

RITE

Residency In-service
Training Examination

2026 DISCUSSION &
REFERENCE MANUAL

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Question

5 ADULT NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

Frontotemporal dementia is characterized by a strong gradient of atrophy, typically involving the frontal or temporal lobe. As shown in this patient's images, there is anterior to posterior atrophy along the temporal lobe bilaterally, with asymmetry on the left side more than the right.

In Alzheimer disease, atrophy occurs throughout the temporal lobe, and hippocampal atrophy is common. As the disease progress, increased involvement is seen in the mesial temporal structures, specifically the precuneus cingulate gurus and parietal lobe. Binswanger disease is characterized by subcortical foci of patchy T2 hyperintensities in white matter, a finding not seen here. Although there is ventriculomegaly, it is in proportion to the cortical atrophy, making normal pressure hydrocephalus an unlikely diagnosis. The regional pattern of atrophy seen here is not characteristic of dementia with Lewy bodies.

Planche V, Mansencal B, Manjon JV, et al; Frontotemporal Lobar Degeneration Neuroimaging Initiative and the National Alzheimer's Coordinating Center cohort. Anatomical MRI staging of frontotemporal dementia variants. *Alzheimer's Dement*. 2023 Aug;19(8):3283-3294.



Question

20 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

This patient's presentation is consistent with medial prefrontal cortex dysfunction, which can be seen with anterior communicating artery aneurysm, parasagittal tumor, or anterior cerebral artery stroke. This type of disorder is associated with apathy, decreased goal-oriented behavior, decreased initiation of motor activity, and decreased spontaneous speech/abulia.

Right ventrolateral prefrontal dysfunction manifests as impaired spatial attention. Orbitofrontal cortex dysfunction is associated with personality change, disinhibition, impaired social judgment, hyperphagia, hypersexuality, and increased risk taking. Lesions of the frontopolar region result in disorganized behavior (eg, difficulty making decisions on what to wear), impaired time estimation, and deficits in creativity, analogical thinking, and impaired multitasking. Hippocampal dysfunction leads to impairment in processing speed, executive functioning, and working memory.

Jones DT, Graff-Radford J. Executive dysfunction and the prefrontal cortex. *Continuum Lifelong Learning Neurol.* 2021 Dec;27(6):1586-1601.

Diamond A. Executive functions. *Annu Rev Psychol.* 2013;64:135-168.

Question

34 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient has problems with procedural memory, which is the ability to acquire (with practice) cognitive and behavioral skills that subsequently operate automatically. Procedural memory is associated with lesions of the basal ganglia–cerebellum–supplementary motor area system. Difficulties are commonly reported in patients with Parkinson disease (PD), affecting tasks such as playing a musical instrument or golfing.

Episodic memory localizes to the medial temporal lobe–Papez circuit system, semantic memory to the anterior and inferior temporal lobes, and working memory to the prefrontal cortex–subcortex–parietal–association cortex system. Bálint syndrome localizes to the posterior parietal regions and consists classically of the triad of optic ataxia, ocular dysmetria, and simultagnosia. Episodic memory deficits are typical of Alzheimer disease (AD), as is Bálint syndrome. Semantic memory deficits are typical of AD and frontotemporal lobar degeneration (FTD). Working memory deficits can result from multiple cerebrovascular events, AD, FTD, PD, dementia with Lewy bodies, and traumatic brain injury.

Matthews BR. Memory dysfunction. *Continuum Lifelong Learning Neurol*. 2015 Jun;21(3):613-626.

Finney GR. Perceptual-motor dysfunction. *Continuum Lifelong Learning Neurol*. 2015 Jun;21(3):678-689.

47 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

This patient presents with isolated anterograde memory issues in the setting of recent exertion concerning for transient global amnesia (TGA). TGA is characterized by isolated anterograde memory difficulty and usually resolves within 24 hours. Though patients should be evaluated for alternative etiologies, namely stroke or seizure, TGA is self-limited and does not require treatment.

Spiegel DR, Smith J, Wade RR, et al. Transient global amnesia: current perspectives. *Neuropsychiatr Dis Treat*. 2017 Oct 24;13:2691-2703.

Question

58 ADULT NEUROLOGY**Clinical Aspects of Disease**

Limbic-predominant age-related transactive response TDP-43 encephalopathy (LATE) is commonly seen in people older than age 75 years and is principally characterized by amnesic impairment only.

When compared with Alzheimer disease, frontotemporal dementia, or dementia with Lewy bodies, LATE progresses very slowly and is accompanied by hippocampal sclerosis. Despite the presence of hippocampal sclerosis, LATE is not associated to increased seizure prevalence. Other than imaging findings, this patient's presentation with gradual memory difficulties suggests a cognitive disorder rather than a focal seizure disorder.

Ramanan VK, Graff-Radford J. LATE, hippocampal sclerosis, and primary age-related tauopathy. *Continuum Lifelong Learning Neurol.* 2024 Dec;30(6):1726-1743.

65 ADULT NEUROLOGY

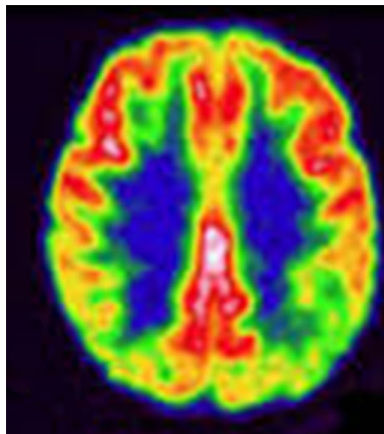
SUBSPECIALTY KNOWLEDGE

Neuroimaging|Clinical Aspects of Disease

This patient has visuospatial impairment consistent with Bálint syndrome (simultanagnosia, ocular apraxia, optic ataxia), cognitive decline, REM sleep behavior disorder, and temporo-parieto-occipital hypoperfusion on PET imaging. These findings meet the criteria for dementia with Lewy bodies. Although temporo-parietal hypoperfusion is also seen in Alzheimer dementia, occipital hypoperfusion typically is not. The "cingulate island" sign (ie, sparing of the posterior cingulate) on nuclear imaging studies is specific for dementia with Lewy bodies. The posterior cingulate is typically hypometabolic on PET scan in Alzheimer disease.

Galvin JE. Lewy body dementia. *Continuum Lifelong Learning Neurol.* 2024 Dec;30(6):1673-1689.

Image credit: Galvin JE. Lewy body dementia. *Continuum Lifelong Learning Neurol.* 2024 Dec;30(6):1673-1689.



Question

73 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

Shuddering spells are benign, nonepileptic events that begin in infancy, characterized by rapid shivering of the head, shoulders, and occasionally the trunk with no alteration in consciousness. Events are brief, typically lasting only a few seconds and are frequently seen during the day such as during eating or in moments of excitement. The diagnosis is generally clinical, and the pathophysiology is unknown. Infantile spasms differ in clinical presentation from shuddering spells. Episodes consist of involuntary flexion or extension that lasts about 1 second, whereas the continuous movement of shuddering spells lasts several seconds. Infantile spasms often cluster and can occur in children in overlapping age ranges. While each individual spasm is brief, many occur back to back in a "cluster." These spasms are also frequently seen in the transition from wake to sleep or vice versa.

Absence seizures are epileptic in nature, characterized by behavioral arrest, alteration in consciousness, and staring. Automatisms, such as lip smacking or eye blinking can also be seen. Absence seizures are not associated with large motor movements of the extremities, such as seen in shuddering spells. In breath-holding spells, a child appears to stop breathing in response to anger, frustration, pain, or injury. Children may even appear cyanotic. During this time, children are unresponsive. In contrast, during shuddering spells, children can respond and do not stop breathing. Infantile gratification syndrome, also known as self-stimulatory behavior or masturbatory behavior, occurs in young children as well. In this syndrome, genital stimulation occurs, frequently through body positioning such as stiffening or crossing of the legs. Facial flushing, grunting, and sweating may be seen. No alteration of consciousness occurs.

Wang JJ, Goldman RD. Shuddering attacks: a benign phenomenon in children. *Can Fam Physician*. 2021 Feb;67(2):107-108.

Tibussek D, Karenfort M, Mayatepek E, et al. Clinical reasoning: shuddering attacks in infancy. *Neurology*. 2008 Mar 25;70(38):e38-e41.

Question

87 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Patients with frontotemporal dementia have been shown to manifest a variety of behavioral changes, including hoarding of items and nascent musical and/or artistic expression. This combination of behaviors is usually not seen in other degenerative dementias.

Knopman DS, DeKosky ST, Cummings JL, et al. Practice parameter: diagnosis of dementia. Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001 May;56(9):1143-1153. Reaffirmed October 2024.

Seeley WW. Behavioral variant frontotemporal dementia. *Continuum Lifelong Learning Neurol*. 2019 Feb;25(1):76-100.

Erkkinen MG, Zúñiga RG, Pardo CC, et al. Artistic renaissance in frontotemporal dementia. *JAMA*. 2018 Apr 3;319(13):1304-1306.

Finger EC. Frontotemporal dementias. *Continuum Lifelong Learning Neurol*. 2016 Apr;22(2):464-489.

95 ADULT NEUROLOGY

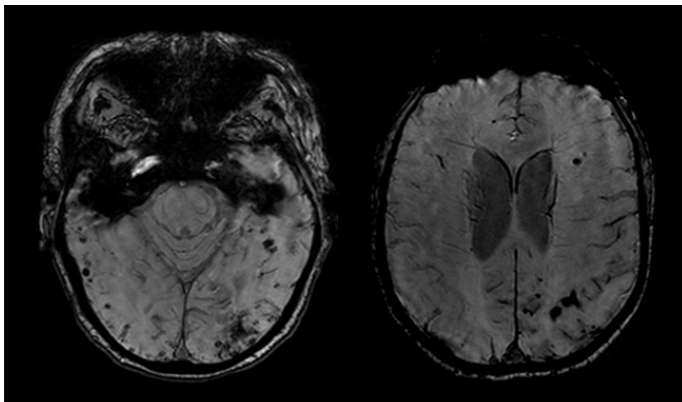
CORE KNOWLEDGE

Neuroimaging

Beta-amyloid deposition resulting in amyloid angiopathy is most frequently seen in cortical and subcortical locations, whereas hypertensive microhemorrhage due to small vessel ischemic disease is more often seen in the deep gray and periventricular white matter.

Amyloid deposition results in increased microhemorrhages, best seen on GRE T2* imaging. Susceptibility-weighted imaging is a form of GRE T2* imaging with phase information to enhance the ability to detect hemorrhages and small veins.

Atlas SW (ed). *Magnetic Resonance Imaging of the Brain and Spine*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2017.



Question

102 NO SPECIFIED PATIENT AGE**Diagnostic Procedures**

Aphemia, also known as apraxia of speech, is characterized by occasional mutism, diminished fluency, and deficits in articulation. Despite appearing to have nonfluent aphasia, patients with aphemia have retained the ability to write.

Kasturiarachi BM, Krishnaiah B. Recognizing aphemia and how to differentiate from aphasia in the era of telemedicine. *Neurohospitalist*. 2021 Oct;11(4):348-350.

Ottomeyer C, Reuter B, Jager T, et al. Aphemia: an isolated disorder of speech associated with an ischemic lesion of the left precentral gyrus. *J Neurol*. 2009 Jul;256(7):1166-1168.

113 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Normal pressure hydrocephalus is characterized by cognitive difficulties, gait apraxia, and urinary incontinence. Imaging studies typically demonstrate a communicating hydrocephalus. Gait abnormalities are most likely to improve after ventriculoperitoneal shunting.

Williams MA, Relkin NR. Diagnosis and management of idiopathic normal-pressure hydrocephalus. *Neurol Clin Pract*. 2013 Oct;3(5):375-385.

Malm J, Eklund A. Idiopathic normal pressure hydrocephalus. *Pract Neurol*. 2006;6:14-27.

Question

130 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Diagnostic Procedures

Disturbing, vivid dreams are associated with REM sleep behavior disorder, a syndrome that occurs more frequently in patients with alpha-synucleinopathies such as Parkinson disease, dementia with Lewy bodies (DLB), and multiple-system atrophy. Detailed visual hallucinations are seen in DLB.

Among imaging modalities, DaT (dopamine transporter) scans have been FDA approved for the detection of DLB. Skin biopsy is now used to diagnose synucleinopathies, along with CSF testing for alpha-synuclein aggregates.

Synuclein CSF testing follows the same principle as RT-QulC for prion proteins. That is, CSF from patients is incubated with recombinant alpha-synuclein. If synuclein aggregates are found in the sample, the aggregates are amplified by converting recombinant synuclein to aggregates as well.

Tau PET imaging can be helpful to identify Alzheimer disease but is less useful in DLB. CSF or serum testing for amyloid helps confirm Alzheimer disease, and CSF testing for prion protein helps confirm Creutzfeldt-Jakob disease.

Schindler SE, Petersen KK, Saef B, et al; Alzheimer's Disease Neuroimaging Initiative (ADNI) Foundation for the National Institutes of Health (FNIH) Biomarkers Consortium Plasma A_β and Phosphorylated Tau as Predictors of Amyloid and Tau Positivity in Alzheimer's Disease Project Team. Head-to-head comparison of leading blood tests for Alzheimer's disease pathology. *Alzheimers Dement*. 2024 Nov;20(11):8074-8096. Erratum in: *Alzheimers Dement*. 2025 Feb;21(2):e14494.

Samudra N, Fischer DL, Lenio S, et al. Clinicopathological correlation of cerebrospinal fluid alpha-synuclein seed amplification assay in a behavioral neurology autopsy cohort. *Alzheimers Dement*. 2024 May;20(5): 3334-3341.

Orad RI, Shiner T. Differentiating dementia with Lewy bodies from Alzheimer's disease and Parkinson's disease dementia: an update on imaging modalities. *J Neurol*. 2022 Feb;269(2):639-653.

McCleery J, Morgan S, Bradley KM, et al. Dopamine transporter imaging for the diagnosis of dementia with Lewy bodies. *Cochrane Database Syst Rev*. 2015 Jan 30;1(1):CD010633.

Question

149 ADULT NEUROLOGY**Clinical Aspects of Disease**

Amnesic mild cognitive impairment is characterized by a memory complaint with otherwise normal cognition, normal activities of daily living, and objective memory impairment. It is thought to be a precursor to Alzheimer disease.

Peterson RC. Mild cognitive impairment. *New Engl J Med*. 2011 Jun 9;364(23):2227-2234.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th Edition. Arlington, VA: American Psychiatric Association; 2013.

161 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Bradycardia and resultant syncope are side effects of acetylcholinesterase inhibitors such as donepezil. Such agents should be discontinued if patients develop bradycardia and/or syncope.

Geldmacher DS. Treatment of Alzheimer disease. *Continuum Lifelong Learning Neurol*. 2024 Dec;30(6):1823-1844.

176 ADULT NEUROLOGY**Neuropathology**

In all pathologies associated with frontotemporal lobar degeneration (FTLD), signs of neurodegeneration involving the frontal and/or temporal lobes are seen, specifically neuronal loss, gliosis, and microvacuolation. Most patients have either abnormal accumulations of the protein tau (FTLD-TAU) or 43-kD TAR-DNA-binding protein (TDP-43) (FTLD-TDP). A minority of patients (10%) have pathology associated with the protein fused in sarcoma (FTLD-FUS).

Pathogenic variants in valosin-containing protein result in a small percentage of patients with FTD but in combination with myopathy and Paget disease of bone. Amyloid accumulation is most commonly associated with Alzheimer disease but can be seen to some extent in aging brains. Alpha-synuclein accumulation is most commonly associated with Parkinson disease. Amyloid and alpha-synuclein accumulation would not be expected in a 56-year-old patient.

Carlos AF, Josephs KA. Frontotemporal lobar degeneration with TAR DNA-binding protein 43 (TDP-43): its journey of more than 100 years. *J Neurol*. 2022 Aug;269(8):4030-4054.

Neumann M, Lee EB, Mackenzie IR. Frontotemporal lobar degeneration TDP-43-immunoreactive pathological subtypes: clinical and mechanistic significance. *Adv Exp Med Biol*. 2021;1281:201-217.

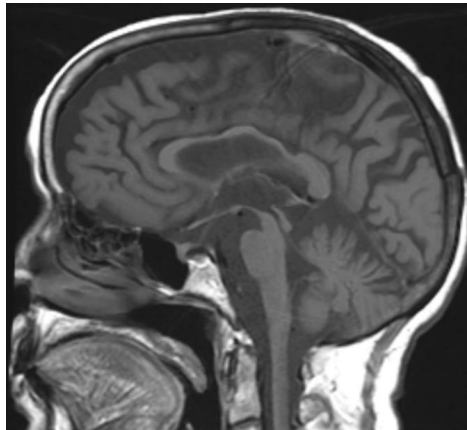
Question

188 ADULT NEUROLOGY**Neuroimaging|Clinical Aspects of Disease**

This patient most likely has progressive supranuclear palsy (PSP). The typical features of this disorder include marked postural instability, axial rigidity, parkinsonism without tremor, pseudobulbar palsy, and impairment of voluntary gaze. Most patients develop a subcortical dementia in the course of their illness. MRI scans characteristically show significant atrophy of the midbrain tegmentum (hummingbird sign), corpus callosum, and anterior cingulate gyrus. The patient's clinical presentation and radiographic features fit best with PSP as compared with the other disorders listed (frontotemporal dementia, paraneoplastic cerebellar degeneration, dementia with Lewy bodies, corticobasal degeneration).

Galasko D. The diagnostic evaluation of a patient with dementia. *Continuum Lifelong Learning Neurol.* 2013 Apr;19(2):397-410.

Pantelyat A. Progressive supranuclear palsy and corticobasal syndrome. *Continuum Lifelong Learning Neurol.* 2022 Oct;28(5):1364-1378.

**211** ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient's cognitive symptoms, specifically executive dysfunction and fluent aphasia with paraphasic errors, along with FDG-PET findings of hypometabolism in the parietal and left temporal and frontal regions, indicate Alzheimer disease. MRI findings consistent with cerebral amyloid angiopathy further support this diagnosis, given her age (54 years) and negative history of head injury or bleeding disorders. This pattern aligns with the dysexecutive variant of early-onset Alzheimer disease.

McDade EM. Alzheimer disease. *Continuum Lifelong Learning Neurol.* 2022 Jun;28(3):648-675.

Question

226 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

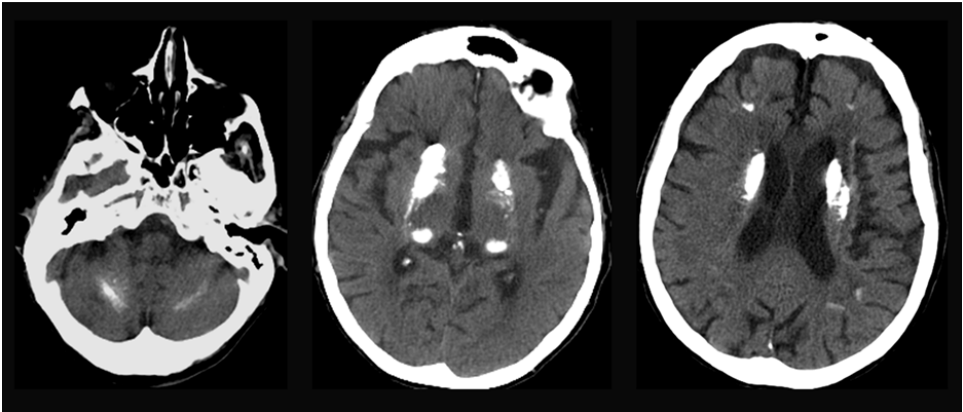
Neuroimaging

Fahr disease (or syndrome) is characterized by calcium deposition and cell loss in the basal ganglia and the cerebral cortex. It is an autosomal dominant degenerative neurologic disorder resulting in parkinsonism, dementia, and depression, among other symptoms.

Wilson disease and carbon monoxide toxicity are associated with hypodensities in the basal ganglia. Carbon monoxide induces hypoxia and resultant hypoattenuation of the globus pallidus.

Nonhemorrhagic (nonacute) iron deposition is poorly determined by CT as compared to calcium. Acute hemorrhage appears as hyperdensities in the brain parenchyma, subarachnoid space, or intraventricular space due to the high density of protein-rich blood compared to brain tissue.

Salzman KL, Jhaveri MD, Osborn AG (eds). *Diagnostic Imaging: Brain*. 5th ed. Philadelphia: Elsevier; 2025.



Question

239 NO SPECIFIED PATIENT AGE**Contemporary Issues**

Sensitivity is calculated as the true positives divided by the sum of true positives plus false negatives ($TP / [TP + FN]$) and is therefore the proportion of people with a disease who test positive. More sensitive tests minimize the rate of false-negative results.

Specificity is calculated as the true negatives divided by the sum of true negatives plus false positives ($TN / [TN + FP]$) and is therefore the proportion of people without a disease who test negative. More specific tests minimize the rate of false positives.

Positive predictive value (PPV) is the proportion of positive test results that are true positives ($TP / [TP + FP]$), and negative predictive value (NPV) is the proportion of negative test results that are true negatives ($TN / [TN + FN]$). While sensitivity and specificity are fixed properties of a test, PPV and NPV are influenced by the prevalence of the disease in the population tested.

Palmqvist S, Tideman P, Mattsson-Carlgren N, et al. Blood biomarkers to detect Alzheimer disease in primary care and secondary care. *JAMA*. 2024 Oct 15;332(15):1245-1257.

Aschengrau A, Seage GR. *Essentials of Epidemiology in Public Health*. Jones & Bartlett Learning. 4th ed. Burlington, MA: Jones & Bartlett Learning; 2020.

243 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

Anosognosia, which is the inability to appreciate one's neurologic impairment, may be seen with right frontoparietal lesions, as in this patient who is reported to ignore objects on his left side. Other neglect syndromes may also be seen. Right-left confusion and alexia without agraphia generally result from dominant hemisphere lesions. Prosopagnosia results from lesions in occipital and/or temporal lobes. Acalculia results from lesions in the dominant hemisphere.

Ropper AH, Samuels MA, Klein JP, Prasad S (eds). *Adams and Victor's Principles of Neurology*. 12th ed. New York: McGraw Hill; 2023.

Question

255 ADULT NEUROLOGY

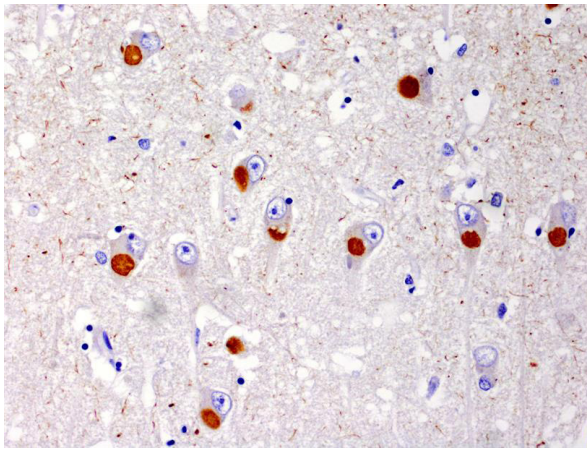
CORE KNOWLEDGE

Neuropathology

The two primary protein-related pathologies seen in patients with frontotemporal dementia are tau and TDP-43. The image shows classic tau-immunoreactive Pick bodies within the neuronal cytoplasm. Marked frontotemporal lobe atrophy with shrunken, firm-appearing hippocampi are typical features. Pick bodies are generally widespread but seen in great abundance in the limbic and paralimbic cortices and in the ventral temporal lobe, including the dentate nucleus and pyramidal cells of the dentate nucleus.

Suzuki H, Kubota M, Kurose S, et al. Neuropathological correlations of 18F-florbetapir PET in a case with Pick's disease. *EJNMMI Res.* 2025 Jul 31;15(1):96.

Smith C, Perry A, Kovacs G, et al (eds). *Greenfield's Neuropathology*. 10th ed. Boca Raton, FL: CRC Press; 2024.

**279** ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Clinical features suggestive of dementia with Lewy bodies include fluctuating cognition, visual hallucinations, and parkinsonian features. Patients are known to have sensitivity to both typical and atypical antipsychotics, most likely due to low expression of striatal dopamine D2 receptors. However, quetiapine can be useful and is better tolerated. Clonazepam can be used for REM sleep behavior disorder, and SSRIs are used for depression and emotional lability.

Armstrong MJ. Lewy body dementia. *Continuum Lifelong Learning Neurol.* 2019 Feb;25(1):128-146.

Mayo MC, Bordelon Y. Dementia with Lewy bodies. *Semin Neurol.* 2014 Apr;34(2):182-188.

Question

290 ADULT NEUROLOGY

Treatment/Management

Quetiapine and clozapine are atypical antipsychotic medications that antagonize dopamine receptors and, as such, are frequently used for Parkinson disease (PD) psychosis (hallucinations, delusions). Only pimavanserin is nondopaminergic and selectively targets serotonin 5HT_{2A} and 5HT_{2C} receptors to treat PD psychosis.

Clozapine is an antipsychotic medication approved for treatment-resistant schizophrenia. Donepezil and memantine are medications for Alzheimer disease but have no additional indication in PD or PD psychosis. Donepezil is a cholinesterase inhibitor resulting in increased synaptic acetylcholine. Memantine is an NMDA receptor antagonist that reduces excitotoxicity.

Isaacson SH, Ballard CG, Kreitzman DL, et al. Efficacy results of pimavanserin from a multi-center, open-label extension study in Parkinson's disease psychosis patients. *Parkinsonism Relat Disord.* 2021 Jun;87:25-31.

Stahl SM. Mechanism of action of pimavanserin in Parkinson's disease psychosis: targeting serotonin 5HT_{2A} and 5HT_{2C} receptors. *CNS Spectr.* 2016 Aug;21(4):271-275.

Cummings J, Isaacson S, Mills R, et al. Pimavanserin for patients with Parkinson's disease psychosis: a randomised, placebo-controlled phase 3 trial. *Lancet.* 2014 Feb 8;383(9916):533-540.

294 ADULT NEUROLOGY

Contemporary Issues

The MacArthur Competency Assessment Tool, as described here, is a validated tool to guide interview for competence that has been used in patients with neurologic disorders and cancer. While aphasia and verbal semantic performance are associated with competence, having aphasia does not automatically exclude the possibility of competence.

This patient has demonstrated competence by repeating that he understands the prognosis, risks, side effects, and outcomes, with and without standard cancer treatment. As such, he does not need permission to refuse treatment, though a family meeting could be helpful for other reasons. Even if the described standard treatment is evidence-based, patients can choose not to follow guidelines and standards.

Simel DL, Rennie D (eds). *The Rational Clinical Examination: Evidence-Based Clinical Diagnosis.* New York: McGraw-Hill Education; 2009.

Question

311 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Dopamine agonist therapy has been associated with several impulse control and repetitive behaviors in Parkinson disease. These behaviors include new-onset gambling, compulsive shopping and eating, hypersexuality, and punding (ie, repetitive performance of pointless actions). This appears to be a class effect with dopamine agonists. Risk factors for the development of these disorders have been associated with younger age, unmarried status, and family history of gambling disorders.

Pringsheim T, Day GS, Smith DB, et al. Dopaminergic therapy for motor symptoms in early Parkinson disease. Practice guideline summary: a report of the AAN Guideline Subcommittee. *Neurology*. 2021 Nov;97(20):942-957. Reaffirmed February 2025.

Weintraub D, Koester J, Potenza MN, et al. Impulse control disorders in Parkinson's disease: a cross-sectional study of 3090 patients. *Arch Neurol*. 2010 May;67(5):589-595.

Voon V, Potenza MN, Thomsen T. Medication-related impulse control and repetitive behaviors in Parkinson's disease. *Curr Opin Neurol*. 2007 Aug;20(4):484-492.

Question

324 ADULT NEUROLOGY

CORE KNOWLEDGE

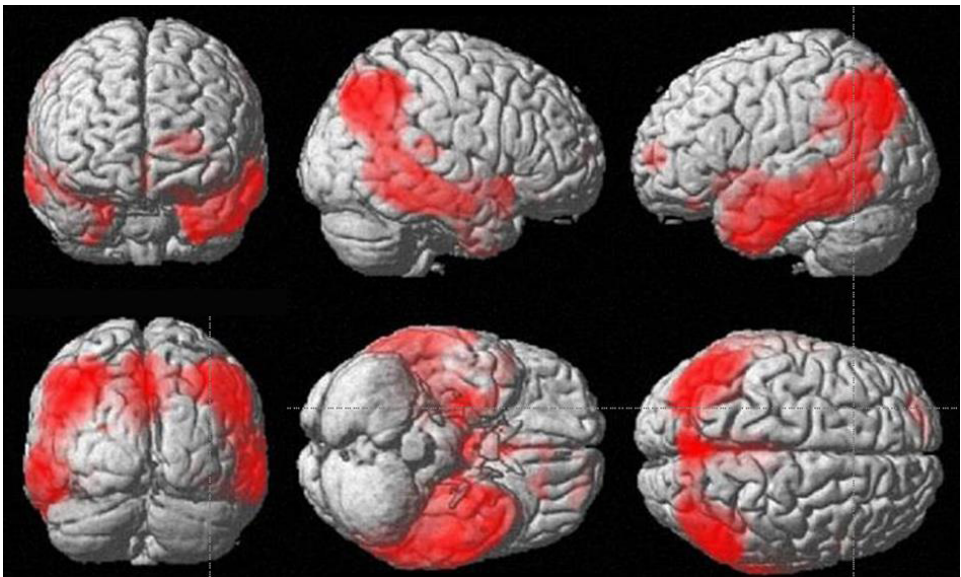
Neuroimaging

This image is a statistical parametric map in which an individual patient's raw PET data are compared with a database of healthy controls. The red areas indicate areas of decreased metabolism. The pattern of decreased metabolism in the association cortex of the parietal and temporal lobes and in the retrosplenial region is characteristic of Alzheimer disease.

Corticobasal degeneration shows decreased metabolism in the association cortex of one hemisphere but not the other, with a marked hemispheric asymmetry not present in this patient. Diffuse Lewy body disease is associated with occipital hypometabolism. Frontotemporal lobar degeneration is associated with decreased frontal metabolism. Vascular dementia does not typically show such symmetric regional predilection.

Smith NM, Ford JN, Haghdel A, et al. Statistical parametric mapping in amyloid positron emission tomography. *Front Aging Neurosci.* 2022 Apr 25;14:849932.

Masdeu JC, Zubietta JL, Arbizu J. Neuroimaging as a marker of the onset and progression of Alzheimer's disease. *J Neurol Sci* 2005 Sep 15;236(1-2):55-64.



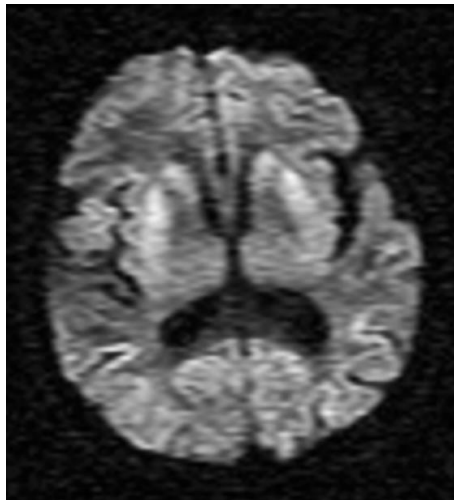
Question

339 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

The patient's presentation is strongly suggestive of Creutzfeldt-Jakob disease (CJD). His normal CSF parameters are consistent with CJD, and his diffusion-weighted MRI scan demonstrates restricted diffusion in the cortical mantle (cortical ribboning) and basal ganglia, findings characteristic of this disorder. Of the biomarkers listed, real-time quaking-induced conversion (RT-QuIC) is the most specific and sensitive, followed by neuron-specific enolase and 14-3-3 protein.

Manara R, Fragiaco F, Ladogana A, et al. MRI abnormalities in Creutzfeldt-Jakob disease and other rapidly progressive dementia. *J Neurol*. 2024 Jan;271(1):300-309.

Hamlin C, Puoti G, Berri S, et al. A comparison of tau and 14-3-3 protein in the diagnosis of Creutzfeldt-Jakob disease. *Neurology*. 2012 Aug 7;79(6):547-552. "



Question

359 NO SPECIFIED PATIENT AGE

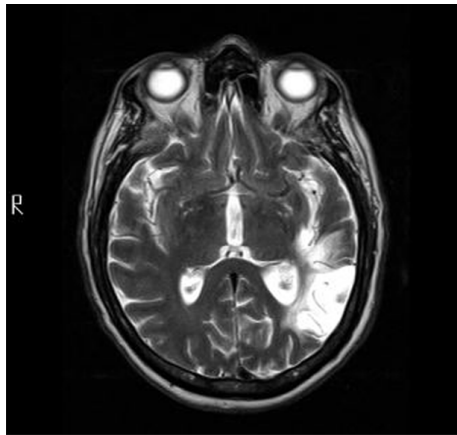
CORE KNOWLEDGE

Neuroimaging

The image shown depicts a wedge-shaped left temporal infarction that is most commonly associated with Wernicke (fluent) aphasia, a disorder characterized by the ability to produce fluent speech that is grammatically correct but lacks meaning. Wernicke's area is located in the posterior temporal lobe.

Kandel ER, Koester JD, Mack SH, et al, (eds). Principles of Neural Science. 6th ed. New York: McGraw-Hill, 2021.

Heilman KM, Valenstein E. Clinical Neuropsychology. 5th ed. New York: Oxford University Press, 2012.

**369** ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient's presentation has all the elements of the normal pressure hydrocephalus triad, specifically gait and/or balance disturbances, urinary symptoms, and cognitive impairment.

The other disorders listed are considered Parkinson plus syndromes. Asymmetric findings are seen in Parkinson disease, corticobasal syndrome, and multiple-system atrophy, parkinsonian type. Symmetric findings are seen in progressive supranuclear palsy, and multiple-system atrophy, cerebellar type. Patients with progressive supranuclear palsy also demonstrate truncal rigidity but typically do not have a stooped posture. Those with multiple-system atrophy, cerebellar type, have cerebellar findings not described here.

Vertes AC, Beato MR, Sonne J, et al. Parkinson-plus syndrome. [Updated 2023 Jun 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-.

Prajwal P, Kolanu ND, Reddy YB, et al. Association of Parkinson's disease to Parkinson's plus syndromes, Lewy body dementia, and Alzheimer's dementia. Health Sci Rep. 2024 Mar 31;7(4):e2019.

Question

370 ADULT NEUROLOGY**CORE KNOWLEDGE****Contemporary Issues**

Patients receiving genetic testing should undergo genetic counseling before and after genetic testing. The other tests listed (brain MRI, neuropsychological testing, serum vitamin B12, and thyroid-stimulating hormone) may be reasonable in the appropriate clinical setting but are not required prior to genetic testing in an asymptomatic patient, regardless of strong family history of a specific disorder.

Chiong W, Tsou AY, Simmons Z, et al; Ethics, Law, and Humanities Committee (a joint committee of the American Academy of Neurology, American Neurological Association, and Child Neurology Society). Ethical considerations in dementia diagnosis and care: AAN position statement. *Neurology*. 2021 Jul 13;97(2):80-89.

398 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroanatomy**

This patient suddenly cannot perform calculations or write a sentence. Her exam is indicative of mild finger agnosia and dysgraphia. This constellation of symptoms is part of Gerstmann syndrome, which localizes to the left angular gyrus.

Rusconi E, Pinel P, Dehaene S, et al. The enigma of Gerstmann's syndrome revisited: A telling tale of the vicissitudes of neuropsychology. *Brain*. 2010 Feb;133Pt 2):320-332.

Vallar G. Spatial neglect, Balint-Homes' and Gerstmann's syndrome, and other spatial disorders. *CNS Spectr*. 2007 Jul;12(7):527-536.

Question

4

ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

Patients who develop fulminant liver failure are more prone to hepatic encephalopathy. In patients with hepatic encephalopathy-induced coma, up to 80% develop cerebral edema, which is the leading cause of death in these patients. It is one of the leading causes of death in patients with acute liver failure.

Maheer S, Schreiberman R. The clinical spectrum and manifestations of acute liver failure. *Clin Liver Dis*. 2018 May;22(2):361-374.

Schwendimann R, Minagar A. Liver disease and neurology. *Continuum Lifelong Learning Neurol*. 2017 Jun;23(3):762-777.

12

PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Contemporary Issues

This pediatric patient (20 months) meets the prerequisites for declaration of death by neurologic criteria ("brain death"), including loss of brainstem reflexes >24 hours after an incident that would be expected to result in irreversible injury, with normothermia and findings not confounded by medication.

Like declaration of brain death in adults, clinical examination is the next step in evaluation, with assessment of brainstem responses, including cold caloric testing as noted, followed by apnea testing. Patients should undergo preoxygenation with 100% oxygen for 10 minutes, followed by passive administration of 100% oxygen while disconnected from ventilatory support for a period long enough to achieve a PaCO₂ of 60 mm Hg while assessing for clinical evidence of respiratory evidence.

Ancillary testing should be reserved for situations in which a complete clinical exam cannot be performed. The other tests listed (EEG, MRI with MR angiography, and radionuclide imaging for cerebral blood flow) are associated with a high incidence of false-negative results.

Greer DM, Shemie SD, Lewis A, et al. Determination of brain death/death by neurologic criteria: The World Brain Death Project. *JAMA*. 2020 Sep 15;324(11):1078-1097.

Question

69 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

Posttraumatic headache begins within 7 days of a traumatic brain injury and can be classified as acute or persistent. This patient with a concussion that occurred during a soccer game, with symptoms gradually improving after a week, is most likely to recover within a month, even without intervention; therefore, preventive medication is not indicated at this time. A broad range of headache phenotypes is possible, but these more often resemble migraines with accompanying nausea, vomiting, and photophobia. Tension-type headache is the second most common phenotype but is not a factor in return to sports decisions.

Even when patients remain symptomatic, current sports concussion guidelines cite early return to physical activity as beneficial, beginning with symptom-limited activity then progressing in a stepwise fashion over at least 7 days before resuming full contact participation.

CGRP antagonists have not been approved for postconcussion headache, although this is an area of research. Headaches from medication overuse are more common when another primary headache disorder is present, such as persistent posttraumatic headache, defined as headache lasting longer than 3 months after concussion, which is not present in this case.

Patricios JS, Schneider KJ, et al. Consensus statement on concussion in sport: The 6th International Conference on Concussion in Sport-Amsterdam, October 2022. *Br J Sports Med.* 2023 Jun;57(11):695-811.

Blumenfeld A, McVige J, Kneivel K. Post-traumatic headache: pathophysiology and management - a review. *J Concussion.* 2022 May 9;6:205970022210934.

Kamins J, Charles A. Posttraumatic headache: basic mechanisms and therapeutic targets. *Headache.* 2018 Jun;58(6):811-826.

Question

131 ADULT NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

The image shows a right subdural hematoma, a left epidural hematoma, bilateral brain contusions, right uncus herniation, and left scalp hematoma.

Salzman KL, Jhaveri MD, Osborn AG (eds). *Diagnostic Imaging: Brain*. 5th ed. Philadelphia: Elsevier; 2025.

**225** ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

Autonomic dysreflexia is a common complication in patients with spinal cord injury above T6. Episodes are characterized by headaches, diaphoresis, hypertension, and bradycardia, and caused by noxious stimuli below the level of injury such as bladder distention, fecal impaction and pressure sores.

Cowan H, Lakra C, Desai M. Autonomic dysreflexia in spinal cord injury. *BMJ*. 2020 Oct 2;371:m3596.

288 NO SPECIFIED PATIENT AGE**Neuroanatomy**

Contrecoup contusions occur in the brain away from the point of impact and do not directly underlie the site of skull fractures. Orbital surfaces of the frontal lobe are the most common location; contrecoup contusions at this site usually occur as a result of a fall on the occiput with the sudden deceleration of the head. Parasagittal contusions, also called gliding contusions, occur in association with diffuse brain damage and diffuse axonal injury.

Smith C, Perry A, Kovacs G, et al (eds). *Greenfield's Neuropathology*. 10th ed. Boca Raton, FL: CRC Press; 2024.

Question

323 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient has a cervical central spinal cord syndrome manifested by lower motor findings in his hands, upper motor neuron hyperreflexia in his legs, and a classic sensory disturbance in which secondary order neurons subserving pain and thermal sense are interrupted as they decussate in the central spinal cord. The primary order neuronal axons in the dorsal columns subserving fine touch and proprioception are spared. Central spinal cord syndrome most commonly results from syringomyelia or intrinsic tumors.

Brachial plexopathy produces focal dermatomal/nerve distribution deficits and often decreased reflexes and motor weakness in the limb; it would not explain increased lower extremity reflexes or preserved vibration with selective hand pain/temperature loss.

Posttraumatic syringomyelia can produce a similar "cape-like" spinothalamic loss and therefore can mimic central cord syndrome. However, posttraumatic syrinx formation is usually progressive and often delayed for months after injury and is distinguished by MRI demonstration of a fluid cavity and frequently by segmental lower motor neuron signs in the hands. Imaging differentiates central cord injury from syringomyelia.

Brown-Séquard syndrome is caused by cord hemisection, which gives ipsilateral loss of vibration/position and weakness below the lesion and contralateral loss of pain/temperature below the lesion. The preserved vibration/joint position sense in this patient makes this diagnosis unlikely.

Posterior (dorsal column) cord syndrome would produce loss of vibration and proprioception with preserved pain/temperature — the opposite of this patient's findings.

Brazis PW, Masdeu JC, Biller J (eds). *Localization in Clinical Neurology*. 8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2022.

Question

377 ADULT NEUROLOGY

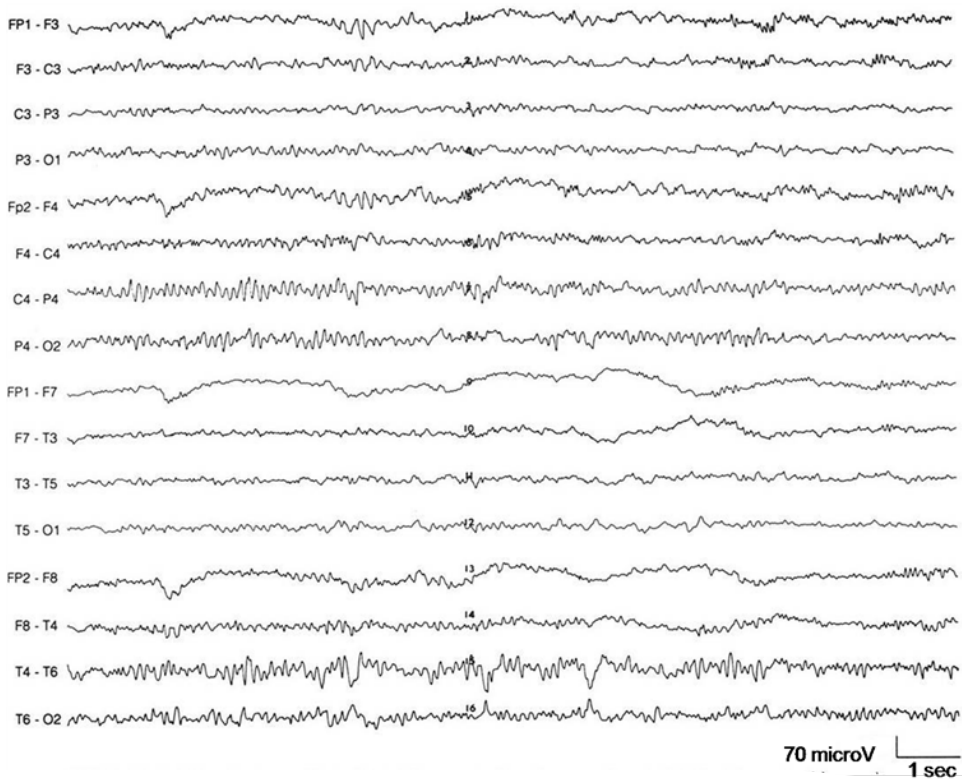
CORE KNOWLEDGE

Diagnostic Procedures

The principal finding in the EEG shown is hemispheric amplitude asymmetry. In the absence of a skull defect, the side of the lower voltage alpha activity is usually the abnormal one. In this case of a patient with a traumatic brain injury, the left hemispheric attenuation is due to a large left hemispheric subdural hematoma.

Alpha coma and hepatic encephalopathy both produce bilateral EEG abnormalities. Right-sided middle cerebral artery stroke might be expected to produce focal slowing in the affected distribution. There is no evidence of ongoing epileptiform activity to support a diagnosis of status epilepticus.

Rubin DI (ed). Clinical Neurophysiology. 5th ed. New York: Oxford University Press; 2021.



Question

400 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

Large cerebellar strokes can result in elevated intracranial pressure due to fourth ventricular and brainstem compression. Suboccipital decompressive craniectomy is the treatment most likely to confer a mortality benefit for this patient's condition. The other treatment options listed (IV hypertonic saline, IV mannitol, hypothermia, external CSF drainage) are temporizing measures and not likely to significantly reduce posterior fossa intracranial pressure. External CSF drainage may even precipitate an upward herniation syndrome by increasing the pressure gradient between the posterior and the middle fossa compartments.

Posner JB, Saper CB, Schiff ND, et al (eds). Plum and Posner's Diagnosis and Treatment of Stupor and Coma. 5th ed. New York: Oxford University Press; 2019.

Freeman D. Management of intracranial pressure. Continuum Lifelong Learning Neurol. 2015 Oct;21(5):1299-1323.

Question

11

PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroscience and Mechanism of Disease

Alternating hemiplegia of childhood (AHC) is a paroxysmal disorder, with onset typically before age 1 year. Although its name is derived from episodes of alternating hemiplegia that can last several minutes to several days, the paroxysmal episode may also consist of paroxysmal nystagmus or dystonia. Bilateral paralysis with associated mutism has been reported, as have swallowing difficulties and drooling. Symptoms disappear upon falling asleep but can resume upon awakening. AHC is most commonly caused by *ATP1A3* pathogenic variants.

Dravet syndrome (developmental and epileptic encephalopathy [DEE]) classically presents in the first year of life with prolonged, drug-resistant, febrile or afebrile hemiclonic or generalized clonic seizures. Development is normal until seizure onset. Dravet syndrome is most commonly associated with pathogenic variants in *SCN1A*. Epilepsy of infancy with migrating focal seizures (EIMFS) typically presents within the first 6 months of life and is characterized by drug-resistant, focal motor clonic or tonic seizures that migrate from one hemisphere to the other on EEG during a seizure. Early infantile developmental and epileptic encephalopathy (EIDEE) presents within the first 3 months of life with drug-resistant, focal tonic, generalized tonic, myoclonic, focal clonic, and epileptic spasms. The EEG characteristically shows a burst suppression pattern.

Paroxysmal kinesigenic dyskinesia presents from age 1 up to age 20 years. Features include episodes of dystonic or choreoathetoid movements that last <1 minute and are triggered by sudden movements. It responds well to antiseizure medications and is most often associated with pathogenic variants in *PRRT2*. Somatic mutations in *GNAQ* can result in Sturge Weber syndrome, in which prolonged hemiconvulsions (from the hemisphere affected by leptomeningeal angiomatosis) can result in progressive weakness over time.

Uchitel J, Helseth A, Prange L, et al. The epileptology of alternating hemiplegia of childhood. *Neurology*. 2019 Sept;93(13):e1248-1259. Erratum: 2020 Oct;95(15):708.

Zuberi SM, Wirrell E, Yozawitz E, et al. ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: Position statement by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1349-1397.

Xu JJ, Li HF, Wu ZY. Paroxysmal kinesigenic dyskinesia: genetics and pathophysiological mechanisms. *Neurosci Bull*. 2024 Jul;40(7):952-962.

Magrinelli F, Bhatia KP. Paroxysmal movement disorders. *Handb Clin Neurol*. 2024;203:145-156.

Question

22 NO SPECIFIED PATIENT AGE**Treatment/Management**

Many antiseizure medications can cause a slight decrease in free T4 with normal or increased levels of thyroid-stimulating hormone, placing patients with epilepsy at risk for hypothyroidism. Of the medications listed (lamotrigine, levetiracetam, vigabatrin, and topiramate), valproate is associated with the highest risk of hypothyroxinemia. Other risk factors include use of older antiseizure medications, polytherapy, older patient age, and female sex. Thyroid function should be monitored in patients with epilepsy for this reason.

Rochtus AM, Herijgers D, Jansen K, et al. Antiseizure medications and thyroid hormone homeostasis: literature review and practical recommendations. *Epilepsia*. 2022 Feb;63(2):259-270.

32 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neurophysiology

Because alpha rhythm frequency varies depending on the behavioral state of the individual, it should be measured only when it is clear the subject is awake and not drowsy. Additionally, as one of the cardinal features of alpha rhythm is reactivity (attenuation) to eye opening, the rhythm should be evaluated in the eyes closed state.

Wusthoff CJ, Tatum WO. Normal adult and pediatric EEG. In: Husain M (ed). *Current Practice of Clinical Electroencephalography*. 5th ed. Wolters Kluwer Health; 2023, pp 72-121.

Question

39 NO SPECIFIED PATIENT AGE**Neurophysiology**

The video shows a right temporal seizure characterized by staring, vocalizations, oral and hand automatisms, and ictal speech. Temporal intermittent rhythmic delta activity is a form of lateralized rhythmic delta activity associated with temporal lobe seizures and is an interictal epileptiform abnormality.

Frontal intermittent rhythmic delta activity is a nonspecific and nonlocalizing abnormality. Generalized rhythmic delta activity is a nonspecific abnormality indicative of generalized cerebral dysfunction. Occipital intermittent rhythmic delta activity is associated with generalized epilepsies such as childhood absence epilepsy. Subclinical rhythmic electrographic discharge of adults (SREDA) is a benign pattern consisting of bursts of rhythmic, sharply contoured, 5- to 7-Hz theta over the temporoparietal areas that mimics an electrographic seizure.

Wusthoff CJ, Tatum WO. Normal adult and pediatric EEG. In: Husain AM (ed). *Current Practice of Clinical Electroencephalography*. 5th ed. Lippincott Williams & Wilkins: Philadelphia, PA; 2024, pp 72-1121.

Johnson EL. Generalized and focal nonepileptic EEG abnormalities. In: Husain AM (ed). *Current Practice of Clinical Electroencephalography*. 5th ed. Lippincott Williams & Wilkins: Philadelphia, PA; 2024, pp 308-349.

Video credit: Tatum WO. EEG essentials. *Continuum Lifelong Learning Neurol*. 2022 Apr;28(2):261-305.

Question

43 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient's interictal EEG shows generalized 1- to 2-Hz spike and sharp and slow wave complexes, along with generalized paroxysmal fast activity during sleep. The ictal EEG shows generalized voltage attenuation with superimposed 10- to 11-Hz alpha activity and increased myogenic artifact, findings expected of a generalized tonic seizure. The history of intellectual disability, multiple seizure types, including generalized tonic seizures, along with EEG findings of generalized slow spike and wave complexes and generalized paroxysmal fast activity, meet the diagnostic criteria for Lennox-Gastaut syndrome (LGS) but are not consistent with the other syndromes listed (epilepsy with eyelid myoclonia, epilepsy with myoclonic atonic seizures, Dravet syndrome, or juvenile myoclonic epilepsy).

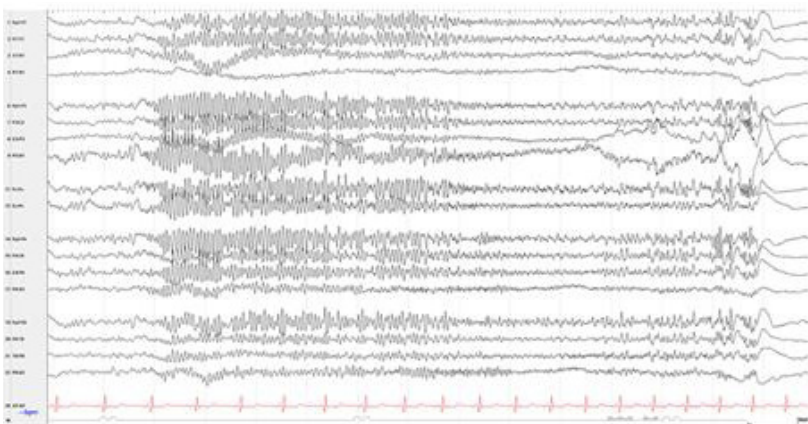
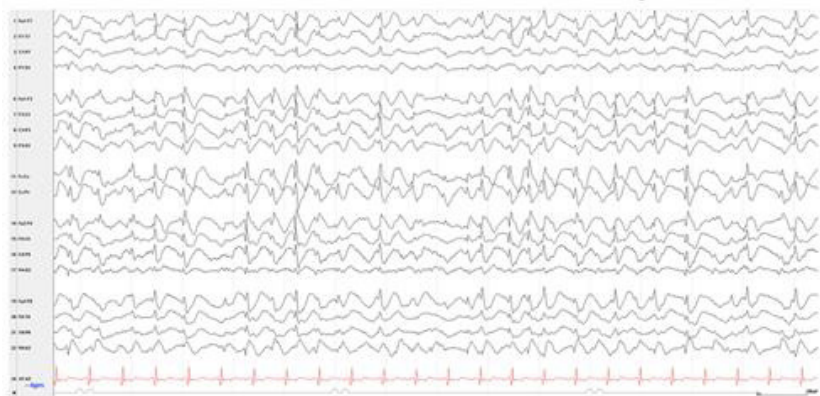
Zuberi SM, Wirrell E, Yozawitz E, et al. ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: Position statement by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1349-1397.

Specchio N, Wirrell EC, Scheffer IE, et al. International League Against Epilepsy classification and definition of epilepsy syndromes with onset in childhood: Position paper by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1398-1442.

(continues)

Question

Sensitivity 7 $\mu\text{V}/\text{mm}$, HFF 70 Hz, LFF 1 Hz



Question

54 NO SPECIFIED PATIENT AGE**Treatment/Management**

Vagal nerve stimulation (VNS) is a treatment option for patients with refractory focal or generalized epilepsy, though it has the potential to exacerbate the physiology underlying obstructive sleep apnea (OSA), which is why OSA is considered a relative contraindication to VNS.

Comorbid OSA should not preclude VNS implantation in otherwise eligible candidates; however, patients who are at risk for or with known OSA and typical symptoms need monitoring both before and after implantation and implementation/optimization of OSA-directed treatments to ensure adequate disease control.

The other disorders listed (depression, irritable bowel syndrome, inflammatory arthritis, Parkinson disease) are not known to worsen after VNS implantation. In fact, VNS has FDA approval for depression, though a VNS device is rarely implanted solely for this indication. Systematic reviews suggest comorbid depression may improve after VNS implantation in patients with refractory epilepsy.

Seth J, Couper RG, Burneo JG, et al. Effects of vagus nerve stimulation on the quality of sleep and sleep apnea in patients with drug-resistant epilepsy: A systematic review. *Epilepsia*. 2024 Jan;65(1):73-83.

Assenza G, Tombini M, Lanzzone J, et al; Epilepsy Study Group of the Italian Neurological Society. Antidepressant effect of vagal nerve stimulation in epilepsy patients: A systematic review. *Neurol Sci*. 2020 Nov;41(11):3075-3084.

63 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Clinical Aspects of Disease

Sudden unexpected death in epilepsy (SUDEP) is relatively infrequent (1.2 per 1000), but its incidence is higher in patients with drug-resistant epilepsy and in those who have seizures during sleep or generalized tonic-clonic seizures. Improved seizure control, having a bed partner, not sleeping prone, and use of seizure detection devices may reduce the risk of SUDEP. Zonisamide does not increase the risk of SUDEP.

Haridas B, Chuan DT, Nei M, et al. Sudden unexpected death in epilepsy: Pathogenesis, risk factors, and prevention. *Semin Neurol*. 2022 Oct;42(5):658-664.

Harden C, Tomson T, Gloss D, et al. Practice guideline summary: Sudden unexpected death in epilepsy incidence rates and risk factors: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2017 Apr 24;88(17):1674-1680. Reaffirmed October 2023.

Keller AE, Whitney R, Li SA, et al. Incidence of sudden unexpected death in epilepsy in children is similar to adults. *Neurology*. 2018 Jul 10;91(2):e107-e111.

Question

72 NO SPECIFIED PATIENT AGE**Neuroanatomy**

Seizures arising from the supplementary motor area, also known as the supplementary sensorimotor area (SSMA), are of brief duration, usually lasting 10 to 40 seconds. Rapid onset of asymmetric tonic posturing involving one or more extremities is characteristically observed. SSMA seizures may be frequent and can occur in clusters. They also tend to occur primarily in sleep. The clinical picture with involvement of all four extremities and simultaneous preservation of awareness can inadvertently lead to a misdiagnosis of psychogenic seizures.

Chowdhury FA, Silva R, Whatley B, et al. Localisation in focal epilepsy: a practical guide. *Prac Neurol*. 2021 Dec;21(6):481-491.

Question

79 NO SPECIFIED PATIENT AGE

Neuroimaging

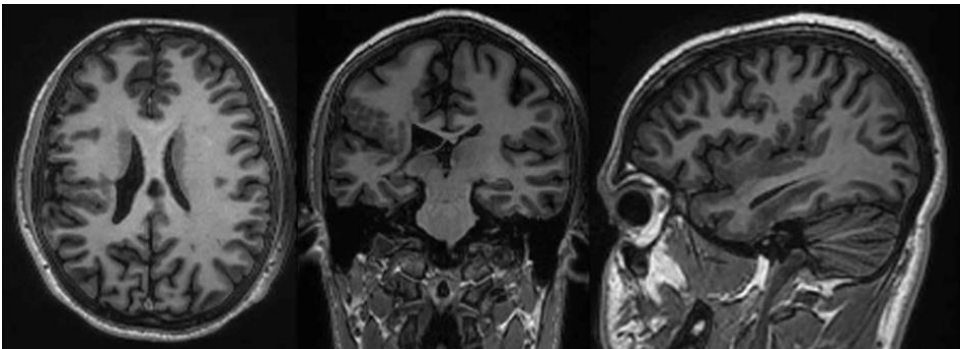
This patient's MRI scans are consistent with unilateral closed-lip schizencephaly, with associated polymicrogyria involving the right perisylvian region. Schizencephaly is a malformation of cortical development that arises during the stage of neuronal organization. In schizencephaly, a cleft disrupts the cortex at the pial surface and may or may not extend all the way to the ependymal surface (open-lip and closed-lip schizencephaly, respectively). The cleft is often lined with abnormal gray matter (either polymicrogyria or gray matter heterotopia). The underlying cause usually cannot be confirmed, though there is a consensus theory that a destructive insult during fetal development (such as a stroke or infection) is likely involved, particularly in unilateral cases.

Seizure semiology refers to behavioral or perceptual phenomena that occur during a seizure which serve as clues to seizure localization. In this case, the cortical abnormality involves the right lateral perisylvian region (which includes face motor cortex). Of the choices presented, the most likely is left face clonic jerking.

Formed visual hallucinations are seen in seizures involving posterior temporal cortex. Olfactory auras tend to be seen in mesial temporal seizures. Mirthless laughter is seen in gelastic seizures, which are associated with hypothalamic hamartomas (but may also be seen in temporal lobe seizures). Startle-induced asymmetric tonic seizures are a hallmark of the supplementary motor cortex (medial frontal).

Beniczky S, Tatum WO, Blumenfeld H, et al. Seizure semiology: ILAE glossary of terms and their significance. *Epileptic Disord.* 2022 Jun 1;24(3):447-495. Erratum in: *Epileptic Disord.* 2024 Aug;26(4):561-565.

Russ JB, Agarwal S, Venkatesan C, et al. Fetal malformations of cortical development: Review and clinical guidance. *Brain.* 2025 Jun 3;148(6):1888-1903.



Question

84 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Diagnostic Procedures

This patient has had episodes refractory to two different antiseizure medications. Before proceeding with a specific course of treatment, EEG in an epilepsy monitoring unit is indicated to determine if the episodes are epileptic or nonepileptic events. Epilepsy and functional neurologic disorder are both on the differential. Serum prolactin is occasionally obtained immediately after an event to help differentiate epileptic seizures from functional seizures; though it has high specificity, sensitivity is only moderate, and it does not distinguish seizures from syncope -- thus its use has not been recommended. This patient first requires monitoring in the epilepsy monitoring unit for characterization of events.

Hopp JL. Nonepileptic episodic events. *Continuum Lifelong Learning Neurol.* 2019 Apr;25(2):492-507.

Nass RD, Sassen R, Elger CE, et al. The role of postictal laboratory blood analyses in the diagnosis and prognosis of seizures. *Seizure.* 2017 Apr;47:51-65.

92 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

Potassium influx during a nerve action potential limits the duration of the action potential by repolarizing (and actually hyperpolarizing) the neuron. This change in voltage allows voltage-gated sodium channels to move from a deactivated state to a ready state. Some potassium currents are activated by calcium entry but not chloride channels.

Kandel ER, Schwartz JH, Jessel TM (eds). *Principles of Neural Science.* 6th ed. New York: McGraw-Hill Education; 2021.

Question

105 PEDIATRIC NEUROLOGY**Diagnostic Procedures**

This patient's history is characteristic of the focal seizures seen in self-limited epilepsy with centrotemporal spikes (SeLECTS), a childhood seizure syndrome previously known as benign rolandic epilepsy, benign epilepsy with centrotemporal spikes, and childhood epilepsy with centrotemporal spikes. Seizure onset is typically between ages 4 and 10 years, and seizures typically stop by midadolescence. EEG shows centrotemporal spikes or sharp discharges that are activated in drowsiness and sleep.

Focal seizures with the classic frontoparietal operculum features and/or nocturnal bilateral tonic-clonic seizures are required for the diagnosis. The classic semiology of focal seizures in SeLECTS consists of four components: 1) unilateral sensory changes involving the tongue, lips, gum, and inside cheek; 2) orofacial motor signs such as tonic or clonic contraction of one side of the face, mouth, or tongue, then involving one side of the face; 3) speech arrest (inability to speak or difficulty speaking during episode); and 4) sialorrhea as an ictal symptom. Hence, a sleep-deprived EEG is the next most appropriate step in workup to evaluate for sleep-activated focal abnormalities.

Although episodes originate from sleep, they do not represent a primary sleep disorder; thus, polysomnography is not a useful diagnostic study. Excess drooling during an episode is part of the ictal phenomenon. A swallow study would be normal in an otherwise normally developing child, as there is no issue with drooling or swallowing outside of the time of the seizure. Imaging studies in these patients are classically normal, and there is no reason to believe a structural abnormality is present. Therefore, imaging studies are not necessarily indicated.

Specchio N, Wirrell EC, Scheffer IE, et al. International League Against Epilepsy classification and definition of epilepsy syndromes with onset in childhood: Position paper by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1398-1442.

Question

110 PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Fenfluramine, an antiseizure medication that affects serotonin levels, is approved for treatment of seizures in both Dravet and Lennox–Gastaut syndromes. As an amphetamine derivative, its primary side effect is anorexia. Because of rare occurrences of valvular heart disease and pulmonary artery hypertension when fenfluramine was used in combination with phentermine for weight loss, a risk evaluation and mitigation (REMS) program is in place consisting of periodic monitoring with echocardiography. Neither of these adverse effects occurred in trials of fenfluramine for Dravet or Lennox–Gastaut syndromes.

Simon K, Sheckley H, Anderson CL, et al. A review of fenfluramine for the treatment of Dravet syndrome patients. *Curr Res Pharmacol Drug Discov*. 2021 Dec 16;3:100078.

Cross JH, Galer BS, Gil-Nagel A, et al. Impact of fenfluramine on the expected SUDEP mortality rates in patients with Dravet syndrome. *Seizure*. 2021 Dec;93:154-159.

Bishop KI, Isquith PK, Gioia GA, et al. Fenfluramine treatment is associated with improvement in everyday executive function in preschool-aged children (<5 years) with Dravet syndrome: a critical period for early neurodevelopment. *Epilepsy Behav*. 2023 Jan;138:108994.

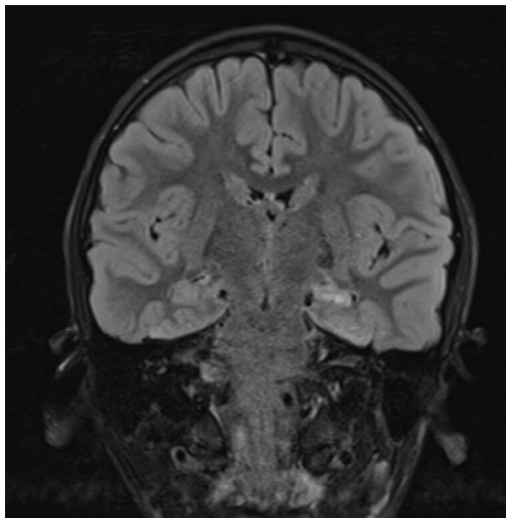
120 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroimaging

The MRI scan shows increased T2-weighted signal along the right medial hippocampus as well as hippocampal atrophy, characteristic of mesial temporal sclerosis.

Skidmore CT. Neuroimaging in epilepsy. *Continuum Lifelong Learning Neurol*. 2025 Feb;31(1):61-80.



Question

133 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Progressive myoclonus epilepsies (PMEs) are a rare and heterogeneous group of disorders characterized by stimulus-sensitive myoclonus, generalized tonic-clonic seizures, and variable disease progression over time. Valproate is most commonly used in treatment, though should be avoided in the mitochondrial form of PME (myoclonic epilepsy with ragged-red fibers [MERRF]).

Other antiseizure medicines used include levetiracetam, topiramate, clonazepam, and zonisamide. While lamotrigine can be used, in rare instances the drug can make seizures worse. While the mechanism is not completely understood, some antiseizure medications, particularly those with prominent sodium channel inhibition such as carbamazepine, oxcarbazepine, and phenytoin, usually do not help and can often worsen myoclonus.

Riney K, Bogacz A, Somerville E, et al. International League Against Epilepsy classification and definition of epilepsy syndromes with onset at a variable age: position statement by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022;63(6):1443-1474.

Kälviäinen R. Progressive myoclonus epilepsies. *Semin Neurol*. 2015 Jun;35(3):293-299.

143 ADULT NEUROLOGY**Treatment/Management**

Lamotrigine and estrogen are metabolized via glucuronidation, and estrogen-containing compounds increase the metabolism of lamotrigine. Therefore, when a patient taking lamotrigine starts or increases the dose of an estrogen-containing preparation, the lamotrigine level must be monitored and the dose adjusted.

Bui E. Women's issues in epilepsy. *Continuum Lifelong Learning Neurol*. 2022 Apr 1;28(2):399-427.

Johnson EL, Kaplan PW. Caring for transgender patients with epilepsy. *Epilepsia*. 2017 Oct;58(10):1667-1672.

Question

153 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

The most common cause of symptomatic neonatal seizures is hypoxic ischemic encephalopathy (HIE), a disorder that occurs in approximately 1 to 2 in 1,000 live births. Diverse causes include infection, acute metabolic hypoglycemia, hypocalcemia, hypomagnesemia, and hyponatremia or hypernatremia. Withdrawal syndromes are associated with maternal drug use. Most neonatal seizures are acute symptomatic seizures and not due to epilepsy.

Stieren ES, Rottkamp CA, Brooks-Kayal AR. Neonatal seizures. *Neoreviews*. 2024 Jun 1;25(6):e338-e349.

Question

164 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

This patient's EEG tracings show a 20-second burst of generalized 3-Hz spike and slow wave discharges, characteristic of an absence seizure. Given the child's age (5 years) and normal development, neurologic examination, and EEG background, the most likely diagnosis is childhood absence epilepsy.

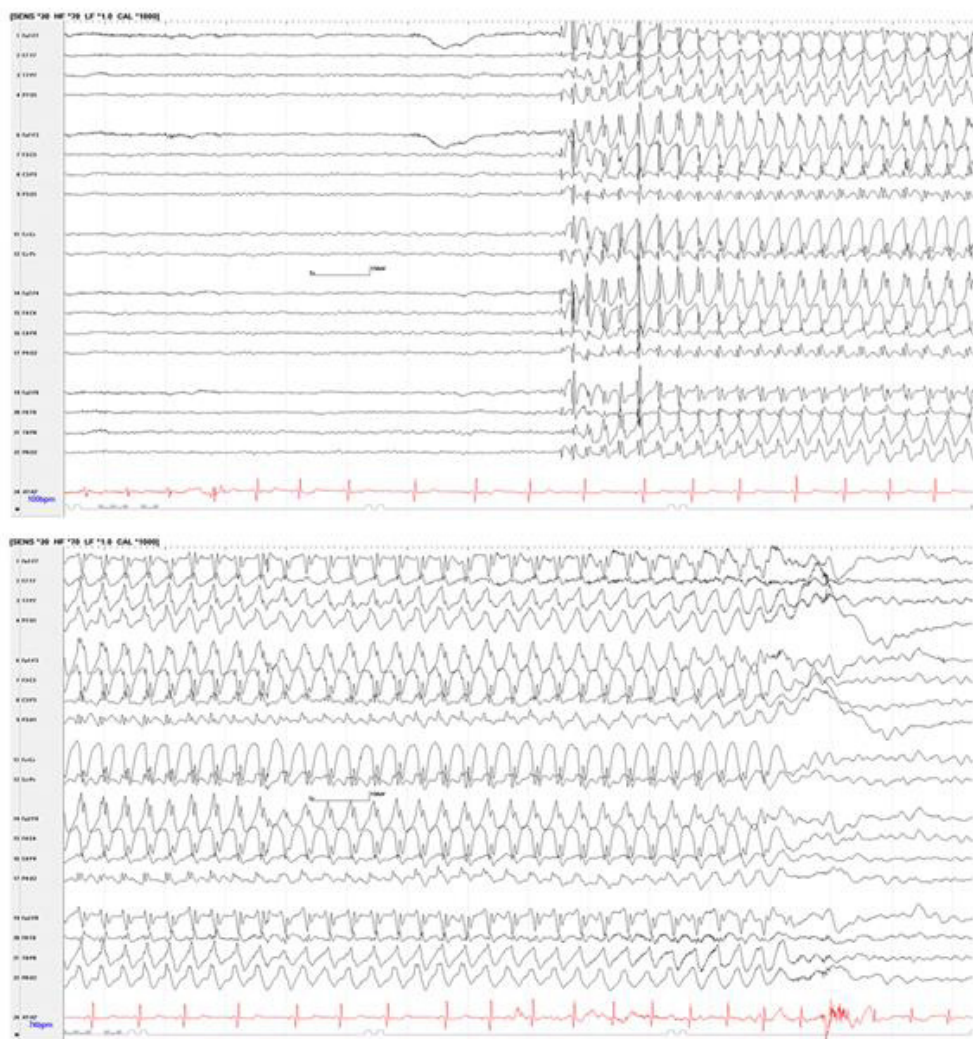
The landmark Childhood Absence Epilepsy Study reported that ethosuximide is the treatment of choice over lamotrigine and valproate. Ethosuximide is more efficacious than lamotrigine and better tolerated than valproate. Levetiracetam is not a first-line treatment for childhood absence epilepsy and is not known to work well for typical absence seizures. Oxcarbazepine may exacerbate absence seizures.

Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: efficacy and tolerability of the new antiepileptic drugs I: treatment of new-onset epilepsy: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Neurology*. 2018 Jul 10;91(2):74-81. Reaffirmed October 2024.

Hirsch E, French J, Scheffer IE, et al. ILAE definition of the idiopathic generalized epilepsy syndromes: position statement by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022;63(6):1475-1499.

(continues)

Question



Question

179 PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

The combination of tonic seizures and a burst suppression pattern on EEG is consistent with early infantile epileptic encephalopathy (Ohtahara syndrome). This syndrome, which can also include myoclonic seizures and focal seizures, frequently evolves into infantile epileptic spasms syndrome at 4 to 6 months of age. Causes have included brain malformations, as well as metabolic syndromes such as glycine encephalopathy and mitochondrial disorders.

Aicardi syndrome occurs in girls and is associated with retinal colobomas, agenesis of the corpus collosum, and epileptic spasms of infancy. EEG patterns in self-limited (familial) infantile epilepsy (SeLFIE) are normal or mildly abnormal, but do not show burst suppression. Dravet syndrome typically presents between age 4 to 12 months with a prolonged generalized tonic-clonic or hemiclonic seizure during fever; tonic seizures are not seen at presentation in Dravet syndrome.

Wyllie E, Gidal BE, Goodkin HP, et al (eds). *Wyllie's Treatment of Epilepsy: Principles and Practice*. 7th ed. Philadelphia: Wolters Kluwer; 2020.

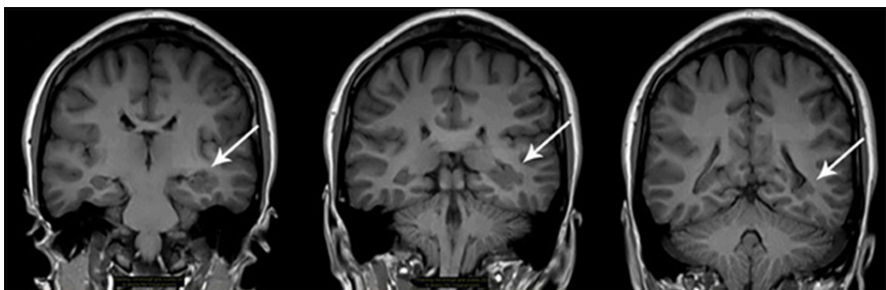
Arzimanoglou A, O'Hare A, Johnston M, et al (eds). *Aicardi's Diseases of the Nervous System in Childhood*. 4th ed. London: Mac Keith Press; 2018.

183 NO SPECIFIED PATIENT AGE

Neuroimaging|Neuroscience and Mechanism of Disease

The coronal T1-weighted MRI scan shows left temporal cortical heterotopia (neuronal migration defect) involving the left temporal parahippocampal and fusiform gyri (white arrows). The area appears to have increased cortical volume rather than the volume loss seen with an old stroke. A multiple sclerosis plaque should not involve only the cortex and again demonstrate volume loss. Hemorrhage may be hyperintense or hypointense on T1-weighted images. Mesial temporal sclerosis demonstrates atrophy of the hippocampus, which is not seen here.

Yoo JY, Panov F. Identification and treatment of drug-resistant epilepsy. *Continuum Lifelong Learning Neurol*. 2019 Apr;25(2):362-380.



Question

191 NO SPECIFIED PATIENT AGE**Treatment/Management**

Perampanel is the first-in-class antiseizure medication that inhibits the postsynaptic AMPA receptor. The mechanism of action that carbamazepine, lamotrigine, phenytoin, topiramate, valproic acid, and zonisamide have in common is slow recovery of voltage-gated sodium channels. Phenobarbital and primidone increase the duration of GABA channel opening. Clobazam increases the frequency of GABA channel opening.

Steinhoff BJ, Ben-Menachem E, Ryvlin P, et al. Efficacy and safety of adjunctive perampanel for the treatment of refractory partial seizures: a pooled analysis of three phase III studies. *Epilepsia*. 2013 54(8):1481-1489.

203 PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

This patient has Dravet syndrome, likely due to a pathogenic variant in the *SCN1A* gene that encodes for a sodium channel subunit. Mutations in *SCN1A* can cause a spectrum of epilepsies, including Dravet syndrome. Clinical features include epilepsy onset at age <1 year, history of normal development, and episodes that often but not always include a prolonged febrile or afebrile convulsion. Typical seizure types include hemiclonic (as described), generalized tonic-clonic, myoclonic, and other generalized seizure types, though tonic seizures should not be a prominent seizure type.

Cannabidiol in a high-dose formulation has been studied in both randomized controlled studies and open label studies, with efficacy in treating seizures in Dravet syndrome reported. In 2008, the FDA approved this formulation in the United States for children ages 2 and older with Dravet syndrome. Ethosuximide is indicated for absence seizures. Gabapentin, lamotrigine, and tiagabine are contraindicated for Dravet syndrome.

Myers KA. Genetic epilepsy syndromes. *Continuum Lifelong Learning Neurol*. 2022 Apr;28(2):339-362.

Question

212 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Diagnostic Procedures

According to the Salzburg criteria, epileptiform discharges averaging >2.5 Hz for ~10 seconds or any pattern with definite evolution and lasting for ~10 seconds is considered an electrographic seizure. Of the options listed, only generalized, 2.75–Hz periodic discharges meet this criterion.

The other patterns listed (bilateral, asynchronous, temporal, with 1.5–Hz periodic discharges; generalized, with 2.5–Hz extreme delta brush pattern; generalized, rhythmic, with 0.5–Hz delta; and generalized, with burst attenuation) are not ictal in the absence of a clinical correlate. However, with the exception of generalized, with burst attenuation pattern, the others fall under the ictal-interictal continuum, which refers to possible electrographic seizures. The term ictal-interictal continuum indicates that the pattern may be clinically significant and contributing to the altered mental status and other clinical symptoms. Treatment may be warranted.

Hirsch LJ, Fong MWK, Leitinger M, et al. American Clinical Neurophysiology Society's standardized critical care EEG terminology: 2021 version. *J Clin Neurophysiol*. 2021 Jan;38(1):1-29.

Rubinos C. Emergent management of status epilepticus. *Continuum Lifelong Learning Neurol*. 2024 Jan;30(3):682-720.

227 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

Status epilepticus (SE) is defined as repeated seizures lasting at least 5 minutes or recurrent seizures without interictal recovery of awareness. Recent studies report that in SE there is both loss of inhibitory GABA-A receptors and accrual of excitatory NMDA receptors. Implications of these findings suggest that antiseizure medications with GABA-agonist activity (midazolam, propofol) may be less effective with progression of SE, whereas NMDA antagonists (ketamine) may be more efficacious in late stages of SE.

Alkhachroum A, Der-Nigoghossian CA, Mathews E, et al. Ketamine to treat super-refractory status epilepticus. *Neurology*. 2020 Oct 20;95(16):e2286-e2294.

Hocker SE. Status epilepticus. *Continuum Lifelong Learning Neurol*. 2015 Oct;21(5):1362-1383.

Question

238 NO SPECIFIED PATIENT AGE**Treatment/Management**

N-desmethyclobazam levels (the metabolite of clobazam) increase significantly in combination with cenobamate, leading to intolerable fatigue that can be improved by reducing the dose of clobazam. Reducing clobazam earlier in the titration of cenobamate is recommended to decrease the risk of side effects. There is evidence for synergy between these two medications, so a small dose of clobazam is often retained after the dose is lowered to help with seizure control. Reducing levetiracetam is not likely to improve sedation significantly. Adding a stimulant may help, but it would be best to decrease (rather than increase) the medication if the same level of seizure control can be achieved.

Osborn M, Abou-Khalil B. The cenobamate-clobazam interaction- evidence of synergy in addition to pharmacokinetic interaction. *Epilepsy Behav.* 2023 May;142:109156.

Elakkary S, Hagemann A, Klimpel D, et al. A retrospective non-interventional study evaluating the pharmacokinetic interactions between cenobamate and clobazam. *Epilepsia.* 2023 Apr;64(4):e36-e42.

Rosenfeld WE, Abou-Khalil B, Aboumatar S, et al. Post hoc analysis of a phase 3, multicenter, open-label study of cenobamate for treatment of uncontrolled focal seizures: effects of dose adjustments of concomitant antiseizure medications. *Epilepsia.* 2021 Dec;62(12):3016-3028.

Question

249 NO SPECIFIED PATIENT AGE

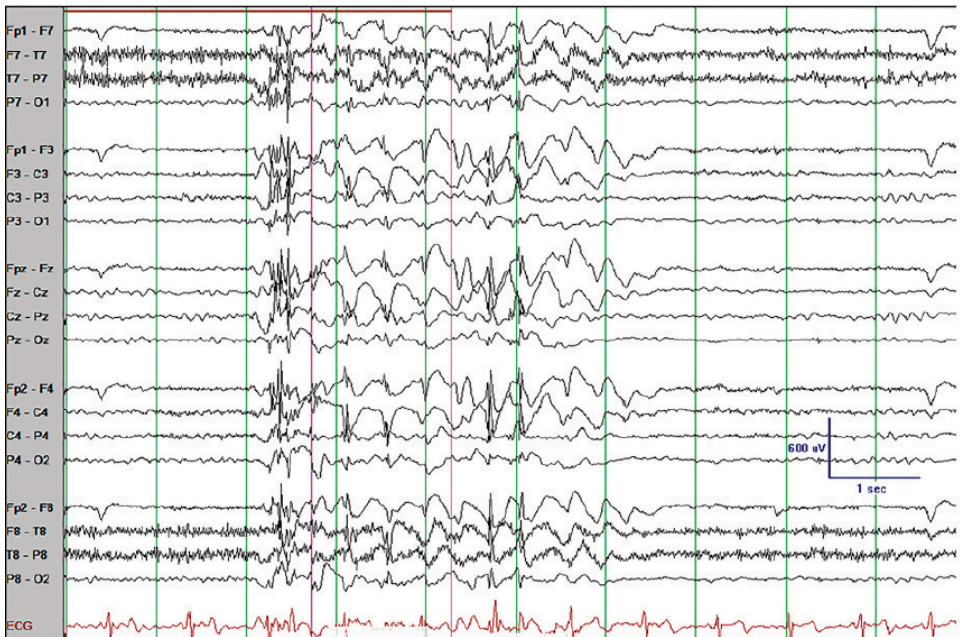
CORE KNOWLEDGE

Clinical Aspects of Disease

This patient most likely has juvenile myoclonic epilepsy characterized by generalized tonic-clonic seizures, absence seizures, and myoclonic jerks. The EEG demonstrates 4- to 6-Hz spike wave discharges, polyspikes, and a normal background.

Hirsch E, French J, Scheffer IE, et al. ILAE definition of the idiopathic generalized epilepsy syndromes: position statement by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1475-1499.

Wirrell E. Infantile, childhood, and adolescent epilepsies. *Continuum Lifelong Learning Neurol*. 2016 Feb;22(1):60-93.



Question

260 PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroimaging

This patient's MRI scan shows a midline mass of the hypothalamus, a finding consistent with hypothalamic hamartoma. The MRI scan is also typical of a hamartoma of the tuber cinereum, which is generally associated with premature maturity, seizures, hyperactivity, and rapid changes in weight. Pituitary macroadenoma are sellar lesions. Craniopharyngioma generally presents with heterogeneous T1 signal and no contrast enhancement. Aneurysm would demonstrate flow signal void.

Cohen NT, Cross JH, Arzimanoglou A, et al. Hypothalamic hamartomas: evolving understanding and management. *Neurology*. 2021 Nov;97(18):864-873.

**261** ADULT NEUROLOGY**Contemporary Issues**

This patient has REM sleep behavior disorder (RBD), a syndrome that has a up to 96% rate of conversion to a neurodegenerative disorder, most likely a synucleinopathy, after 14 years. The most recent guidance for communicating this information is to provide the patient and family the option of disclosure about prognosis.

Malkani RG, Wenger NS. REM sleep behavior disorder as a pathway to dementia: if, when, how, what, and why should physicians disclose the diagnosis and risk for dementia. *Curr Sleep Med Rep*. 2021;7(3):57-64.

Malkani R. REM sleep behavior disorder and other REM parasomnias. *Continuum Lifelong Learning Neurol*. 2023 Aug;29(4):1092-1116.

Question

273 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

When selecting antiseizure medications (ASMs), not only is it necessary to consider the specific epilepsy syndrome, but it is also important to consider medical comorbidities that might be affected by the ASM. For example, in elderly patients taking multiple cardiovascular medications, it is preferable to avoid ASMs with multiple drug interactions, typically those that induce hepatic enzymes (phenytoin, carbamazepine, phenobarbital, and primidone). Both topiramate and zonisamide can suppress appetite and lead to weight loss. Valproic acid, gabapentin, pregabalin, and carbamazepine are associated with weight gain, which would be relatively contraindicated in obesity.

Kanner AM, Ashman E, Gloss D, et al. Practice guideline update summary: Efficacy and tolerability of the new antiepileptic drugs I: treatment of new-onset epilepsy: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018 Jul 10;91(2):74-81. Codeveloped with the American Epilepsy Society. Reaffirmed October 2024.

French JA, Gazzola DM. Antiepileptic drug treatment: new drugs and new strategies. *Continuum Lifelong Learning Neurol*. 2013 Jun;19(3):643-655.

Question #

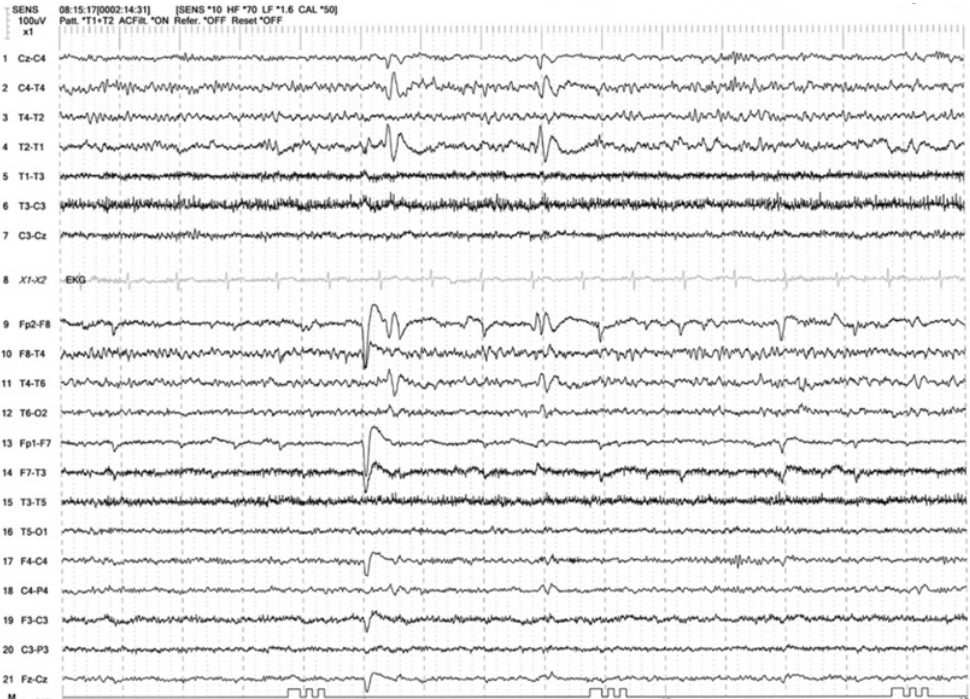
295 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neurophysiology

The EEG shown reveals right anterior temporal sharp waves.

Skidmore CT. Adult focal epilepsies. Continuum Lifelong Learning Neurol. 2016 Feb;22(1):94-115.



Question

304 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

The antiseizure medications with the lowest risk of major congenital malformations are lamotrigine, levetiracetam, and oxcarbazepine, with respective unadjusted birth prevalence risk of 3.1%, 3.5%, and 3.1%. Valproate had the highest risk at 9.7% with carbamazepine, phenytoin, and topiramate falling in between.

Perucca P, Battino D, Bromley R, et al. Epilepsy-pregnancy registries: an update. *Epilepsia*. 2025 Jan;66(1):47-59.

315 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

Developmental and/or epileptic encephalopathy with spike-wave activation in sleep (DEE-SWAS or EE-SWAS) is characterized by a variable degree of cognitive, language, behavioral, or motor regression associated with a marked increase in spike-and-wave discharges (generalized or focal) in sleep. Seizures are typically infrequent, and regression is seen within weeks of the EEG pattern, though specific changes can sometimes be hard to assess. Landau-Kleffner syndrome is a specific subtype of EE-SWAS in which regression affects mainly language (classically, an acquired auditory agnosia).

Silbersweig D, Safar LT, Daffner KR (eds). *Neuropsychiatry and Behavioral Neuroscience: Principles and Practice*. New York: McGraw-Hill; 2021.

Question

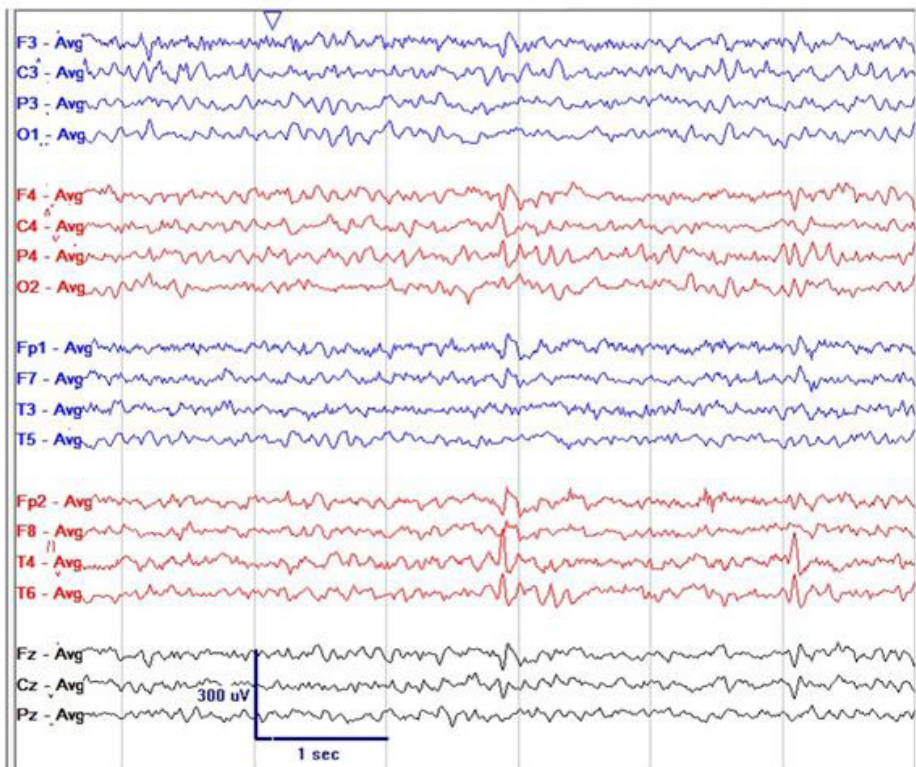
331 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neurophysiology

The EEG record is generated by recording electrical potential differences between pairs of electrodes or between an electrode and a reference. The universal convention is that negative potential differences are represented by a deflection above the baseline (ie, up). In this case, the montage shown is average, so each electrode shown is being compared to an average of all of the electrodes. In this montage, the electrode with the highest amplitude upward deflection of the sharp wave indicates the place at which there is maximal negativity (ie, the negative end of the dipole).

Schomer D, Lopez de Silva F (eds). *Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields*. 7th ed. New York: Oxford University Press; 2018.



Question

341 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

Hippocampal sclerosis, more broadly referred to as mesial temporal sclerosis (MTS) and includes the amygdala, is highly associated with focal epilepsy. MTS is seen at a high rate in people with a history of prolonged febrile convulsions during childhood (febrile status epilepticus).

The hallmark MRI findings include hippocampal atrophy, T2 hyperintensity of the hippocampus, and loss of observable internal architecture. The other imaging findings listed may be associated with seizures and/or epilepsy, but are not strongly associated with prolonged febrile childhood convulsions.

Encephalomalacia involving the orbitofrontal cortices is commonly seen in association with traumatic brain injury and may occur with posttraumatic focal epilepsy. Contrast enhancement of the leptomeninges can be seen in meningitis or other inflammatory or neoplastic conditions. Temporal encephaloceles may also be seen in the setting of increased intracranial pressure and can be associated with focal epilepsy.

Lewis DV, Nordli DR Jr, Nordli DR 3rd, et al. Febrile status epilepticus and epileptogenesis: The FEBSTAT study. *Epilepsia Open*. 2024 Aug 6.

Walker MC. Hippocampal sclerosis: causes and prevention. *Semin Neurol*. 2015 Jun;35(3):193-200.

Question

354 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Diagnostic Procedures

Exome sequencing is now the recommended first-line genetic test for most patients with epilepsy. It targets the exome—the portion of the genome composed of all protein-coding exons—which accounts for approximately 2% of the entire human genome. Also known as whole exome sequencing, this approach detects variants in genes already associated with epilepsy and can also uncover novel gene variants that may not yet be linked to the condition. In a population of patients with epilepsy, exome sequencing has the highest diagnostic yield.

Gene panels also evaluate large numbers of genes known to be associated with a specified disease category (such as epilepsy) but decode variants in fewer genes than would be included in exome sequencing. A chromosomal microarray identifies copy number variations (deletions or duplications) across regions of chromosomes that include multiple genes, but it does not provide information about base-pair level variants. Targeted gene testing is used to sequence a single gene for evaluation of pathogenic variants when clinical information is highly indicative of a specific diagnosis.

Kessler SK. Epilepsy genetics. *Continuum Lifelong Learning Neurol*. 2025 Feb;31(1):81-94.

Smith L, Malinowski J, Ceulemans S, et al. Genetic testing and counseling for the unexplained epilepsies: an evidence-based practice guideline of the National Society of Genetic Counselors. *J Genet Couns*. 2023 Apr;32(2):266-280.

Question

366 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Valproate increases lamotrigine serum levels by inhibiting the hepatic glucuronidation of lamotrigine. Because of this interaction, titration of lamotrigine in a patient taking valproate must start and end at lower doses. Cenobamate and phenytoin induce the metabolism of lamotrigine, decreasing its serum concentration.

Abou-Khalil BW. Update on antiseizure medications 2022. Continuum Lifelong Learning Neurol. 2022 Apr;28(2):500-535.

376 NO SPECIFIED PATIENT AGE**Neurophysiology**

The location of ictal focus is the most important factor in determining seizure onset during chronic intracranial EEG monitoring and thus is best represented by ictal onset. The subsequent expression of the ictal discharge, while important, is less useful in localizing the epileptogenic zone.

Rubin DI (ed). Clinical Neurophysiology. 5th ed. New York: Oxford University Press; 2021.

Question

386 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

This patient presents with a history of a single seizure. Lateral tongue bite, urinary incontinence, and postictal confusion increase the likelihood that the event was an epileptic seizure; however, a single unprovoked seizure is not sufficient to diagnose epilepsy. According to the International League Against Epilepsy (ILAE), epilepsy is defined by any of the following:

- At least two unprovoked seizures occurring >24 hours apart
- One unprovoked seizure and a probability of further seizures similar to the general recurrence risk after two unprovoked seizures ($\geq 60\%$) (This criterion could be satisfied by an epileptogenic lesion on MRI, or epileptiform abnormalities on EEG.)
- Diagnosis of an epilepsy syndrome

Both generalized and focal epilepsy syndromes may present with unrecognized nonmotor seizures. In focal epilepsy, focal impaired awareness seizures (FIAS), particularly those of temporal lobe origin, often feature bland staring with automatic behavior (oral or manual automatisms). These episodes would be highly suggestive of focal epilepsy and would substantiate a diagnosis of an epilepsy syndrome, prompting initiation of an antiseizure medication.

It is important to know that the diagnosis of epilepsy is often delayed in patients with predominantly nonmotor seizures, as the history is often not elicited at the time a seizure occurs and sometimes requires collateral information from witnesses, as patients with FIAS may not remember the events. History should also try to identify focal aware seizures, which may cause brief, stereotyped sensations ascribable to the localization of the seizure (eg, déjà vu, epigastric rising sensation, or unprovoked panic in patients with temporal lobe epilepsy).

Serum prolactin has high specificity and low sensitivity when drawn soon after an epileptic convulsive seizure and has utility in differentiating epileptic from nonepileptic seizures when the suspicion for mimics like syncope is low. However, in this case it cannot help substantiate a diagnosis of epilepsy.

(continues)

Question

Arachnoid cysts are a common incidental MRI finding and do not appear to be associated with epilepsy in large epidemiologic studies; the prevalence of epilepsy/seizures in individuals with arachnoid cysts is not significantly higher than those without cysts. Thus, arachnoid cysts generally should not be considered an epileptogenic lesion unless they substantially disrupt overlying cortex. Epileptogenic lesions typically involve or disrupt the cortex and should have reasonable causal connection to epilepsy. These may include remote symptomatic lesions such as cortical strokes, cortical encephalomalacia from traumatic brain injury, brain tumors that disrupt the cortex, various vascular malformations, and hippocampal sclerosis.

Wicket waves are a benign EEG variant whose presence does not support a diagnosis of epilepsy.

History of concussion with brief loss of consciousness represents a mild head injury. Mild head injuries are associated with a slight increased risk in developing epilepsy, but the presence of a mild risk factor is not sufficient for diagnosis of epilepsy.

Vossler DG. First seizures, acute repetitive seizures. *Continuum Lifelong Learning Neurol.* 2025 Feb;31(1):95-124.

Jandhyala N, Ferrer M, Pellinen J, et al; for Human Epilepsy Project Investigators. Unrecognized focal nonmotor seizures in adolescents presenting to emergency departments. *Neurology.* 2024 May;102(10):e209389.

Del Brutto OH, Mera RM, Kiernan J, et al. Supratentorial arachnoid cysts and seizures/epilepsy: a population study in community dwellers aged ≥ 20 years. *Epilepsia.* 2019 Aug;60(8):e83-e87.

Macorig G, Crespel A, Nilo A, et al. Can epilepsy affect normal EEG variants? A comparative study between subjects with and without epilepsy. *Neurophysiol Clin.* 2024 Feb;54(1):102935.

Karlander M, Ljungqvist J, Zelano J. Post-traumatic epilepsy in adults: a nationwide register-based study. *J Neurol Neurosurg Psychiatry.* 2021 Mar 9;92(6):617-621.

Question

394 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

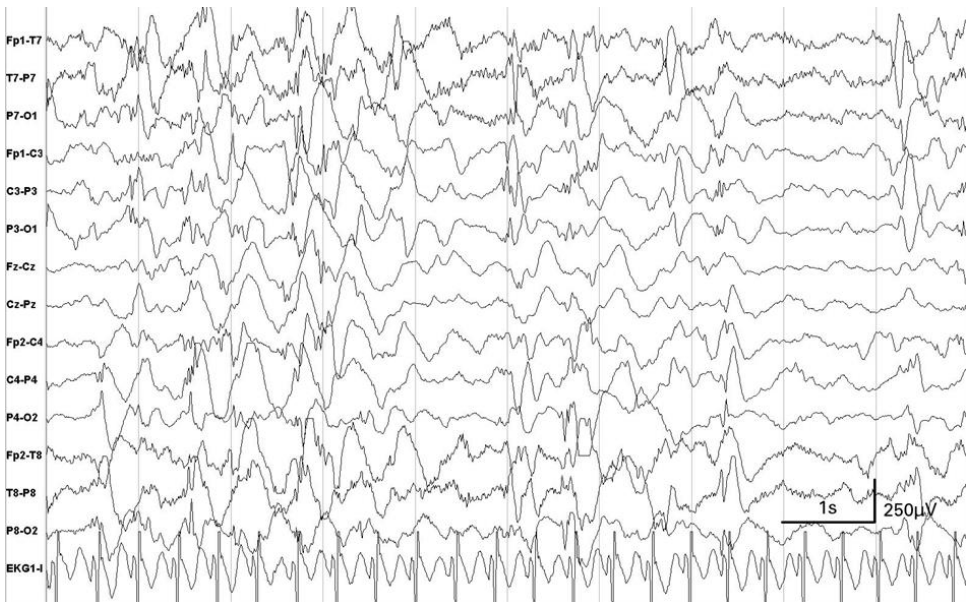
Diagnostic Procedures

The EEG shows hypsarrhythmia (interictal high-amplitude, arrhythmic delta activities with independent multifocal spike discharges), an interictal pattern characteristic (though not always present) of infantile epileptic spasms syndrome (IESS). The ictal patterns of epileptic spasms can vary and include electrodecrement, paroxysmal fast activity, and a high-voltage generalized slow spike and wave discharge. Many infants with IESS progress to develop Lennox–Gastaut syndrome, which is characterized by the other seizure types listed (myoclonic, absence, tonic, generalized tonic clonic).

Katyayan A, Diaz-Medina G. Epilepsy: epileptic syndromes and treatment. *Neurol Clinics* 2021;39(3):779-795.

International League Against Epilepsy. Infantile epileptic spasms syndrome (IESS). <https://www.epilepsydiagnosis.org/syndrome/west-syndrome-overview.html>. Accessed Oct 14, 2025.

Zuberi SM, Wirrell E, Yozawitz E, et al. ILAE classification and definition of epilepsy syndromes with onset in neonates and infants: position statement by the ILAE Task Force on Nosology and Definitions. *Epilepsia*. 2022 Jun;63(6):1349-1397.



Question

7 PEDIATRIC NEUROLOGY

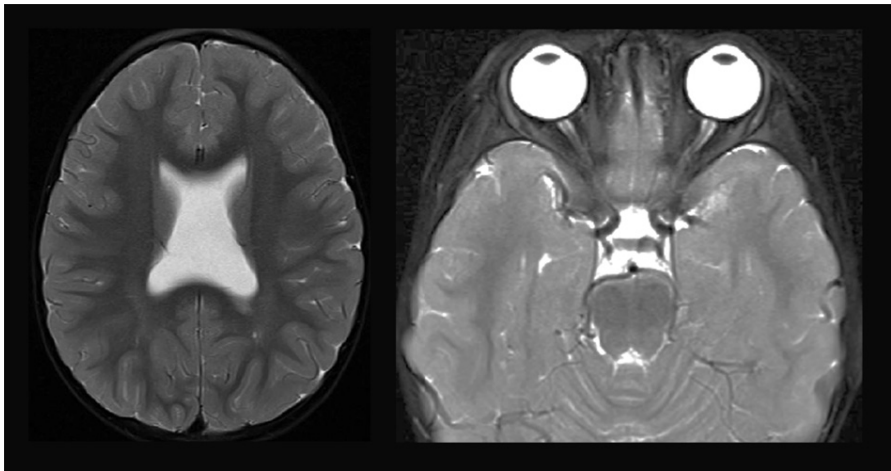
CORE KNOWLEDGE

Neuroimaging|Clinical Aspects of Disease

This patient's MRI scans show small optic nerves/chiasm and absence of the septum pellucidum, findings compatible with septo-optic dysplasia. Up to 90% of patients have associated brain abnormalities and 45% have pituitary insufficiency. Clinical findings include short stature, endocrine dysfunction, normal or color blindness, vision loss, nystagmus, and strabismus, with or without intellectual disability, spasticity, microcephaly, and anosmia.

Signorini SG, Decio A, Fedeli C, et al. Septo-optic dysplasia in childhood: the neurological, cognitive and neuro-ophthalmological perspective. *Dev Med Child Neurol*. 2012 Nov;54(11):1018-1024.

Webb EA, Dattani MT. Septo-optic dysplasia. *Eur J Hum Genet*. 2010 Apr;18(4):393-397.



24 PEDIATRIC NEUROLOGY

Clinical Aspects of Disease

Kearns-Sayre syndrome is caused by large deletions in mitochondrial DNA. Neurologic manifestations include ophthalmoplegia, ptosis, generalized weakness, and often eventually progress to dementia, hearing loss, retinitis pigmentosa, and autonomic neuropathy. Systemic manifestations include heart block, cardiomyopathy, and diabetes mellitus. Mitochondrial DNA deletions (as opposed to mutations) are almost always sporadic.

Arzimanoglou A, O'Hare A, Johnston M, et al (eds). *Aicardi's Diseases of the Nervous System in Childhood*. 4th ed. London: Mac Keith Press; 2018.

Question

42 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Neuroscience and Mechanism of Disease

This patient's presentation (right finger weakness and numbness, history of foot drop) and family history of similar symptoms are consistent with hereditary neuropathy with liability to pressure palsy (HNPP). This disorder is characterized by *PMP22* deletion causing episodic peripheral nerve dysfunction. Pathogenic variants in *TRPV4* or *PCK2* are seen in autosomal recessive Charcot-Marie-Tooth (CMT) disease, and variations in *GJB1* are seen in X-linked CMT. Pathogenic variations in *SOD* are associated with ALS.

Hayes LH, Sadjadi R. Hereditary neuropathies. Continuum Lifelong Learning Neurol. 2023 Oct;29(15):1514-1537.

60 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Diagnostic Procedures

This 5-year-old child's presentation is consistent with autism, as demonstrated by speech regression around 18 months, difficulties with social interactions (poor eye contact), lack of joint attention, and stereotypies. Of the tests listed here, the best for diagnosing autism is the Autism Diagnostic Observation Schedule (ADOS). The NICHQ Vanderbilt Assessment Scale and Connors Continuous Performance Test (CPT) help in the diagnosis of attention-deficit/hyperactivity disorder; the Verbal Fluency Test and the Wechsler Intelligence Scale (WISC) for Children are helpful in evaluating cognitive capacity.

Fulceri F, Caruso A, Micai M, et al. Autism diagnosis in children and adolescents: a systematic review and meta-analysis of test accuracy. Neurosci Biobehav Rev. 2025 Jun;173:106164.

Lebersfeld JB, Swanson M, Clesi CD, et al. Systematic review and meta-analysis of the clinical utility of the ADOS-2 and the ADI-R in diagnosing autism spectrum disorders in children. J Autism Dev Disord. 2021 Nov;51(11):4101-4114.

Barbaresi W, Cacia J, Friedman S, et al. Clinician diagnostic certainty and the role of the autism diagnostic observation schedule in autism spectrum disorder diagnosis in young children. JAMA Pediatr. 2022 Dec;176(12):1233-1241.

Question

76 PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Ketogenic diet is a treatment for refractory epilepsy. In a classic 4:1 ratio ketogenic diet, 90% of calories come from fat with the remainder from carbohydrates and protein, leading to a metabolic state in which the brain's major energy source is ketone bodies (acetone, acetoacetic acid, beta-hydroxybutyric acid) instead of glucose. Beta-oxidation of fatty acids is the process by which fatty acids (breakdown products of fat metabolism) are converted to acetyl-CoA, which enters the citric acid cycle.

Ketogenic diet is the treatment of choice for glucose transporter 1 (GLUT1) deficiency, a disorder characterized by impaired glucose transport to the brain. The diet offers a way to sidestep this problem. Pyruvate dehydrogenase deficiency is a rare disorder of carbohydrate metabolism for which a ketogenic diet has often been used as treatment but is not always successful. This disorder is not to be confused with pyruvate carboxylase deficiency, which is also a contraindication to use of a ketogenic diet because it requires a diet low in fat and high in carbohydrates and protein.

Gavrilovici C, Rho JM. Metabolic epilepsies amenable to ketogenic therapies: indications, contraindications, and underlying mechanisms. *J Inherit Metab Dis*. 2021 Jan;44(1):42-53.

91 PEDIATRIC NEUROLOGY

Neuroscience and Mechanism of Disease

In imaging studies that reveal a large posterior fossa and fourth ventricle that opens to a large cyst, the cyst wall is the roof of the fourth ventricle. The vermis may be either absent entirely or hypoplastic in Dandy-Walker malformation, in association with an enlarged posterior fossa and frequent brainstem microscopic developmental abnormalities.

The Chiari malformations are characterized by a small posterior fossa. Rhombencephalosynapsis is characterized by absence of the vermis and continuity of the cerebellar hemispheres, dentate nuclei, and superior cerebellar peduncles. Craniorachischisis is a neural tube that is mostly open from one end to the other. Imaging studies of a patient with Joubert syndrome show a "molar tooth" abnormality of the brainstem.

Smith C, Perry A, Kovacs G, et al (eds). *Greenfield's Neuropathology*. 10th ed. Boca Raton, FL: CRC Press; 2024.

Question

107 ADULT NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

This patient's MRI scan shows descent of the cerebellar tonsils beneath the foramen magnum, evidence characteristic of a Chiari type I malformation. Surgical decompression relieves pressure on the brainstem and spinal cord by creating more space at the base of the skull.

Pituitary hormone replacement would be indicated for a pituitary disorder but is not seen here. Anticoagulation with low-molecular-weight heparin is typically indicated for sinus venous thrombosis, which can present with headaches; however, the imaging study shows no evidence of that disorder. There is no obstructive hydrocephalus, which would be treated with a ventriculoperitoneal shunt. The headaches described (subacute onset, worsen with straining) are not consistent with migraine, which can be treated with CGRP inhibitors.

Gaitanis J, Tauri T. Nervous system malformations. *Continuum Lifelong Learning Neurol.* 2018 Feb;24(1):72-95.

Starling AJ. Unusual headache disorders. *Continuum Lifelong Learning Neurol.* 2018 Aug;24(4):1192-1208.



Question

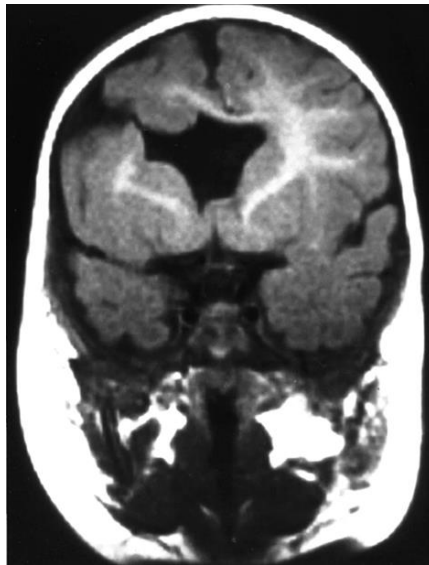
125 PEDIATRIC NEUROLOGY

Neuroimaging

The MRI scan shown is consistent with schizencephaly. A porencephalic cyst would be lined with white matter, whereas the cavity in schizencephaly is lined with heterotopic gray matter.

Lissencephaly refers to absence or extremely poor sulcation within the brain. Holoprosencephaly results from failure of lateral cleavage into distinct cerebral hemispheres and failure of transverse cleavage into the diencephalon and telencephalon. Perisylvian polymicrogyria would be centered around the lateral sulcus and characterized by a textured appearance to the overlying cortex.

Salzman KL, Jhaveri MD, Osborn AG (eds). *Diagnostic Imaging: Brain*. 5th ed. Philadelphia: Elsevier; 2025.



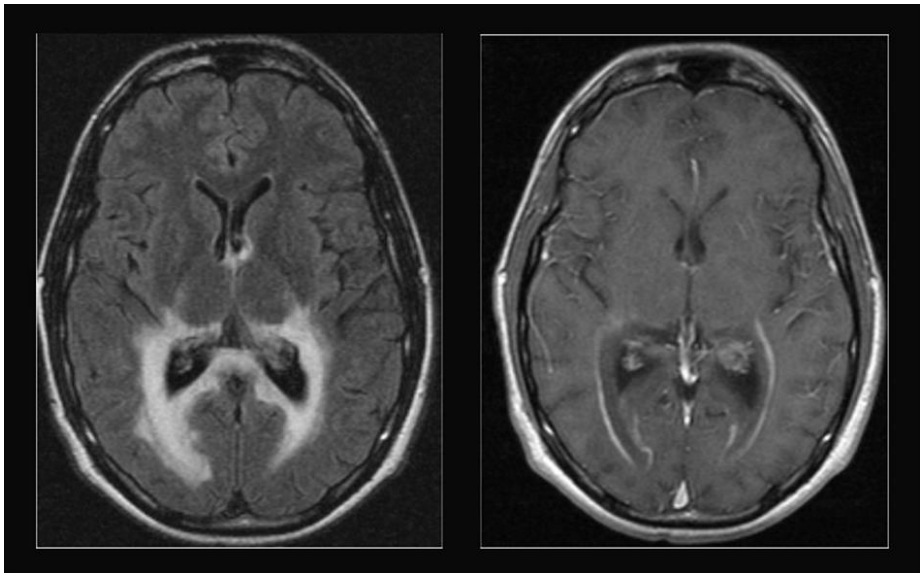
Question

139 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

X-linked adrenoleukodystrophy frequently presents with abnormal white matter hyperintensities in a parieto-occipital distribution, thus leading to issues in visuospatial functioning. Attentional symptoms of later onset than those seen in typical attention-deficit/hyperactivity disorder are common, as is progressive cognitive decline. Psychiatric symptoms are seen relatively early in the disease. The "leading edge" of the myelin loss, seen in the images, is also quite characteristic of the disorder.

In contrast, for Pelizaeus–Merzbacher disease, an X-linked disorder, the white matter in the centrum semiovale is isodense with the cortical ribbon on T1-weighted imaging. In Sandhoff disease and GM2 gangliosidosis, cortical atrophy may be seen. Alexander disease is more commonly characterized by demyelination in the frontal regions.

Ashwal S, Pearl PL, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 7th ed. Philadelphia: Elsevier, 2025.



Question

150 PEDIATRIC NEUROLOGY**Neuroscience and Mechanism of Disease**

This patient's history is consistent with Dravet syndrome, a disorder resulting from a pathogenic variant in one copy of the *SCN1A* gene that encodes for the alpha subunit of the NaV1.1 channel. Haploinsufficiency of this gene leads to loss of channel function.

Clinical features include onset of epilepsy before age 1 year, often associated with febrile seizures, followed by development of other seizure types, including hemiclonic, generalized tonic-clonic, and myoclonic. Development is initially normal but becomes impaired over time.

Because Dravet syndrome is a voltage-gated sodium channel loss of function disorder, sodium channel-blocking antiseizure medications are contraindicated as they may exacerbate seizures.

Helbig I. *SCN1A* – this is what you need to know. Beyond the ion channel. Understanding epilepsy genetics. <https://epilepsygenetics.blog/the-epilepsiome/scn1a-this-is-what-you-need-to-know/>. Accessed September 27, 2025.

Wirrell EC, Hood V, Knupp KG, et al. International consensus on diagnosis and management of Dravet syndrome. *Epilepsia*. 2022 Jul;63(7):1761-1777.

Brunklaus A, Zuberi SM. Dravet syndrome—from epileptic encephalopathy to channelopathy. *Epilepsia*. 2014 Jul;55(7):979-984.

158 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Diagnostic Procedures

The American Academy of Medical Genomics recommends ordering exome sequencing as a first-tier test for global developmental delays. Unless history and physical examination suggest a specific phenotype or group of disorders, tier 1 testing (as recommended by the American Academy of Pediatrics) consists of either genome sequencing or exome sequencing with chromosomal microarray.

Waggoner D, Wain KE, Dubuc AM, et al; ACMG Professional Practice and Guidelines Committee. Yield of additional genetic testing after chromosomal microarray for diagnosis of neurodevelopmental disability and congenital anomalies: a clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2018 Oct;20(10):1105-1113.

Manickam K, McClain MR, Demmer LA, et al; ACMG Board of Directors. Exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability: an evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). *Genet Med*. 2021 Nov;23(11):2029-2037.

Rodan LH, Stoler J, Chen E, et al; Council on Genetics. Genetic evaluation of the child with intellectual disability or global developmental delay: clinical report. *Pediatrics*. 2025 Jul 1;156(1):e2025072219.

Question

173 PEDIATRIC NEUROLOGY**Other Neuroscience/Mechanism of Disease**

Neuronal migration disorders are a group of embryologic disorders caused by the abnormal migration of neurons from the periventricular zone to their location.

Of the disorders listed, only polymicrogyria is considered a neuronal migration disorder. Anencephaly is due to failure of closure of the anterior neuropore, whereas hydranencephaly results from early neonatal hypoxic/ischemic injury. Dandy–Walker malformation is a posterior fossa disorder in which some or all of the cerebellar vermis is absent together with cystic dilation of the fourth ventricle. Agenesis of the corpus callosum represents a midline pattern defect that can occur alone or in the context of other developmental abnormalities.

Smith C, Perry A, Kovacs G, et al (eds). Greenfield's Neuropathology. 10th ed. Boca Raton, FL: CRC Press; 2024.

Question

198 ADULT NEUROLOGY

CORE KNOWLEDGE

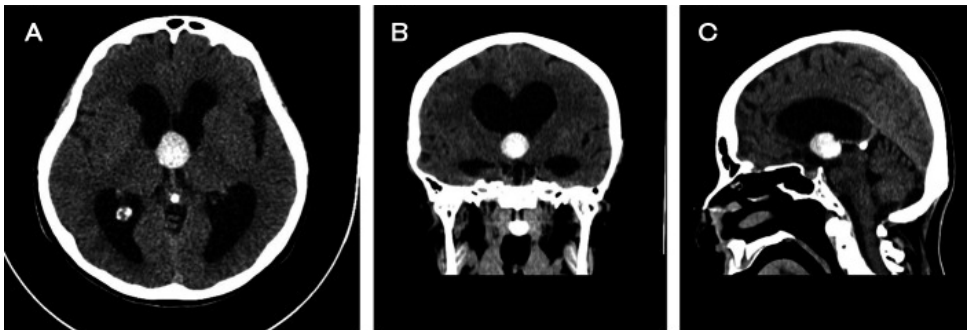
Clinical Aspects of Disease

This patient's MRI scans show acute hydrocephalus and a hyperdense lesion in the anterosuperior third ventricle. This lesion is most likely a colloid cyst that has acutely obstructed outflow from both lateral ventricles, resulting in acute enlargement and ballooning of the third ventricle that causes effacement of the interpeduncular and suprasellar cisterns.

The scans do not show visible subarachnoid bleeding, and subarachnoid hemorrhage does not explain the dense lesion in the third ventricle. The patient does not have fever or report neck stiffness to suggest bacterial meningitis, and symptoms have been present for several weeks. Bacterial meningitis does not explain the dense lesion in the third ventricle, nor is the MRI scan consistent with pituitary apoplexy given the location of the lesion. Pseudotumor cerebri does not produce obstructive hydrocephalus.

Humphries RL, Stone CK, Bowers RC. Colloid cyst: A case report and literature review of a rare but deadly condition. *J Emerg Med.* 2011 Jan;40(1):e5-e9.

Jarquín-Valdivia AA, Rich AT, Yarbrough JL, et al. Intraventricular colloid cyst, hydrocephalus and neurogenic stunned myocardium. *Clin Neurol Neurosurg.* 2005 Aug;107(5):361-365.



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Question

213 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Adrenomyeloneuropathy constitutes up to 46% of male X-linked adrenoleukodystrophy (X-ALD) involving the dorsal column and corticospinal tracts in the lower thoracic and lumbar regions. In men, disease onset typically occurs in the late 20s (mean, 28 years), with approximately 40% of patients having or developing cerebral involvement.

About 70% of all male patients with X-ALD have primary adrenocortical insufficiency (Addison disease); thus, evaluation of adrenocortical function is indicated every 6 months. Hydrocortisone supplementation and glucose are needed during times of stress and illness to prevent adrenal shock and hypoglycemia. ACTH is a treatment for secondary (not primary) adrenal insufficiency.

Raymond GV, Moser AB, Fatemi A, et al. X-linked adrenoleukodystrophy. GeneReviews® [Internet]. University of Washington, Seattle 1999 [updated Feb 2018].

Moser HW, Mahmood A, Raymond GV. X-linked adrenoleukodystrophy. *Nat Clin Pract Neurol*. 2007 Mar;3(3):140-151.

230 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

Rett syndrome is an X-linked disorder seen in young girls, characterized by developmental arrest, stereotypic hand movements, deceleration of head growth, and loss of communication skills. Between 80% and 85% of patients with classic Rett syndrome have an abnormality in the *MECP2* gene, whereas only approximately 50% of patients with atypical Rett syndrome have this gene abnormality.

Ashwal S, Pearl PL, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 7th ed. Philadelphia: Elsevier, 2025.

Question

246 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

The CT and MRI scan findings shown are highly consistent with Sturge–Weber syndrome. Cerebral lesions in patients with this disorder are most frequently seen in the parieto–occipital area. On CT scans, parenchymal calcification is seen adjacent to the leptomeningeal lesions in a pericapillary distribution in the fourth cortical layer, possibly secondary to chronic tissue hypoxia.

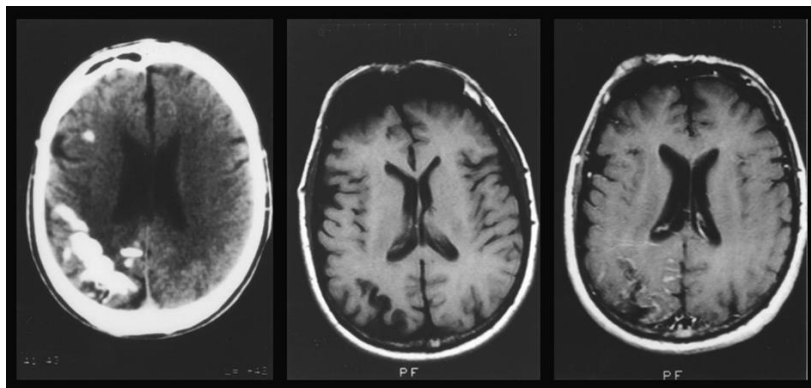
Noncontrast MRI scans typically show unilateral cerebral atrophy with enlargement of the ipsilateral subarachnoid spaces and ventricular cavities. Enlarged tubular regions of flow void and gyriform hypointensities (ie, decreased signal on T1- and T2-weighted images) reflect venous collateralization and cortical “serpentine” calcification, respectively.

Contrast-enhanced MRI is best for demonstrating the salient CNS vascular abnormalities. The leptomeninges show intense enhancement overlying the involved cortical region, secondary to leptomeningeal (pial) angiomatosis or a compromised blood–brain barrier secondary to chronic cortical ischemia. This meningeal enhancement often extends well beyond the region of parenchymal atrophy.

Fahr disease is characterized by bilateral symmetric calcium deposition in the brain parenchyma and typically presents in adulthood. Congenital toxoplasmosis can also be characterized by brain calcifications, but in this case they are small randomly distributed foci. Rasmussen encephalitis is a pediatric autoimmune disorder that typically presents with severe epilepsy and progressive hemispheric atrophy; calcifications are not seen. MRI scans in MELAS show characteristic stroke-like lesions with gyral swelling and T2/FLAIR hyperintensity, often affecting the parieto–occipital regions and cortex without following typical vascular territories but often involving both hemispheres.

Smith C, Perry A, Kovacs G, et al (eds). *Greenfield’s Neuropathology*. 10th ed. Boca Raton, FL:CRC Press; 2024.

Varadkar S, Bien CG, Kruse CA, et al. Rasmussen’s encephalitis: clinical features, pathobiology, and treatment advances. *Lancet Neurol*. 2014 Feb;13(2):195-205.



Question

263 PEDIATRIC NEUROLOGY**Treatment/Management**

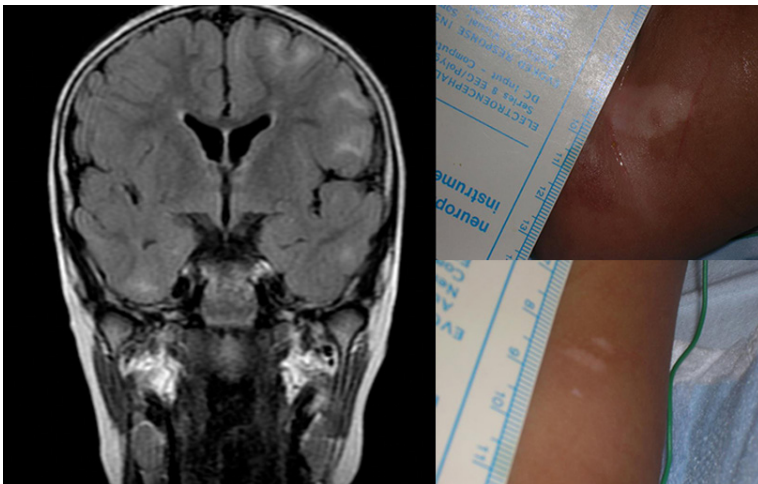
Infantile spasms are characterized by episodes of sudden, brief flexion or extension of the body, often involving the extremities and head/neck. Clinical trial evidence supports the use of high-dose oral corticosteroids, ACTH, or vigabatrin as first-line therapy, except in patients with tuberous sclerosis, where evidence strongly supports vigabatrin as first-line therapy.

Tuberous sclerosis is a disorder caused by pathogenic variants in *TSC1* or *TSC2*, which encode for proteins in the mTOR pathway. This disorder is characterized by one or more (typically many) areas of focal cortical dysplasia (tubers) and later by development of subependymal giant cell astrocytomas. Other organ systems involved include the heart (rhabdomyomas at birth that regress), eyes (ocular hamartomas), kidneys (renal angiomyolipomas), and skin (hypomelanotic macules, as pictured). These macules are also known as ash-leaf spots and can manifest as raised red bumps on the face (facial angiofibromas), rough patches of skin on the back (shagreen patches), and fibromas around and under the nails (periungual fibromas).

Go CY, Mackay MT, Weiss SK, et al. Evidence-based guideline update: medical treatment of infantile spasms: report of the Guideline Development Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology*. 2012 Jun;78(24):1974-1980. Reaffirmed May 2021.

Grinspan ZM, Knupp KG, Patel AD, et al. Comparative effectiveness of initial treatment for infantile spasms in a contemporary US cohort. *Neurology*. 2021 Sep 20;97(12):e1217-e1228.

van der Poest CE, Jansen FE, Braun KPJ, et al. Update on drug management of refractory epilepsy in tuberous sclerosis complex. *Pediatr Drugs*. 2020 Feb;22(1):73-84.



Question

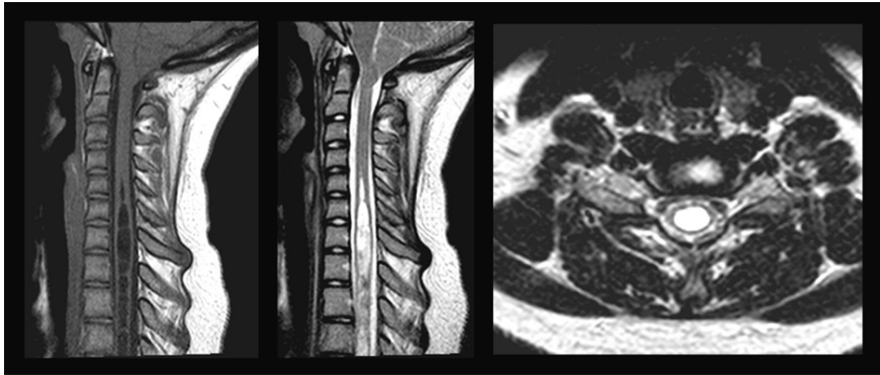
280 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroimaging

This patient's MRI scans demonstrate dilation of the spinal cord around a central cystic cavity, a finding consistent with syringohydromyelia. Note also on the sagittal images that the inferior portion of the cerebellum has herniated down into the upper cervical canal, a finding diagnostic of a Chiari malformation. Hydromyelia is commonly seen in association with both Chiari type I and II malformations.

Greenberg JO. Neuroimaging: A Companion to Adams and Victor's Principles of Neurology. New York: McGraw-Hill;1999.

**296** NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Neuroscience and Mechanism of Disease

This patient's presentation is consistent with spinal bulbar muscular atrophy (Kennedy syndrome), which is inherited in an X-linked recessive manner as a CAG triplet repeat expansion. This syndrome is characterized by upper and lower extremity weakness, hyporeflexia, infertility, gynecomastia, and bulbar fasciculations.

Stavros K. Genetic myelopathies. Continuum Lifelong Learning Neurol. 2024 Feb;30(1): 119-132.

Question

305 NO SPECIFIED PATIENT AGE**Neuropathology**

This patient has Down syndrome due to an extra copy of chromosome 21. The gene for amyloid precursor protein is also on chromosome 21; thus, patients overexpress amyloid-beta at an early age. Most individuals with Down syndrome have dementia, similar to Alzheimer disease, by age 40.

Degeneration of small blood vessels, seen in CADASIL/CARASIL, is due to a pathogenic variation in *NOTCH3*, leading to buildup of excess proteins in the smooth muscle cells of small arteries. This results in migraines and dementia. Increased alpha-synuclein is seen in dementia with Lewy bodies, a syndrome not commonly associated with Down syndrome.

Accumulation of abnormal GFAP protein aggregates occurs in Alexander disease, a disorder caused by a gain of function mutation in the gene encoding for *GFAP*. Although there is an association between moyamoya vasculopathy and Down syndrome, vasculopathy alone would not be expected to cause progressive memory loss.

Fortea J, Zaman SH, Hartley S, et al. Alzheimer's disease associated with Down syndrome: a genetic form of dementia. *Lancet Neurol*. 2021 Nov;20(11):930-942.

Question

310 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

The axial views show markedly enlarged lateral and third ventricles, with a small (or absent) cerebral aqueduct on sagittal views. These findings are most consistent with aqueductal stenosis, resulting in obstructive hydrocephalus.

In Dandy–Walker malformation, there is partial absence of the vermis of the cerebellum, not present here. Miller–Dieker syndrome is characterized by lissencephaly, also not present here. Alexander disease causes acquired macrocephaly but is associated with diffuse white matter changes. Periventricular leukomalacia is characterized by injury to the white matter surrounding the ventricles, most common in preterm infants, and typically results in *ex vacuo* dilation of the ventricles.

Salzman KL, Jhaveri MD, Osborn AG (eds). *Diagnostic Imaging: Brain*. 5th ed. Philadelphia: Elsevier; 2025.



Question

330 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

This 3-year-old patient's clinical presentation (loss of developmental skills, liver failure, worsening encephalopathy, ophthalmoplegia, myoclonus, ataxia, dystonia, and seizures) and MRI findings (FLAIR abnormalities in the bilateral basal ganglia, caudate, thalamic and dentate, with diffuse restriction in the caudate, basal ganglia, and scattered areas in the cortical and subcortical regions bilaterally) are consistent with mitochondrial disease, specifically Leigh disease.

Propionic acidemia is associated with metabolic abnormalities such as ketonuria and hypoglycemia. Both propionic acidemia and glutaric acidemia, which are assessed on the newborn screen, typically have a more acute time course and are not associated with ophthalmoplegia. Opsoclonus–myoclonus–ataxia syndrome is characterized by chaotic involuntary eye movements but not ophthalmoplegia.

Ball M, Thorburn DR, Rahman S. Mitochondrial DNA-associated Leigh syndrome spectrum. 2003 Oct 30 [Updated 2024 May 9]. In: Adam MP, Feldman J, Mirzaa GM, et al (eds). GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025.

Question

346 PEDIATRIC NEUROLOGY

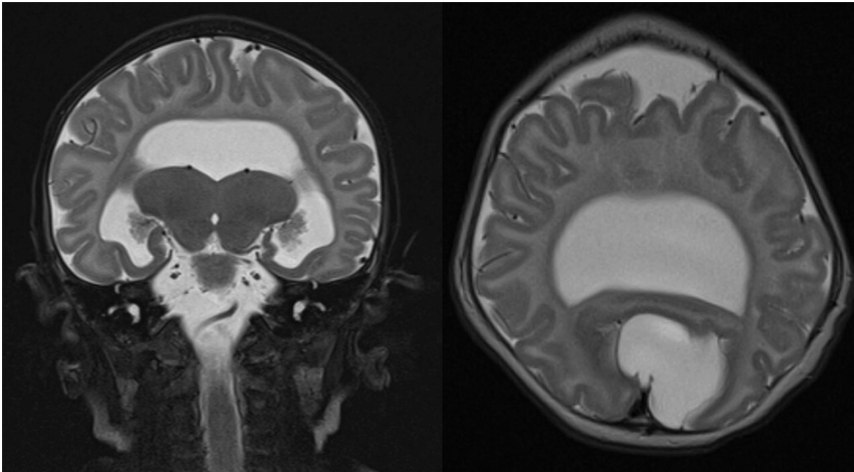
CORE KNOWLEDGE

Neuroimaging

This patient's imaging studies show fusion of the thalami and continuity of cerebral tissue across the midline with a continuous "horseshoe" mono-ventricle, rather than a third and two distinct lateral ventricles. This morphology, characterized by the failure of formation of separate right and left cerebral hemispheres, is consistent with holoprosencephaly. The volume of brain and configuration of the CSF-containing structures suggests this patient's anomaly falls in the range of semilobar holoprosencephaly.

Canavan disease is a leukodystrophy associated with large, rather than small, head size. Anencephaly is characterized by absence of the major portions of the hemispheres and diencephalon. Hydrocephalus refers to abnormal expansion of the ventricles. Periventricular leukomalacia is characterized by abnormal loss of white matter in the peritrigonal region.

Gomez GD, Corrêa DG, Trap B, et al. Holoprosencephaly spectrum: an up-to-date overview of classification, genetics and neuroimaging. *Jpn J Radiol*. 2025 Jan;43(1):13-31.

**361** NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Neuroimaging

This patient exhibits physical signs of a hereditary connective tissue disorder, most likely Marfan syndrome. Dural ectasia, a widening of the dural sac, is a cardinal feature of Marfan syndrome seen in 80% of patients. The sac compresses on the nerve roots over time and thins the cortex of the vertebral bodies and pedicles; this can cause back pain.

(continues)

Question

Scoliosis is commonly seen in Marfan syndrome but is not expected to cause severe back pain. Both a herniated disk and spondylolisthesis can cause back pain, but neither is a cardinal feature of Marfan syndrome. Tethered cord and filum terminale paragangliomas are not associated with Marfan syndrome.

Zeigler SM, Sloan B, Jones JA. Pathophysiology and pathogenesis of Marfan syndrome. *Adv Exp Med Biol*. 2021;1348:185-206.

372 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

Tuberous sclerosis is characterized by widespread hamartomas and benign, or rarely malignant, neoplasms in the brain, skin, retina, kidneys, heart, and lungs. Common manifestations include cortical tubers (ie, areas of focal cortical dysplasia), subependymal nodules, retinal abnormalities, cardiac rhabdomyoma, lymphangioleiomyomatosis, renal angiomyolipoma, and skin lesions. The disorder is caused by pathogenic variants in *TSC1* or *TSC2*, and inheritance pattern is autosomal dominant, though the mutation often occurs *de novo* in affected children.

Baldassari S, Picard F, Verbeek NE, et al. The landscape of epilepsy-related GATOR1 variants. *Genet Med*. 2019 Feb;21(2):398-408.

Randle SC. Tuberous sclerosis complex: a review. *Pediatr Ann*. 2017 Apr 1;46(4):e166-e171.

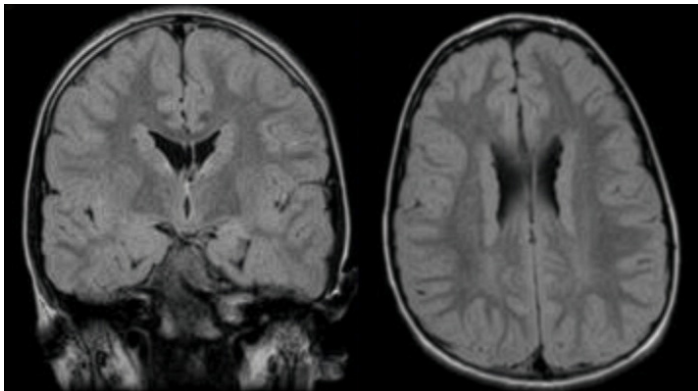
393 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

These FLAIR sequence images show tissue with signal intensity identical to that of cortical gray matter along the lateral subependymal aspect of each ventricle, representing heterotopic gray matter.

Salzman KL, Jhaveri MD, Osborn AG (eds). *Diagnostic Imaging: Brain*. 5th ed. Philadelphia: Elsevier; 2025.



Question

19

ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment Management

Carbamazepine and oxcarbazepine, both of which act as sodium channel blockers, are first-line treatment of trigeminal neuralgia, especially the classical and idiopathic types. These agents are effective but carry the risk of hyponatremia; thus, serum sodium level should be monitored periodically during treatment. Symptomatic hyponatremia is seen in up to 7% of patients taking oxcarbazepine, though most have mild symptoms. Risk factors include old age, polytherapy, and higher doses. CBC should be monitored with carbamazepine because of its rare but serious hematologic side effects (agranulocytosis and aplastic anemia), but serial monitoring is not necessary with oxcarbazepine.

Routine monitoring of carbamazepine or oxcarbazepine levels is not indicated unless there are concerns for toxicity. Urinalysis has no role in the monitoring of first-line preventive therapies. Urinalysis may be considered as part of the diagnostic evaluation of hyponatremia. While ECG may be obtained in patients with notable cardiac risk factors, it is not required for ongoing routine monitoring. Thyroid-stimulating hormone testing is unrelated to trigeminal neuralgia or the use of the aforementioned preventive medications.

Ashina S, Robertson CE, Srikiatkachorn A, et al. Trigeminal neuralgia. *Nat Rev Dis Primers*. 2024 May 30;10(1):39.

Question

41 ADULT NEUROLOGY**Treatment/Management**

This patient's symptoms are most consistent with classical trigeminal neuralgia, a disorder caused by neurovascular compression. The trigeminal nerve can be compressed vascularly by the superior cerebellar artery, anterior inferior cerebellar artery, trigeminal vein, or superior petrosal vein. This patient's classical trigeminal neuralgia is refractory to multiple pharmacologic treatments; therefore, microvascular decompression is the most appropriate next option in this otherwise healthy patient. If microvascular decompression is contraindicated, gamma knife radiosurgery, botulinum toxin injections, and radiofrequency ablation can be considered. Tramadol is an analgesic that targets mu-opioid receptors and inhibits the reuptake of norepinephrine and serotonin. Opioid medications are not indicated in trigeminal neuralgia, especially because of its habit-forming properties.

Ashina S, Robertson CE, Srikiatkachorn A, et al. Trigeminal neuralgia. *Nat Rev Dis Primers*. 2024;10:39.

Gronseth G, Cruccu GJ, Alksne C, et al. Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurologic Societies. *Neurology*. 2008 Oct 7;71(15):1183-1190. Reaffirmed May 2021.

129 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

The trigeminal autonomic cephalgias are a group of primary headache disorders characterized by short-lasting episodes of severe unilateral headaches associated with ipsilateral cranial autonomic symptoms. This patient has short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome. As well described by the name, SUNCT syndrome is characterized by very brief attacks of periorbital pain with ipsilateral tearing and eye redness. Attacks of SUNCT syndrome resemble those of cluster headaches but are differentiated primarily by the much briefer attack duration and greater frequency in SUNCT than in cluster headache. Primary stabbing headache (also known as ice pick headaches) should not be associated with cranial autonomic symptoms.

Newman LC. Trigeminal autonomic cephalgias. *Continuum Lifelong Learning Neurol*. 2015 Aug;21(4):1041-1057.

Goadsby PJ. Trigeminal autonomic cephalgias. *Continuum Lifelong Learning Neurol*. 2012 Aug;18(4):883-895.

Question

138 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Frontal or occipital headache can develop 12 to 24 hours after lumbar puncture. These headaches are usually worse in a standing position and improve when lying down. Transient symptoms that develop shortly after the procedure can reflect reduced CSF volume and pressure due to the removal of CSF before volume can be regenerated by the choroid plexus. Persistent symptoms suggest continuous CSF leakage from the subarachnoid space at the location of the lumbar puncture.

Using a higher gauge needle, orienting the bevel parallel to the longitudinal fibers, and reinserting the stylet prior to removal of the spinal needle can reduce the risk of postlumbar puncture headaches. Atraumatic (noncutting) needles have a blunt tip that reportedly spread the dural fibers apart rather than cutting them, resulting in a smaller hole and thus a lower risk of postlumbar puncture headache. A 2018 meta-analysis reported a reduction in postlumbar headache with use of an atraumatic needle (4.2%) compared with a conventional needle (11%).

Nath S, Koziarz A, Badhiwala JH, et al. Atraumatic versus conventional lumbar puncture needles: a systematic review and meta-analysis. *Lancet*. 2018 Mar;391(10126):1197-1204.

Arevalo-Rodriguez I, Ciapponi A, Roqué-Figuls M, et al. Posture and fluids for preventing post-dural puncture headache. *Cochrane Database Syst Rev*. 2016;3:CD009199.

Waise S, Gannon D. Reducing the incidence of post-dural puncture headache. *Clin Med (Lond)*. 2013 Feb;13(1):32-34

Question

148 ADULT NEUROLOGY**Contemporary Issues**

This otherwise healthy, physically active 80-year-old patient presents with classic left middle cerebral artery (MCA) stroke. Tenecteplase (TNK) was appropriately administered but did not result in improvement. CT angiogram showed a proximal left MCA occlusion. At this point it would be appropriate to consider, discuss, and offer mechanical thrombectomy to this patient even after TNK. It should not be withheld on the basis of age, as patients older than age 80 may also benefit from mechanical thrombectomy. Therapeutic nihilism is illustrated here: the appropriate management (in this case mechanical thrombectomy) is not offered due to perceived poor tolerance, inability to recover, and futility based on the patient's age.

Beneficence is the obligation to act for the benefit of the patient and to promote the patient's welfare (ie, offer mechanical thrombectomy). Nonmaleficence is the obligation to do no harm (ie, discuss the risks of mechanical thrombectomy). Patients have autonomy through an informed consent process by which they can learn about the risks and benefits of a procedure so they can make a decision consistent with their values.

Varkey B. Principles of clinical ethics and their application to practice. *Med Princ Pract.* 2021;30(1):17-28.

Sedney C, Kurowski-Burt A, Smith M, et al. Therapeutic nihilism of neurological diseases: a comparative qualitative study. *J Clin Neurosci.* 2019 Nov;69:124-131.

Herpich F, Rincon F. Management of acute ischemic stroke. *Crit Care Med.* 2020 Nov;48(11):1654-1663.

Question

170 ADULT NEUROLOGY

Treatment/Management

This patient has idiopathic glossopharyngeal neuralgia. Secondary causes, including skull-based tumors, have been adequately excluded by MRI. Syncope associated with this syndrome results from activation of the carotid sinus branch of the glossopharyngeal nerve, resulting in bradycardia and hypotension due to peripheral arterial vasodilation. Symptomatic therapy is the same as that used for trigeminal neuralgia.

Gronseth G, Cruccu G, Alksne J, et al. Practice Parameter: The diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review). *Neurology*. 2008 Oct 7;71(15):1183-1190.

Rozen TD. Trigeminal neuralgia and glossopharyngeal neuralgia. *Neurol Clin*. 2004 Feb;22(1):185-206.

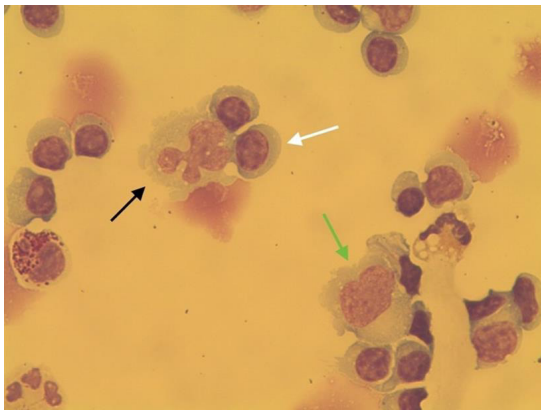
Saper CB. Visceral sensation and visceral sensory disorders. *Continuum Lifelong Learning Neurol*. 2007 Dec;13(6):204-214.

192 ADULT NEUROLOGY

Neuropathology

This patient presents with recurrent aseptic meningitis, which in the absence of drugs or a known autoimmune disease is most typically caused by herpes simplex virus type 2. The black and green arrows on the cytology slide point to irregular monocytes, known as Mollaret cells, which would not be present with any of the other diagnoses listed (cryptococcal meningitis, leptomeningeal carcinomatosis, granulomatosis with polyangiitis, neurosarcoidosis).

Gluck L, Robbins M, Galen B. Mollaret cells in recurrent benign lymphocytic meningitis. *Neurohospitalist*. 2019 Jan;9(1):49-50.



Images reprinted with permission via Creative Commons License from Gluck L, Robbins M, Galen B. Mollaret cells in recurrent benign lymphocytic meningitis. *Neurohospitalist*. 2019 Jan;9(1):49-50.

Question

209 NO SPECIFIED PATIENT AGE**Treatment Management**

This patient's presentation is consistent with paroxysmal hemicrania, a trigeminal autonomic cephalalgia (TAC) characterized by severe, unilateral headaches lasting 2 to 30 minutes, occurring more than five times per day, and accompanied by ipsilateral cranial autonomic symptoms such as conjunctival injection and lacrimation.

A key distinguishing feature of paroxysmal hemicrania and hemicrania continua is an absolute responsiveness to indomethacin, which serves both diagnostic and therapeutic purposes.

In contrast, cluster headache is not an indomethacin-responsive headache disorder. Galcanezumab and verapamil are effective preventive treatment for cluster headache, which is less likely in this case given the brief duration of attacks. Subcutaneous sumatriptan is an effective abortive option for cluster headache, whereas lamotrigine is used as preventive therapy for SUNCT and SUNA, two TACs characterized by even shorter, stabbing attacks.

Burish M. Cluster headache, SUNCT, and SUNA. *Continuum Lifelong Learning Neurol.* 2024 Apr;30(2):391-410.

Question

233 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Clinical Aspects of Disease

The imaging study shown illustrates vascular loops abutting the trigeminal nerve root, which can cause trigeminal neuralgia. Symptoms are described as electrical shocks to the head or face in the distribution of the trigeminal nerve branches, most commonly involving the second (maxillary) and third (mandibular) divisions of the trigeminal nerve.

Lambru G, Zakrzewska J, Matharu M. Trigeminal neuralgia: a practical guide. *Pract Neurol*. 2021 Oct;21(5):392-402.

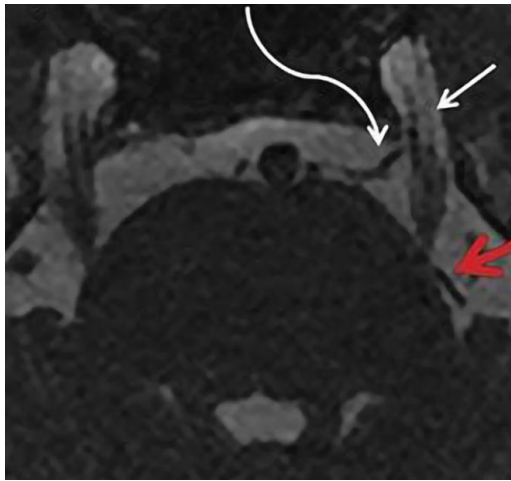


Image credit: Uviyal R, Paliwal VK, Kumar N, et al. Teaching NeurolImages: Amlodipine-responsive trigeminal neuralgia: an alibi for vascular compression theory. *Neurology*. 2017 Jul;89(3):e20.

252 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

Benign paroxysmal vertigo of childhood is often considered a migraine variant or migraine precursor. Episodes are brief (<5 minutes) and not accompanied by any change in consciousness. Patients are normal between episodes.

Arzimanoglou A, O'Hare A, Johnston M, et al (eds). *Aicardi's Diseases of the Nervous System in Childhood*. 4th ed. London: Mac Keith Press; 2018.

Question

264 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

This patient's chronic migraine has been treated with two preventive therapies (topiramate and propranolol) that have had adverse effects. She is eligible for preventive therapies that target calcitonin gene-related peptide such as erenumab or onabotulinumtoxinA.

Amitriptyline and divalproex sodium are not good choices for a patient with a BMI of 30 because of their association with weight gain. Carbamazepine does not have evidence for migraine prevention. Lasmiditan is an acute treatment for migraine that is a 5HT_{1F} receptor agonist.

Ailani J, Burch RC, Robbins MS; Board of Directors of the American Headache Society. The American Headache Society consensus statement: update on integrating new migraine treatments into clinical practice. *Headache*. 2021 Jul;61(7):1021-1039.

293 ADULT NEUROLOGY

CORE KNOWLEDGE

Neurophysiology

The clinical description (wrist pain and tingling paresthesias involving the thumb and index finger, pain that awakens the patient from sleep) is classic for carpal tunnel syndrome. Of the tests listed, median sensory studies are the most sensitive in identifying mild carpal tunnel syndrome. Motor distal latency prolongation and EMG abnormalities in the median territory are seen later in the disease course and indicate more severe nerve compression. The other tests listed pertain to nerves unaffected by carpal tunnel syndrome: ulnar and radial, respectively.

Smith C, Perry A, Kovacs G, et al (eds). *Greenfield's Neuropathology*. 10th ed. Boca Raton, FL: CRC Press; 2024.

Question

306 ADULT NEUROLOGY

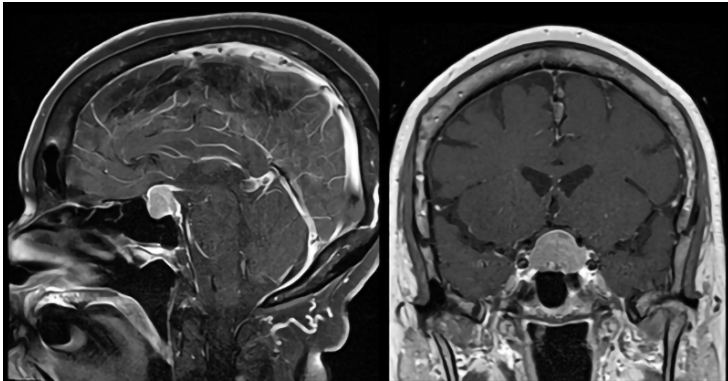
CORE KNOWLEDGE

Neuroimaging|Clinical Aspects of Disease

The images show a large, briskly enhancing sellar mass extending into the suprasellar region, which causes compression of the optic chiasm. No apparent extension from the internal carotid artery is seen to suggest aneurysm.

Tolosa-Hunt syndrome would not have such circumscribed homogenous enhancement. Craniopharyngioma would have more heterogenous enhancement and cystic features. Epidermoid and Rathke cleft cysts typically do not enhance so briskly.

Salzman KL, Jhaveri MD, Osborn AG (eds). Diagnostic Imaging: Brain. 5th ed. Philadelphia: Elsevier; 2025.

**317** ADULT NEUROLOGY

Clinical Aspects of Disease

This patient meets the Budapest criteria for complex regional pain syndrome (CRPS), a pain disorder typically triggered by trauma such as a fracture or surgery. The arms and hands are more likely to be affected than the legs and feet. Diagnostic criteria include the following symptoms: continuing pain disproportionate to the inciting event; at least one sensory symptom such as allodynia; one vasomotor symptom such as a temperature or skin color asymmetry; one sudomotor symptom such as asymmetric edema; and one trophic symptom such as changes in fingernails. Physical examination must show at least one sign in two of these four categories.

(continues)

Question

The consistent pain and history of trauma distinguish CRPS from erythromelalgia. Fabry disease causes an episodic burning pain in the hands and feet without erythema and warmth. Peripheral neuropathies usually do not cause erythema and warmth, and cooling measures typically fail to provide relief. Raynaud syndrome does not follow trauma, and cold temperatures provoke episodes.

Caldito EG, Caldito NG, Kaul S, et al. Erythromelalgia. Part II: differential diagnoses and management. *J Am Acad Dermatol*. 2024 Mar;90(3):465-474.

Abd-Elseyed A, Stark CW, Topoluk N, et al. A brief review of complex regional pain syndrome and current management. *Ann Med*. 2024 Dec;56(1):2334398.

Ferraro MC, O'Connell NE, Sommer C, et al. Complex regional pain syndrome: advances in epidemiology, pathophysiology, diagnosis, and treatment. *Lancet Neurol*. 2024 May;23(5):522-533.

Zahn C, Puga C, Malik A, et al. Painful Raynaud's mimics. *Best Pract Res Clin Rheumatol*. 2024 Mar;38(1):101948.

334 NO SPECIFIED PATIENT AGE**Neuroscience and Mechanism of Disease**

The analgesic effects of pregabalin are related primarily to a decrease in central sensitization and nociceptive transmission to the action on the alpha-2-delta subunit of the calcium channel.

Price R, Smith D, Franklin G, et al. Oral and topical treatment of painful diabetic polyneuropathy: practice guideline update summary: report of the AAN Guideline Subcommittee. *Neurology*. 2022 Jan 4;98(1):31-43. Reaffirmed February 2025.

van Seventer R, Bach FW, Toth CC, et al. Pregabalin in the treatment of post-traumatic peripheral neuropathic pain: a randomized double-trial. *Eur J Neurol*. 2010;17(8):1082-1089.

Question

360 ADULT NEUROLOGY

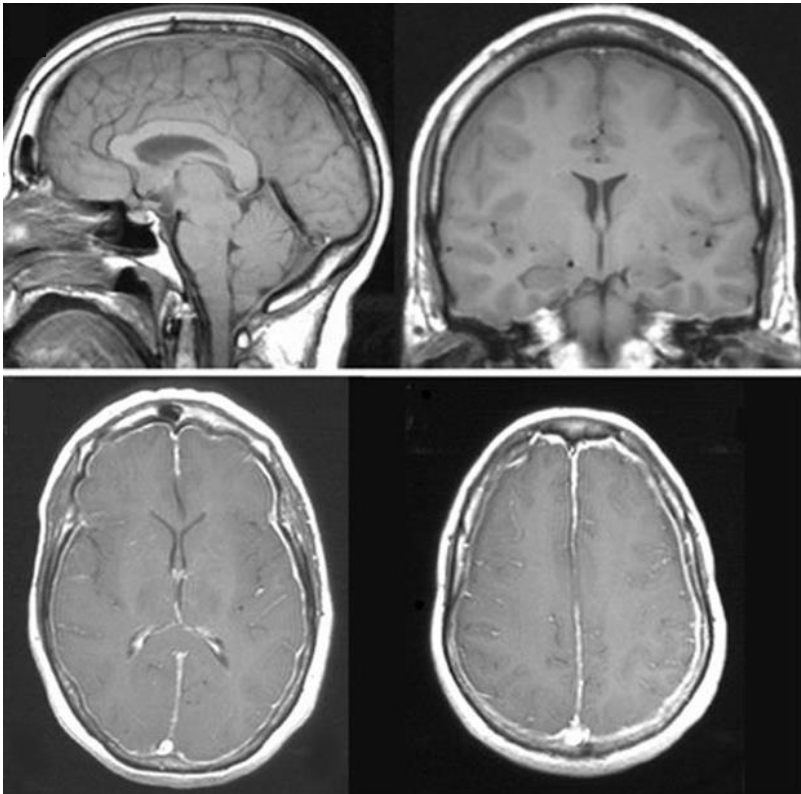
CORE KNOWLEDGE

Neuroimaging|Clinical Aspects of Disease

Gadolinium enhancement of the meningeal structures suggests hypotension, carcinomatosis, or lymphoma. The orthostatic character of the headache, the smooth pachymeningeal enhancement pattern, and the absence of other findings favor intracranial hypotension, also favored by the descended tonsils present in the sagittal image.

Schievink WI, Maya MM, Jean-Pierre S, et al. A classification system of spontaneous spinal CSF leaks. *Neurology*. 2016 Aug;87(7):673-679.

Schievink WI. Spontaneous spinal cerebrospinal fluid leaks and intracranial hypotension. *JAMA*. 2006 May;295(19):2286-2296.



Question

378 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

This patient has a history of migraine with aura but no apparent red flags, so additional diagnostic testing is not warranted. Her attack frequency is not high enough (three episodes in the past year) to consider preventive therapy such as topiramate. Sumatriptan can be continued as it is safe for patients who have migraine with typical aura. Women who have a history of migraine with aura have a slightly elevated relative risk of stroke, which is further increased with use of an estrogen-containing oral contraceptive; therefore, the contraceptive pill should be discontinued.

Pavlovi JM. Headache in women. *Continuum Lifelong Learning Neurol.* 2021 Jun;27(3):686-702.

391 NO SPECIFIED PATIENT AGE**Neuroanatomy**

Patients with cluster headache typically experience weeks or months in which they have frequent attacks, interspersed with periods of attack freedom lasting months or years. While all the structures listed have importance in the pathophysiology of cluster headache, the hypothalamus is the structure whose activation underlies the periodicity of attack periods in which there is repeated activation of the trigeminal-autonomic reflex.

Burish M. Cluster headache, SUNCT, and SUNA. *Continuum Lifelong Learning Neurol.* 2024 Apr;30(2):391-410.

Question

8 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Parkinson disease is a clinical diagnosis, and treatment with a dopamine-blocking agent at the time of diagnosis is an absolute contraindication to confirming the diagnosis. Drug-induced parkinsonism classically presents after several weeks to months of treatment but can occur after chronic use. The best treatment for drug-induced parkinsonism is to discontinue the offending agent, in this case aripiprazole. There is weak evidence to support the use of carbidopa/levodopa, benztropine, and amantadine for treatment of drug-induced parkinsonism. SSRIs are rarely indicated for drug-induced parkinsonism.

Conn H, Jankovic J. Drug-induced parkinsonism: diagnosis and treatment. *Expert Opin Drug Saf.* 2024 Dec;23(12):1503-1513.

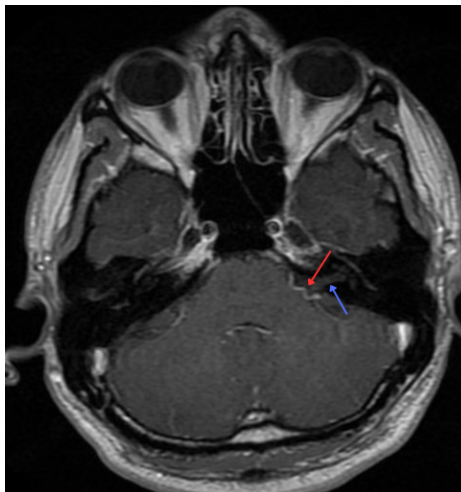
17 ADULT NEUROLOGY

Neuroimaging

This patient's MRI scan shows a small tortuous vessel (red arrow) abutting the proximal left facial nerve (blue arrow), a finding that can be seen in hemifacial spasm. The scan does not show features suggesting demyelination, glioma, or sarcoidosis. There is no apparent pathologic enhancement within the facial nerve, as may occur in Ramsay Hunt syndrome.

Prasad S, Galetta SL. The facial nerve. In: Tasman W, Jaeger EA (eds). *Duane's Ophthalmology*. Philadelphia: Lippincott Williams & Wilkins; 2012, pp 1-44.

Yaltho TC, Jankovic J. The many faces of hemifacial spasm: differential diagnosis of unilateral facial spasms. *Mov. Disord.* 2011 Aug 1;26(9):1582-1592.



Question

23 ADULT NEUROLOGY**Clinical Aspects of Disease**

Progressive supranuclear palsy (PSP) is a neurodegenerative tauopathy that classically presents with early gait impairment with postural instability leading to falls, supranuclear vertical gaze palsy, dysarthria, axial-predominant rigidity with symmetric parkinsonism, and frontal-executive dementia with pseudobulbar palsy (also known as PSP–Richardson syndrome [PSP–RS]). Many additional phenotypes are also seen, including PSP with predominant gait freezing (PSP–PGF), PSP–frontal-behavioral variant, PSP with predominant language and speech dysfunction (PSP–SL), PSP with corticobasal syndrome (PSP–CBS), and PSP–parkinsonism (PSP–P).

Multiple-system atrophy–cerebellar type, vascular parkinsonism, and the postural instability gait disorder subtype of Parkinson disease can present with early gait impairment and falls but not supranuclear gaze palsy. Fragile–X tremor ataxia syndrome (FXTAS) is an X-linked genetic disorder caused by a genetic premutation in FMR1. Classically, FXTAS presents in men older than age 50 and is characterized by gait ataxia, action tremor, parkinsonism, and cognitive impairment. The square wave jerks seen in the video may also be present on examination in these patients, but they will not have a supranuclear gaze palsy.

Adult-onset Niemann–Pick disease type C typically presents with more prominent ataxia on examination but can otherwise be similar to PSP–RS with imbalance and falls, cognitive impairment, dysarthria, and vertical supranuclear palsy. However, these patients do not have the freezing of gait described here.

McFarland NR. Progressive supranuclear palsy and corticobasal syndrome. *Continuum Lifelong Learning Neurol.* 2025 Aug;31(4):1023-1049.

Di Lazzaro V, Marano M, Florio L, et al. Niemann-Pick type C: focus on the adolescent/adult onset form. *Int J Neurosci.* 2016 Nov;126(11):963-971.

27 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroanatomy

The dentatorubrothalamic tract is the pathway through which the cerebellum modulates synergy of movement as part of the corticopontocerebellar functional module of the cerebellum, and its output pathway is through the superior cerebellar peduncle.

Brazis PW, Masdeu JC, Biller J. *Localization in Clinical Neurology.* 8th ed. Philadelphia: Wolters Kluwer Health. 2022.

Question

38 PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Though the symptoms associated with Tourette syndrome frequently improve with time, treatment should be initiated if symptoms cause distress to the patient.

Comprehensive Behavioral Intervention for Tics (CBIT) is more likely to reduce tic severity than psychoeducation and supportive therapy. CBIT is a manualized treatment program consisting of habit reversal training (HRT), relaxation training, and a functional intervention to address situations that sustain or worsen tics. HRT includes building awareness of urges, identifying situations, places, activities, and urges that typically precipitate the behavior, and tolerating urges.

Singer HS. Tics and Tourette syndrome. *Continuum Lifelong Learning Neurol.* 2019 Aug;25(4):936-958.

Pringsheim T, Holler-Managan Y, Okun MS, et al. Comprehensive systematic review summary: treatment of tics in people with Tourette syndrome and chronic tic disorders. *Neurology.* 2019 May;92(19):907-915. Reaffirmed April 2022. Endorsed by the Child Neurology Society and the European Academy of Neurology.

Pringsheim T, Okun MS, Müller-Vahl K, et al. Practice guideline recommendations summary: treatment of tics in people of Tourette syndrome and chronic tic disorders. *Neurology.* 2019 May;92(19):896-906. Reaffirmed April 2022. Endorsed by the Child Neurology Society and the European Academy of Neurology.

45 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

By definition, a tremor is an involuntary, rhythmic, oscillatory movement of a body part. A re-emergent tremor is present at rest, subsides or reduces with a change in limb posture, and then reappears after a delay of a few seconds. This characteristic distinguishes a parkinsonian rest tremor from a rest tremor in essential tremor.

Distractibility is a feature of a nonphysiologic tremor. At onset, a rest tremor in Parkinson disease commonly is unilateral, whereas essential tremor is usually bilateral. A wing-beating tremor is a proximal tremor of the shoulders characteristic of Wilson disease but can be seen in other disorders.

Louis ED. Tremor. *Continuum Lifelong Learning Neurol.* 2019 Aug;25(4):959-975.

Bhatia KP, Bain P, Bajaj N, et al. Consensus statement on the classification of tremors: from the Task Force on Tremor of the International Parkinson and Movement Disorder Society. *Mov Disord.* 2018 Jan;33(1):75-87.

Thenganatt MA, Louis ED. Distinguishing essential tremor from Parkinson's disease: bedside tests and laboratory evaluations. *Expert Rev Neurother.* 2012 Jun;12(6):687-696.

Question

51 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

REM sleep behavior disorder, fatigue, constipation, anosmia, and depression are common premotor features of idiopathic Parkinson disease and other synucleinopathies and can predate the diagnosis by several years. Corticobasal degeneration, progressive supranuclear palsy, and frontotemporal lobar dementia are tauopathies.

Rawls A, Okun MS. Parkinson disease. Continuum Lifelong Learning Neurol. 2025 Aug;31(4):930-955.

Hess C, Okun M. Diagnosing Parkinson disease. Continuum Lifelong Learning Neurol. 2016 Aug;22,(4):1047-1063.

56 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

This patient is experiencing motor fluctuations due to peak-dose dyskinesias associated with use of levodopa. Of the medications listed (amantadine, rasagiline, istradefylline, ropinirole, entacapone), amantadine is the only agent with a demonstrable antidyskinetic effect, sometimes requiring higher doses than for its typical anti-Parkinson effects.

Rawls A, Okun MS. Parkinson disease. Continuum Lifelong Learning Neurol. 2025 Aug;31(4):930-955.

57 ADULT NEUROLOGY

Contemporary Issues

Rescinding a patient's permission to drive is a challenging and necessary step to keep patients and the community safe. In this case, the patient has dementia that will only worsen with time. He also has demonstrated executive dysfunction on formal testing, as well as a Clinical Dementia Rating (CDR) Scale score of 2, which is considered in the moderate dementia range. CDR score is correlated with driving risk with level A evidence, exceeding driver self-report, passenger report, neuropsychological testing or Mini-Mental State Examination results, and accident history.

Although further testing is not necessary in this case, supportive evidence with a driving test or occupational therapy evaluation may help some patients with buy-in or in the event of uncertainty. Every state has its own reporting policies; it is important for neurologists to know their state's rules and discuss with the patient.

Iverson DJ, Gronseth GS, Reger MA, et al. Practice parameter update: evaluation and management of driving risk in dementia: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2010 Apr 12;74(16):1316-1324. Reaffirmed February 2025.

Question

67 PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Benign paroxysmal torticollis is classified as a migraine equivalent by the International Headache Society. Some children may eventually develop migraine with aura.

Paroxysmal kinesigenic dyskinesia is associated with *PRRT2* pathogenic variants and is characterized by dyskinetic movements of the trunk or limbs triggered by voluntary movement. Spasmus nutans has ocular oscillations along with head tilt, and dopa-responsive dystonia usually begins after age 5 years, typically in the lower extremities.

Ashwal S, Pearl PL, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 7th ed. Philadelphia: Elsevier; 2025.

75 ADULT NEUROLOGY

Treatment/Management

This patient has a Parkinson dementia syndrome, either dementia with Lewy bodies (DLB) or Parkinson disease dementia, but more likely the former given the reported time course over the past year.

Rivastigmine inhibits acetylcholinesterase and thus augments cholinergic activity and can decrease fluctuations in sensorium and hallucinations in DLB that is a cholinergic-deficient state. Patients with DLB are often pathologically sensitive to standard neuroleptics (haloperidol), which can cause severe parkinsonism and neuroleptic malignant syndrome. This is an absolute contraindication. Over-the-counter antihistamine and prescription anticholinergic agents (nortriptyline, trihexyphenidyl) should be avoided. Memantine has not been shown to be beneficial for this indication.

Patel B. Dementia with Lewy bodies. Continuum Lifelong Learning Neurol. 2025 Aug;31(4):956-978.

Liepelt I, Maetzler W, Blaicher HP, et al. Treatment of dementia in parkinsonian syndromes with cholinesterase inhibitors. Dement Geriatr Cogn Disord. 2007;23(6):351-367.

Question

94 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuropathology

Corticobasal syndrome (CBS) is a tauopathy that classically presents with hemibody dystonia and parkinsonism, early cognitive impairment with cortical signs, and apraxia. MRI scans show asymmetric frontoparietal atrophy. Multiple pathologies are associated with this presentation, but the classic pathologic change seen in corticobasal degeneration (CBD) is accumulation of four-repeat hyperphosphorylated tau within neurons and glial cells with astrocytic plaques.

Other pathologies, including Alzheimer disease (extracellular beta-amyloid and intraneuronal neurofibrillary tangles), progressive supranuclear palsy (similar pathology to CBD with astrocytic tufts instead of plaques), and FTLD-tau (3-repeat hyperphosphorylated MAPT) can be seen with CBS.

Cortical intraneuronal alpha-synuclein inclusions (Lewy bodies) are seen in Lewy body dementia (LBD), which presents with significant cognitive impairment within the first year of developing motor parkinsonism. However, the MRI findings and prominent apraxia seen in this patient are inconsistent with LBD. Spongiform degeneration, neuronal loss, and astrocytic gliosis are seen in Creutzfeldt-Jakob disease (CJD). Seventy percent of people with CJD die within 1 year.

Olfati N, Akhoundi FH, Litvan I. Atypical parkinsonian disorders. *Neurol Clin.* 2025 May;43(2):249-277.

Hall WA, Masood W. Cruetzfeldt-Jakob Disease. [Updated 2005 Jun 23]. In: StatPearls [Internet]. Treasure Island (FL):StatPearls Publishing; 2025 Jan-.

Question

103 PEDIATRIC NEUROLOGY**Treatment/Management**

If medication is considered as part of the management plan for tics, first-line therapies include cognitive behavioral therapies, alpha-agonists (guanfacine and clonidine), and topiramate. These are considered first line because they have fewer side effects. Second tier medications include antipsychotic medications and vesicular monoamine transporter-2 inhibitors such as tetrabenazine. Although haloperidol could be considered for severe tics, it would not be used first given its extensive side effect profile.

Singer HS. Tics and Tourette syndrome. *Continuum Lifelong Learning Neurol.* 2019 Aug;25(4):936-958.

Pringsheim T, Holler-Managan Y, Okun MS, et al. Comprehensive systematic review summary: treatment of tics in people with Tourette syndrome and chronic tic disorders. *Neurology.* 2019 May;92(19):907-915. Reaffirmed April 2022. Endorsed by the Child Neurology Society and the European Academy of Neurology.

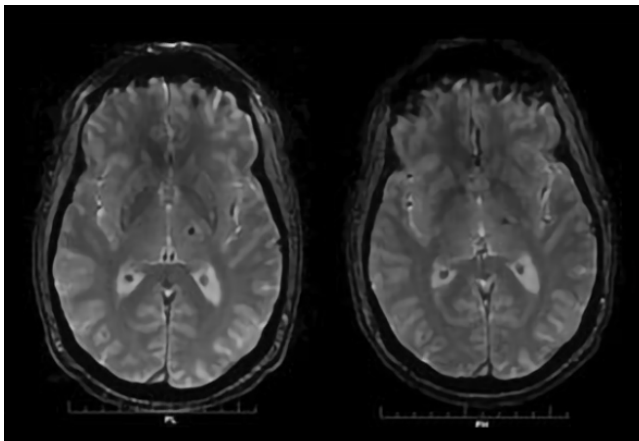
Pringsheim T, Okun MS, Müller-Vahl K, et al. Practice guideline recommendations summary: treatment of tics in people of Tourette syndrome and chronic tic disorders. *Neurology.* 2019 May;92(19):896-906. Reaffirmed April 2022. Endorsed by the Child Neurology Society and the European Academy of Neurology.

111 ADULT NEUROLOGY**Neuroanatomy**

Focused ultrasound involves triangulating ultrasound to lesion a small target in the brain. It is used in essential tremor, and the target (as shown) is the ventral intermediate nucleus of the thalamus.

Louis E. Tremor. *Continuum Lifelong Learning Neurol.* 2019 Aug; 25(4):959-975.

Image Reference: Fasano A, Llinas M, Munhoz RP, et al. MRI-guided focused ultrasound thalamotomy in non-ET tremor syndromes. *Neurology.* 2017 Aug 22;89(8):771-775.



Question

121 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

Hyposmia is found on formal testing (UPSIT or Sniffin Stick tests) in almost all (90%) patients with idiopathic Parkinson disease and reported by about 70% of patients. Normal olfactory function should raise a question about a Parkinson disease diagnosis. The other features listed (limb apraxia as seen in corticobasal syndrome, supranuclear downgaze palsy as seen in progressive supra nuclear palsy, wide-based gait as seen in multiple-system atrophy–cerebellar type, square wave jerks) suggest an atypical parkinsonian syndrome.

Tolosa E, Garrido A, Scholz SW, et al. Challenges in the diagnosis of Parkinson's disease. *Lancet Neurol*. 2021 May;20(5):385-397.

132 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroscience and Mechanism of Disease

Several dopamine-related imaging agents have been developed to assess the integrity of dopaminergic neurons using SPECT or PET. The first FDA-approved diagnostic imaging agent for differentiating Parkinson disease from essential tremor is the DaT-SPECT scan, which binds to the dopamine transporter, the reduction of which correlates with the loss of presynaptic dopamine. With PET imaging, using either ¹¹F dopa or ¹¹C dopa, dopa decarboxylase activity can be seen in images. Similarly, ¹¹C DTBZ with PET imaging can be used to assess the activity of the vesicular monoamine transporter-2.

Pringsheim T, Day GS, Smith DB, et al. Dopaminergic therapy for motor symptoms in early Parkinson disease practice guideline summary: a report of the AAN Guideline Subcommittee. *Neurology*. 2021 Nov;97(20):942-957. Reaffirmed February 2025.

Question

145 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

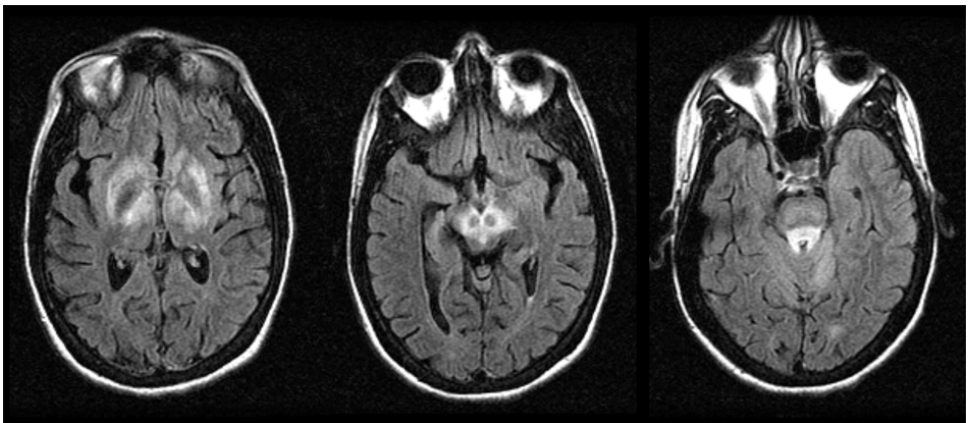
Wilson disease results from accumulation of copper due to a deficiency of ceruloplasmin, its serum transport protein. This disease, also known as hepatolenticular degeneration, affects the liver, brain, and other tissues.

The most common radiographic finding is T2 hyperintensity in the putamen, but it also can be seen in the caudate, thalamus, and brainstem tegmentum. T2 hyperintensity in the tegmentum of the midbrain surrounding the normal red nuclei and substantia nigra can result in the face of the giant panda sign.

Adrenoleukodystrophy typically affects the peritrigonal white matter, not the basal ganglia. Wernicke encephalopathy affects specific sites that differ from what is seen here. Canavan disease is a macrocephalic leukodystrophy that diffusely affects white matter, including subcortical U-fibers. Krabbe disease is a diffuse leukodystrophy that initially spares the subcortical U-fibers, not the distribution seen in this case.

Roberts EA, Schilsky ML. Current and emerging issues in Wilson's disease. *N Engl J Med*. 2023 Sep 7;389(10):922-938.

Hegde AN, Mohan S, Lath N, Lim CCT. Differential diagnosis for bilateral abnormalities of the basal ganglia and thalamus. *Radiographics*. 2011 Jan-Feb;31(1):5-30.



Question

159 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

New treatment guidelines for restless legs syndrome (RLS) published in 2025 recommend against standard use of dopamine agonists due to the concern for augmentation (ie, worsening of symptoms over time) as a long-term side effect. Gabapentin and pregabalin are recommended for treatment. Opiates may also be used but are not first line due to their addictive potential.

Winkelman J, Berkowski JA, DelRosso LM, et al. Treatment of restless legs syndrome and periodic limb movement disorder: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2025 Jan;21(1):137-152.

168 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Diagnostic Procedures

Dopamine transporter (DaT-SPECT) imaging studies can be ordered to help distinguish essential tremor from Parkinson disease. Prior to undergoing this study, patients must discontinue any medications that can impact dopamine transport binding of radiotracers, including bupropion, amphetamines and other stimulants, and haloperidol.

Several medications for Parkinson disease, including carbidopa/levodopa, pramipexole, and amantadine, do not need to be discontinued as they do not impact DaT binding, nor do donepezil or primumdone.

Chahid Y, Sheikh ZH, Mitropoulos M, et al. A systematic review of the potential effects of medications and drugs of abuse on dopamine transporter imaging using [123I]I-FP-CIT SPECT in routine practice. *Eur J Nucl Med Mol Imaging*. 2023 Jun;50(7):1974-1987.

177 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuropathology

The pathology of idiopathic Parkinson disease and dementia with Lewy bodies is characterized by intraneuronal aggregates of alpha-synuclein. The presence of intraneuronal neurofibrillary tangles is characteristic of Alzheimer disease. Neurofibrillary tangles are formed by aggregation and accumulation of phosphorylated microtubule-associated tau protein. This process is believed to impair microtubule-mediated axonal transport and contribute to neuronal degeneration. Tau pathology (tauopathy) is not specific for Alzheimer disease and is detected in frontotemporal dementia, corticobasal degeneration, and progressive supranuclear palsy.

Patel BR. Dementia with Lewy bodies. *Continuum Lifelong Learning Neurol*. 2025 Aug;31(4):956-978.

Question

189 ADULT NEUROLOGY**Neuroimaging**

This patient's abnormal movements (irregular, involuntary, large-amplitude movements of the proximal right arm and leg) are most consistent with hemiballismus, a disorder that typically results from ischemia in the subthalamic nucleus.

A lesion in the internal capsule would be more likely to result in a pure motor syndrome or hemiparesis. A stroke in the ventral pons results in hemiparesis and cranial nerve findings, whereas a stroke in the caudate would present with cognitive and language deficits. Injury to the suprachiasmatic nucleus would manifest as difficulty maintaining sleep-wake cycles.

Cabrero FR, DeJesus O. Hemiballismus. [Updated 2022 Jun 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.

199 NO SPECIFIED PATIENT AGE**Treatment/Management**

Post-anoxic action myoclonus, also known as Lance-Adams syndrome, responds well to treatment with valproic acid, levetiracetam and piracetam, and benzodiazepines (clonazepam). Patients often require multiple agents and long-term treatment. Functional outcomes 12 months after arrest are good in more than half (67%) of patients with this diagnosis.

Xeros H, Sakusic A, Fugate JE, et al. Treatment, diagnostic approach, and long-term outcomes of Lance-Adams syndrome. *Neurocrit Care*. 2026 Feb;44(1):162-175.

Question

201 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

This patient meets the diagnostic criteria for paroxysmal kinesigenic dyskinesia (PKD), which includes the following features: 1) a kinesigenic trigger for the episodes; 2) episode duration <1 minute; 3) no loss of consciousness or pain during episodes; 4) exclusion of other organic diseases and normal neurologic exam; 5) response to antiseizure medications such as phenytoin or carbamazepine; and 6) age at onset between 1 and 20 years. The most common cause of PKD is a pathogenic variant in *PRRT2*, which is linked to self-limited (familial) infantile epilepsy.

The trigger for paroxysmal exercise-induced dyskinesia (PED) is several minutes of exercise, with episode duration between 5 and 30 minutes. PED is a symptom of glucose transporter 1 (Glut1) deficiency syndrome. Autosomal dominant GTP cyclohydrolase deficiency, one cause of dopa-responsive dystonia, typically is asymmetric, involves a leg as an action dystonia initially, and shows diurnal variation. Tic disorder is not triggered by sudden movements with episodes of long duration. Initially, tics usually involve the face, head, or neck.

Landolfi A, Barone P, Erro R. The spectrum of *PRRT2*-associated disorders: update on clinical features and pathophysiology. *Front Neurol*. 2021 Mar 4;12:629747.

Salles PA, Teran-Jimenez M, Vidal-Santoro A, et al. Recognizing atypical dopa-responsive dystonia and its mimics. *Neurol Clin Pract*. 2021 Dec;11(6):e876-e884.

Ueda K, Black KJ. A comprehensive review of tic disorders in children. *J Clin Med*. 2021 Jun 3;10(11):2479.

Silveira-Moriyama L, Kovac S, Kurian MA, et al. Phenotypes, genotypes, and the management of paroxysmal movement disorders. *Dev Med Child Neurol*. 2018 Jun;60(6):559-565.

Wijemanne S, Jankovic J. Dopa-responsive dystonia--clinical and genetic heterogeneity. *Nat Rev Neurol*. 2015 Jul;11(7):414-424.

Question

208 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Diagnostic Procedures

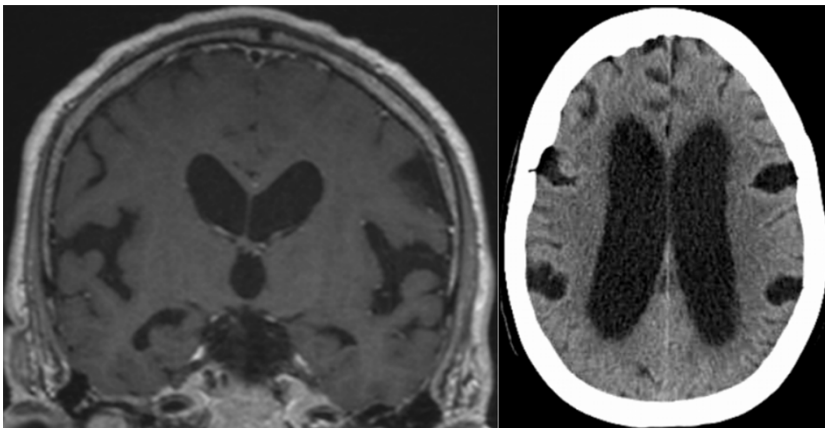
Normal pressure hydrocephalus (NPH) is a slowly evolving neurologic disease, most often seen in elderly persons. NPH is associated with excessive CSF and expansion of the ventricles. Symptoms begin with gait dysfunction, followed by increased urinary frequency and urgency, urinary incontinence, and eventually dementia.

Disproportionally enlarged subarachnoid space hydrocephalus (DESH) on imaging studies includes enlarged CSF spaces in the sylvian and other fissures of the brain coupled with tightening of the sulci at the convexity; these findings are seen on this patient's imaging studies. The presence of these two radiologic characteristics together helps differentiate it from ex vacuo dilation of the ventricles due to atrophy.

A slow, shuffling gait with freezing is characteristic of NPH, but arm movements are preserved, unlike with Parkinson disease. Cognitive decline, either preceding or developing concurrently with gait impairment, raises concern for an alternative diagnosis. Visual hallucinations, dysphagia, and ophthalmoparesis are not characteristic of NPH.

Graff-Radford NR, Jones DT. Normal pressure hydrocephalus. *Continuum Lifelong Learning Neurol.* 2019 Feb;25(1):165-186.

Image credit: Graff-Radford NR, Jones DT. Normal pressure hydrocephalus. *Continuum Lifelong Learning Neurol.* 2019 Feb;25(1):165-186.



Question

219 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Postpump chorea is a rare neurologic syndrome characterized by acute onset of choreiform movements 1 to 2 weeks after cardiopulmonary bypass. This syndrome has been observed in both adults and children. In children, existing developmental delay and/or disability may also be a risk factor.

Etomidate has not been associated with chorea, nor is it observed after blood transfusion, except in rare cases when polycythemia is caused by the transfusion. Myoclonus may be seen with opioids, but chorea is not commonly reported. Neck traction from surgical positioning can cause postoperative peripheral nerve palsies/plexopathies but would not lead to chorea.

Ahn JH, Song J, Choi I, et al. Risk factors and prognosis of adult-onset post-pump chorea. *J Neurol Sci.* 2021 Mar 15;422:117328.

Park KW, Choi N, Ryu HS, et al. Post-pump chorea and progressive supranuclear palsy-like syndrome following major cardiac surgery. *Mov Disord Clin Pract.* 2019 Dec 11;7(1):78-82.

229 PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Ataxia-telangiectasia is an autosomal recessive disorder characterized by ataxia, oculocutaneous telangiectasias, and immunodeficiency. Choreoathetoid movements are seen, even at an early age.

The other physical findings listed are not associated with ataxia-telangiectasia but with other disorders without predominant choreoathetosis. Adenoma sebaceum is seen in tuberous sclerosis. Facial angiomas can be seen independently or in the setting of Sturge-Weber syndrome. Multiple café-au-lait spots are associated with neurofibromatosis types 1 and 2. Retinal angiomas can be seen in von Hippel-Landau syndrome.

Kurian MA, Dale RC. Movement disorders presenting in childhood. *Continuum Lifelong Learning Neurol.* 2016 Aug;22:1159-1185.

Question #

236 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Diagnostic Procedures

Urinary dysfunction related to overactive bladder is seen in both multiple-system atrophy (MSA) and Parkinson disease (PD), but patients with MSA often have neurogenic bladder and therefore an increased postvoid residual. In fact, this finding is listed as a core feature within the diagnostic criteria for MSA.

DaTscan and skin biopsy can be positive in both MSA and PD. Both loss of substantia nigra pigmentation and reduced uptake on MIBG cardiac scan are seen in Parkinson disease.

Wenning GK, Stankovic I, Vignatelli L, et al. The Movement Disorder Society Criteria for the diagnosis of multiple system atrophy. *Mov Disord*. 2022 Jun;37(6):1131-1148.

245 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Neuroanatomy

This patient demonstrates mild gait ataxia, characterized by an intermittently wide-based gait and a tendency to list to the side. It should be noted that it is common for patients with cerebellar ataxia to have a base that is variable, at times narrow and at times wide. This patient has ataxia with oculomotor apraxia type 2, a genetic disorder. He does not demonstrate a cautious, scissoring/spastic, or parkinsonian gait as might be seen in disorders affecting other areas of the brain.

Kuo SH. Ataxia. *Continuum Lifelong Learning Neurol*. 2019 Aug;25(4):1036-1054.

257 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Tardive dyskinesia results from chronic treatment with dopamine D2 receptor blockers. These include the class of high-potency neuroleptics as well as antiemetic agents such as prochlorperazine or metoclopramide. Aripiprazole has a lower risk of causing tardive dyskinesia compared to first-generation antipsychotics, but the risk is still present.

Selfani K, Soland VL, Chouinard S, Huot P. Movement disorders induced by the "atypical" antipsychotic aripiprazole. *Neurologist*. 2017 Jan;22(1):24-28.

Carbon M, Kane JM, Leucht S, Correll CU. Tardive dyskinesia risk with first- and second-generation antipsychotics in comparative randomized controlled trials: a meta-analysis. *World Psychiatry*. 2018 Oct;17(3):330-340.

Question

268 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient's clinical presentation is consistent with cervical dystonia, a disorder characterized by abnormal posturing of the neck with associated neck pain and tremor. Symptoms typically progress over time. Positioning the head away from the side of flexion can worsen the tremor.

Essential tremor causes an action tremor in the hands, and although the tremor can involve the neck, it typically does not cause abnormal posturing or neck pain. Cranial nerve IV palsy can cause diplopia, and patients may have a compensatory head tilt, but should not have associated tremor.

Richardson SP. Dystonia. *Continuum Lifelong Learning Neurol.* 2025 Aug;31(4):1050-1065.

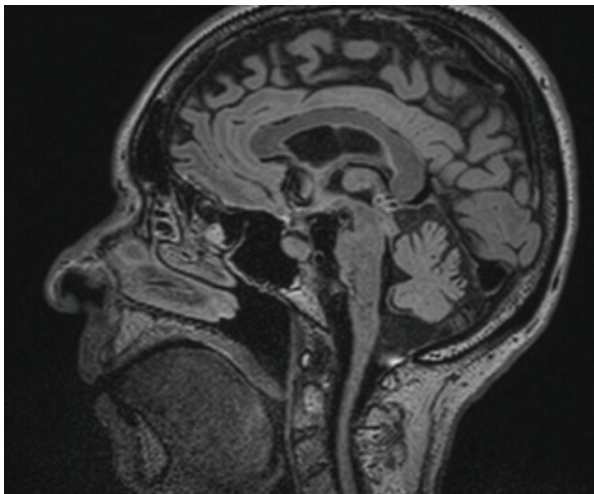
277 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuropathology

The MRI scan shows pontine and cerebellar atrophy, findings consistent with multiple-system atrophy. In multiple-system atrophy, glia (especially oligodendroglia) exhibit cytoplasmic, flame-shaped, silver-positive inclusions that are also immunoreactive for p62, ubiquitin, and alpha-synuclein.

Smith C, Perry A, Kovacs G, et al (eds). *Greenfield's Neuropathology*. 10th ed. Boca Raton, FL: CRC Press; 2024.



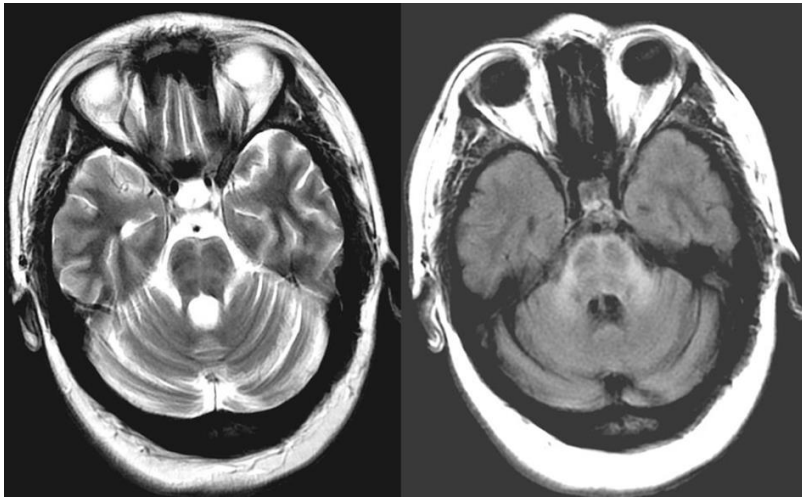
Question

282 ADULT NEUROLOGY

Neuroimaging

This patient's MRI findings demonstrate the "hot cross buns" sign in the pons and hyperintensity in the cerebellar peduncles, findings most suggestive of multiple-system atrophy. The other disorders listed (corticobasal degeneration, vitamin B12 deficiency, spinocerebellar ataxia type 3, progressive supranuclear palsy) typically would not have these characteristic MRI findings.

Salzman KL, Jhaveri MD, Osborn AG (eds). Diagnostic Imaging: Brain. 5th ed. Philadelphia: Elsevier; 2025.

**287** NO SPECIFIED PATIENT AGE

Treatment/Management

Dopa-responsive dystonia (Segawa disease) is a young-onset dystonia syndrome, often beginning in the legs with diurnal fluctuation. This syndrome is often attributable to a pathogenic variant in *GCH1* and is so named due to the robust response to levodopa. Therefore, a levodopa trial is recommended for all patients who present with dystonia at a young age, even though it is not the underlying diagnosis in most pediatric patients with dystonia.

Jinnah HA. The dystonias. Continuum Lifelong Learning Neurol. 2019 Aug;25(4):976-1000.

Question

297 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

This patient's presentation is consistent with Sydenham chorea, the most common acquired chorea in children. Sydenham chorea is an autoimmune response to group A streptococcal infection which occurs, on average, 8 weeks prior to the onset of chorea. In addition to chorea, significant mood lability and other psychiatric symptoms such as obsessive-compulsive disorder are seen. Exam is notable for hypotonia. The diagnosis is clinical. Evidence of prior *Streptococcus* infection is supportive but not required for diagnosis.

Antibiotics are required to prevent recurrence and minimize the risk of rheumatic heart disease. The other treatment approaches listed, specifically antipsychotic or antiseizure medications and immunomodulatory therapies, are directed at symptoms. There are only limited data to support these treatments.

Orsini A, Foiadelli T, Magistrali M, et al. A nationwide study on Sydenham's chorea: clinical features, treatment and prognostic factors. *Eur J Paediatr Neurol*. 2022 Jan;36:1-6.

312 NO SPECIFIED PATIENT AGE**Treatment/Management**

Acute dystonic reactions are often observed after treatment with potent dopamine D2 receptor antagonists, including metoclopramide. Cervical and limb dystonia are the most common. Laryngeal dystonia may be a life-threatening form of dystonic reaction in these patients. Anticholinergic medications, including diphenhydramine, are the most appropriate treatment.

Gaebler JA, Daniels DJ. Dystonic reactions. [Updated 2025 Jan 16]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-.

Question

322 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

Anti-IgLON5 disease, first reported in 2014, is characterized by sleep disorders (100%) such as strider, apnea, and parasomnias, bulbar dysfunction (91%), gait difficulty (73%), ocular motility disorder (59%), cognitive impairment (41%), and chorea (32%). Association with the HLA.DRB1*10:01 and HLA-DQB1*05:01 genotypes has been described. Clinically, anti-IgLON5 disease can mimic many neurodegenerative disorders but progresses more rapidly.

The antibody is believed to disturb the interaction between IgLON5 and the internal cytoskeletal network, leading to neuronal tau accumulation (predominantly in the hypothalamus and brainstem tegmentum) and ultimately neurodegeneration. Suggested treatments include corticosteroids, IVIg, rituximab, and mycophenolate.

Yi-ZongHeng Z, You N, Yi-Ning, et al. Anti-IgLON5 disease: a novel topic beyond neuroimmunology. *Neurol Regen Res*. 2023 May;18(5):1017-1022.

Gaig C, Iranzo A, Cajochen C, et al. Characterization of the sleep disorder of anti-IgLON5 disease. *Sleep*. 2019 Sep 6;42(9):zsz133.

Gaig C, Graus F, Compta Y, et al. Clinical manifestations of the anti-IgLON5 disease. *Neurology*. 2017 May 2;88(18):1736-1743.

329 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Clinical Aspects of Disease**

This patient most likely has Whipple disease, a rare multisystem disorder secondary to infection by *Tropheryma whipplei*, a Gram-positive, non-acid-fast, periodic acid-Schiff (PAS) positive bacillus. Oculomasticatory myorhythmia, a repetitive and rhythmic contraction of ocular and oromandibular muscles, is pathognomonic of Whipple disease.

Celiac disease presents with gastrointestinal complaints either in childhood or adulthood, and the principal neurologic manifestation is ataxia. Progressive supranuclear palsy and multiple-system atrophy develop in a more subacute to chronic manner with other prominent features. Creutzfeldt-Jakob disease usually does not present with prominent gastrointestinal features.

Eggenberger ER. Nystagmus and other abnormal eye movements. *Continuum Lifelong Learning Neurol*. 2009 Aug;15(4):200-212.

Question

337 PEDIATRIC NEUROLOGY**Treatment/Management**

This patient's episodes are consistent with gratification phenomenon, a common condition (previously called infantile masturbation) that starts between ages 3 months and 3 years; it occurs more often in girls. Episodes typically occur when a child is seated with something between the legs such as in a car seat or highchair. Children maintain awareness. Episodes are interruptible, particularly if the child is taken out of the seated position.

When this benign condition is not recognized, it can be mistaken for dystonia or seizures, and unnecessary workup can be ordered. With this characteristic history, normal exam, and development, particularly with a video supportive of the diagnosis, no further evaluation is needed for this patient. Care must be taken in explaining the phenomenon to parents, with emphasis on this being a normal and common behavior that resolves with time and for which no intervention is typically indicated.

Yang ML, Fullwood E, Goldstein J, et al. Masturbation in infancy and early childhood presenting as a movement disorder: 12 cases and a review of the literature. *Pediatrics*. 2005 Dec;116(6):1427-1432.

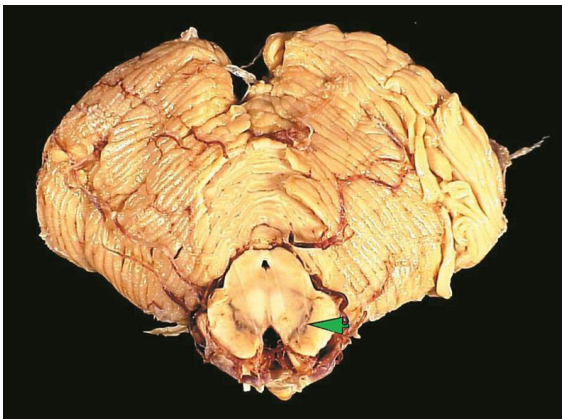
345 ADULT NEUROLOGY

CORE KNOWLEDGE

Neuropathology

The arrow is pointing to the substantia nigra, which normally functions to facilitate voluntary motor activity originating in the prefrontal and motor cortex, ipsilateral to the substantia nigra. Damage to one substantia nigra results in hemiparkinsonism. Because the upper motor neurons of the motor strip are the motor output elements, and these cross at the medullary decussation, the hemiparkinsonism resulting from a unilateral substantia nigra lesion is contralateral to the lesion.

Blumenfeld H. *Neuroanatomy Through Clinical Cases*. 3rd ed. Sunderland: Sinauer Associates; 2021.



Question

352 PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

This patient has glucose transporter type 1 deficiency syndrome (Glut1DS), an autosomal dominant disorder caused by a pathogenic *SLC2A1* mutation that leads to impaired glucose transport to the brain. Clinical manifestations include movement disorders (including ataxia), epilepsy, and mild to severe intellectual disability. CSF evaluation reveals low glucose levels (hypoglycorrachia) in the setting of normoglycemia.

First-line treatment is a ketogenic diet, which provides the developing brain with an alternate fuel source. As this 3-year-old patient is noted to have good seizure control on levetiracetam, adjustments to his maintenance antiseizure medication regimen are not necessary at this time. There are no available antisense oligonucleotide or stem cell therapies for Glut1DS. Gene therapy using adeno-associated virus vectors is being investigated as a potential future treatment.

Klepper J, Akman C, Armeno M, et al. Glut1 deficiency syndrome (Glut1DS): state of the art in 2020 and recommendations of the International Glut1DS Study Group. *Epilepsia Open*. 2020 Aug 13;5(3):354-365.

362 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neurophysiology

Orthostatic tremor is characterized by a very fast (14- to 18-Hz) tremor in the leg muscles on standing still that is relieved with walking or sitting. Patients may report unsteadiness (ie, a sensation they will fall) on standing but no tremor. Likewise, a tremor may not be visible on examination but sometimes can be felt or auscultated.

Babeliowsky WA, Woodward K, Swinnen B, et al. Identifying the diagnostic challenges and indicators of orthostatic tremor: patient perspectives. *Mov Disord Clin Pract*. 2025 Aug;12(8):1124-1131.

Question

371 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

This patient has palatal tremor (formerly known as palatal myoclonus), a clinical finding that occurs following disruption of the Mollaret triangle. The triangle consists of the dentate nucleus, red nucleus, central tegmental tract, and inferior olivary nucleus.

The dorsal motor vagus nucleus does not directly control the pharynx. Rather, it primarily sends parasympathetic signals to the heart and gastrointestinal tract. Motor control of the pharynx comes from the nucleus ambiguus, which sends motor fibers to the muscles of the soft palate, pharynx, and larynx. The nucleus tractus solitarius receives sensory information from the pharynx.

Primiano G, Zanni G, Nardella M, et al. Teaching Video NeurolImages: palatal tremor associated with SPG7 variants. *Neurology*. 2020 May 12;94(19):e2074-e2075.

Aladdin Y, Scozzafava J, Muayqil T, et al. Pearls & oysters: oculopalatal tremor with one-and-a-half syndrome after pontine hemorrhage. *Neurology*. 2008 Oct 14;71(16):e39-e41.

Video credit: Primiano G, Zanni G, Nardella M, et al. Teaching Video NeurolImages: palatal tremor associated with SPG7 variants. *Neurology*. 2020 May 12;94(19):e2074-e2075.

382 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Diagnostic Procedures

Tissue biopsy can assess for alpha-synuclein in the skin of patients with symptoms of parkinsonism. As progressive supranuclear palsy is a tauopathy and not a synucleinopathy, skin biopsy would be negative.

DaTscan does not differentiate between the two because it can be abnormal in both disorders. Amyloid PET is part of the evaluation of Alzheimer disease, but amyloid protein accumulation is not a pathologic component of either Parkinson disease or progressive supranuclear palsy. Postvoid residual is sometimes used to assess for autonomic dysfunction related to multiple-system atrophy compared to Parkinson disease.

Pathogenic variants in *LRRK2* may be found in patients with Parkinson disease. Interestingly, these patients sometimes have alpha-synuclein pathology and sometimes tau pathology. *LRRK2* has incomplete penetrance and thus would not be particularly helpful to differentiate between the two.

Gibbons CH, Levine T, Adler C, et al. Skin biopsy detection of phosphorylated α -synuclein in patients with synucleinopathies. *JAMA*. 2024 Apr 16;331(15):1298-1306.

Question

392 NO SPECIFIED PATIENT AGE**Neuroscience and Mechanism of Disease**

Botulinum neurotoxin (BoNT) is a microbial protein that exists in seven serotypes, designated A through G. Although the individual serotypes are immunologically distinct, all members of the group possess similar subunit structures, act on the same target organs, and produce similar functional outcomes. Each molecule is typically released from bacteria as part of a noncovalent complex with other proteins.

BoNT is an enzyme that acts in the cytosol of nerve endings to cleave three polypeptides that govern exocytosis. Serotypes A and E cleave synaptosomal-associated protein (SNAP)-25, serotypes B, D, F, and G cleave vesicle-associated membrane protein (VAMP), and serotype C cleaves both syntaxin and SNAP-25.^{3,4}

The ability of BoNT to block acetylcholine release at neuromuscular junctions accounts for its therapeutic action to relieve dystonia, spasticity, and related disorders. BoNT has additional therapeutic benefits, not necessarily related to neuromuscular transmission, including blockade of acetylcholine release at autonomic nerve endings and blockade of transmitter release at peripheral nerve endings that use mediators other than acetylcholine.

Berkowitz AL. Tetanus, botulism, and diphtheria. *Continuum Lifelong Learning Neurol.* 2018 Oct;24(5):1459-1488.

Question

6

ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroimaging

The antineutrophilic cytoplasmic antibody (ANCA)-associated vasculitides are a group of disorders characterized by small vessel vasculitis with pathogenic ANCA production. Diagnoses include granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis.

Neurologic involvement is seen in up to 70% of patients, with the peripheral nervous system primarily affected. CNS involvement is seen in <15% of patients, but principally in those with granulomatosis with polyangiitis or microscopic polyangiitis and frequently manifesting as relapsing meningitis.

As with most systemic vasculitides, systemic signs and symptoms typically develop with or precede the onset of neurologic symptoms. Common systemic manifestations include elevated inflammatory markers, fever, nasal crusting, recurrent purulent/bloody sinusitis, nasal ulcers, otitis media, saddle nose deformity, tracheobronchial stenosis, interstitial lung disease, glomerulonephritis, episcleritis, uveitis, and retro-orbital masses.

MRI scans can show pachymeningeal enhancement, with or without leptomeningeal involvement. CSF leak resulting in CSF rhinorrhea indicates a connection between the intrathecal compartment and the nasal cavity and is a risk for bacterial meningitis.

(continues)

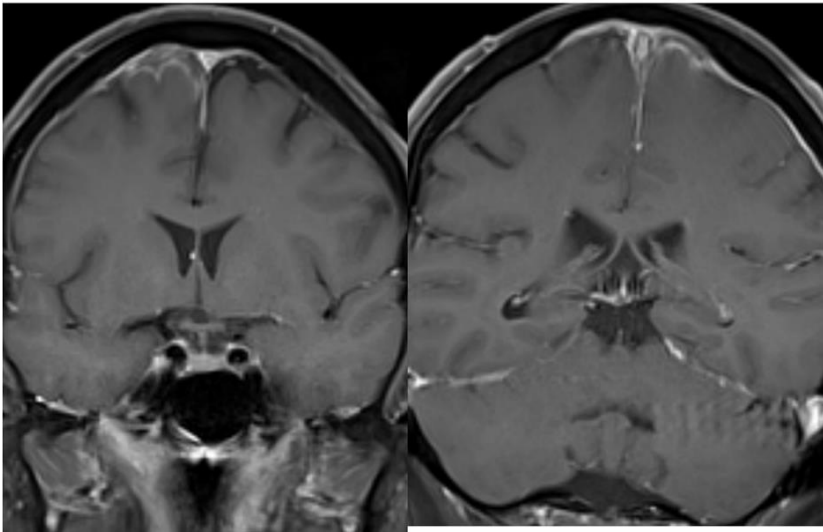
Question

Spontaneous resolution without a course of antimicrobials, normal CSF profile, and absent fevers argues against bacterial or fungal meningitis. Similarly, next-generation metagenomic sequencing or (1,3)- β -d-glucan, a type of glucose polysaccharide found in the cell walls of various fungi, is less likely to be helpful in workup.

Anti-GFAP antibodies can be associated with recurrent meningoencephalitis. Imaging more characteristically demonstrates T2 hyperintensities in the thalamus, basal ganglia, and subcortical and periventricular white matter, as well as a radial perivascular pattern of gadolinium enhancement. Prominent systemic symptoms usually are not seen.

Toledano M. Neurologic manifestations of rheumatologic disease. *Continuum Lifelong Learning Neurol.* 2023 Jun;29(3):734-762.

Graf J. Central nervous system disease in antineutrophil cytoplasmic antibodies-associated vasculitis. *Rheum Clin North Am.* 2017 Nov;43(4):573-578.



Question

16 ADULT NEUROLOGY**Treatment/Management**

This patient likely has the primary progressive form of multiple sclerosis (PPMS). Ocrelizumab, a humanized monoclonal antibody that depletes CD20-expressing B cells and recently approved by the FDA for PPMS, is associated with less disability progression when compared to placebo. Side effects include infusion-related reactions, herpes virus-related infections, and neoplasm.

Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018 Apr;90(17):777-788. Reaffirmed September 2021. Endorsed by the Consortium of Multiple Sclerosis Centers, the Multiple Sclerosis Association of America, and the National Multiple Sclerosis Society.

Rae-Grant A, Day GS, Marrie RA, et al. Comprehensive systematic review summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018 Apr;90(17):789-800. Reaffirmed September 2021. Endorsed by the Consortium of Multiple Sclerosis Centers, the Multiple Sclerosis Association of America, and the National Multiple Sclerosis Society.

Montalban X, Hauser S, Kappos L, et al; ORATORIO Clinical Investigators. Ocrelizumab versus placebo in primary progressive multiple sclerosis. *N Engl J Med*. 2017 Jan 17;376(3):209-220.

29 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

This patient has symptoms of stiff-person syndrome. In a non-neoplastic setting, the most common etiologies are autoimmune glutamic acid decarboxylase or glycine antibodies. However, in the setting of malignancy (particularly breast cancer as suggested in this patient), the most common etiology is paraneoplastic amphiphysin antibodies. Yo and Ma antibodies are paraneoplastic antibodies as well, but they do not result in stiff-person syndrome. These antibodies are associated with cerebellar degeneration (Yo, Ma) and limbic encephalitis (Ma).

Zekeridou A. Paraneoplastic neurological disorders. *Continuum Lifelong Learning Neurol*. 2024 Aug;30(4):1021-1051.

Martinez-Hernandez E, Ariño H, McKeon A, et al. Clinical and immunologic investigations in patients with stiff-person spectrum disorder. *JAMA Neurol*. 2016 Jun 1;73(6):714-720.

Question

35 NO SPECIFIED PATIENT AGE

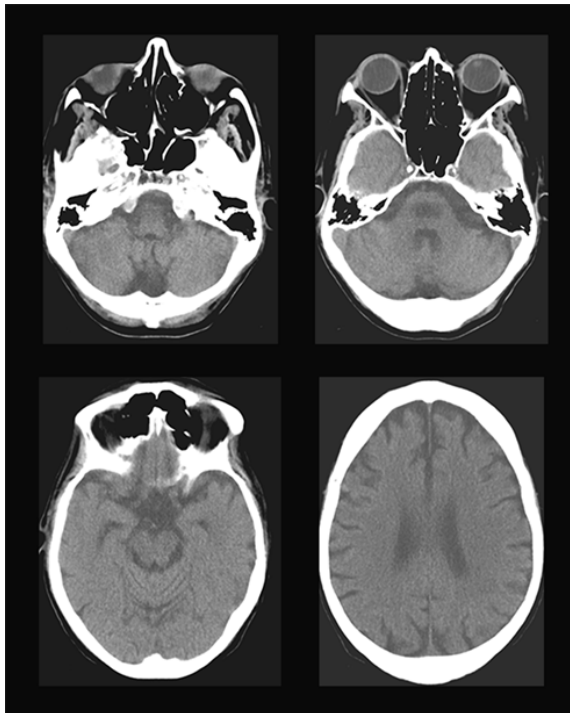
CORE KNOWLEDGE

Neuroimaging

This series of CT images of a patient with central pontine myelinolysis (CPM)—also known as osmotic demyelination syndrome—shows an ovoid hypodensity within the central basis pontis. The lesion does not extend to the anterior or posterior margin of the pons as would be seen with a large pontine infarction, nor is there vasogenic edema as would be seen in an infectious process or tumor.

Although CPM most frequently occurs in the setting of rapid correction of hyponatremia, CPM has been described in patients with chronic alcoholism without hyponatremia, presumably due to rapid osmotic shifts caused by other metabolic derangements. Wernicke encephalopathy can demonstrate some suggestive findings on CT scan, including hypodensity in the fornices and low-density changes along the periaqueductal region and along the margins of the third ventricle. These findings are much better demonstrated on MRI scans, along with signal changes within the mammillary bodies, but are not seen here. Acute alcohol intoxication has no specific imaging findings.

Atlas SW (ed). *Magnetic Resonance Imaging of the Brain and Spine*. 5th ed. Philadelphia, PA: Wolters Kluwer; 2017.



Question

49 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

This clinical presentation is concerning for myocarditis and myasthenia secondary to immune checkpoint inhibitor (ICI) toxicity. The elevated troponin additionally raises concern for myocardial involvement. This triad is a rare and severe complication of ICIs that has a high morbidity and mortality and must be treated promptly. Stopping both the ICIs and initiating steroids is first-line treatment. In refractory cases, plasmapheresis or IVIg are typically used in the acute setting.

Rituximab is considered a third-line agent. Efgartigimod and thymectomy represent treatments used for non-ICI-induced myasthenia, but there is insufficient data for their use in ICI-induced myasthenia. Pyridostigmine potentially provides relief of some myasthenic symptoms but would not address the underlying cause.

Furlepa M, Watts I, Carr AS. Management of triple M syndrome: a narrative review of immune checkpoint inhibitor-induced myasthenia gravis, myositis and myocarditis. *Cancers (Basel)*. 2025 Jun 20;17(13):2063.

Marco C, Simó M, Alemany M, et al. Myasthenia gravis induced by immune checkpoint inhibitors: An emerging neurotoxicity in neuro-oncology practice: Case series. *J Clin Med*. 2022 Dec 24;12(1):130.

Video credit: Gomes de Carvalho Neto E, Ferreira Gomes M, Peurira dos Santos I, et al. Teaching Video Neurolmages: Useful bedside testing for myasthenia gravis: the phenomenon of enhanced ptosis. *Neurology*. 2020 April 28;94(17):e1870-e1871.

53 ADULT NEUROLOGY

Clinical Aspects of Disease

Fatigue, a sense of tiredness or lack of energy that is greater than expected for the effort required for a task or the degree of disability, occurs in up to 75% of patients with multiple sclerosis (MS), often preventing normal activities. It must be differentiated from symptoms of depression, weakness, lack of rest, or excessive exercise. Fatigue in these patients is exacerbated by heat and improves with cooler temperatures; it also is more common than sleep disturbance (58%), depression (50%), euphoria (25%), and pseudobulbar affect (10%).

Marchesi O, Vizzino C, Filippi M, Rocca MA. Current perspectives on the diagnosis and management of fatigue in multiple sclerosis. *Expert Rev Neurother*. 2022 Aug;22(8):681-693.

Question

59 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Uncontrollable laughter and/or crying is typical of pseudobulbar affect. These symptoms can be seen in patients with multiple sclerosis, especially those with a high burden of disease in the brainstem. Dextromethorphan–quinidine is FDA approved for the treatment of pseudobulbar palsy. Clonazepam and chlorpromazine may depress the CNS and help control these emotions, but these medications are not considered first-line agents. Baclofen is typically used for spasticity, and topiramate may be helpful for migraines and paresthesias in patients with multiple sclerosis.

Panitch HS, Thisted RA, Smith RA, et al. Randomized, controlled trial of dextromethorphan/quinidine for pseudobulbar affect in multiple sclerosis. *Ann Neurol*. 2006 May;59(5):780–787.

Question #

68 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Diagnostic Procedures

This patient's presentation is consistent with dorsal root ganglionopathy, also known as sensory neuronopathy. The differential diagnosis is relatively narrow and includes nutritional deficiencies, pyridoxine toxicity, paraneoplastic syndromes (often associated with anti-Hu/ANNA-1), HIV, chemotherapeutic agent toxicity, and Sjögren syndrome.

While antibody testing is rarely negative early in the disease course, the presence of sicca symptoms, and the patient's age (42 years) favor Sjögren syndrome. This syndrome can be seronegative; thus, a lip biopsy demonstrating lymphocytic sialadenitis can help establish the diagnosis.

Sural nerve biopsy can be normal or show nonspecific changes in dorsal root ganglionopathies and as such would not be diagnostic. Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis usually presents as mononeuritis multiplex rather than dorsal root ganglionopathy. CASPR2 antibodies can be associated with peripheral nerve hyperexcitability and neuromyotonia. Dorsal root ganglionopathy is a well-described manifestation of anti-Hu/ANNA-1 paraneoplastic syndrome, which usually occurs in the context of small cell lung cancer.

Toledano M. Neurologic manifestations of rheumatologic disease. *Continuum Lifelong Learning Neurol.* 2023 Jun;29(3):734-762.

Gwathmey KG. Sensory neuronopathies. *Muscle Nerve.* 2016 Jan;53(1):8-19.

NERVE CONDUCTIONS

Nerve	Type	Record Site	Rep Stim	Side	Amp	Normal Amp
Fibular	Motor	EDB		L	3.2	(> 2.0)
Tibial	Motor	AH		L	4.2	(> 4.0)
Sural	Sensory	Ankle		L	NR	(> 0.0)
Ulnar	Motor	ADM		L	7.4	(> 6.0)
Median	Sensory	Dig II		L	NR	(> 15.0)
Ulnar	Sensory	Dig V		L	NR	(> 10.0)

Question

77 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

Paroxysmal tonic spasms are brief (30 seconds to 3 minutes), stereotyped, and often associated with painful unilateral muscle contractions; these spasms are common in patients with multiple sclerosis, especially in the setting of spinal cord lesions. They may be the result of ephaptic transmission, local inflammation, or ion channel dysfunction, and they respond well to carbamazepine.

Although sometimes misdiagnosed as focal-onset seizures, the isolated tonic phase and normal EEG do not support this etiology. C7 radiculopathy would likely include neck pain. Brachial plexitis often features pain followed by persistent weakness, and it is not episodic. Ulnar neuropathy can result in a "claw hand" but would not result in limb posturing and would not likely be episodic.

Freiha J, Riachi N, Chalah MA, et al. Paroxysmal symptoms in multiple sclerosis - a review of the literature. *J Clin Med*. 2020 Oct; 9(10):3100.

89 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroscience and Mechanism of Disease

Dalfampridine is an inhibitor of voltage-dependent potassium channels, and inhibition of these channels improves conduction along demyelinated axons of the CNS in animal studies. Several studies in patients with multiple sclerosis report that treatment with dalfampridine may be associated with improvements in visual function, strength, ambulation, fatigue, and endurance.

Goodman AD, Brown TR, Cohen JA, et al; Fampridine MS-F202 Study Group. Dose comparison trial of sustained-release fampridine in multiple sclerosis. *Neurology*. 2008 Oct 7;71(15):1134-1141.

Question

97 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

Immunosuppression with natalizumab markedly increases the risk of progressive multifocal leukoencephalopathy (PML). The estimated risk of PML is 1:1,000 patients. In one study, all patients in whom PML developed tested positive for anti-JC virus antibodies before the onset of PML. For seropositive patients with prior immunosuppressant use and 25 to 48 months of natalizumab treatment, the estimated rate is 11:1,000.

Ropper AH. Predicting risk of progressive multifocal leukoencephalopathy from natalizumab. *N Engl J Med*. 2012 May 17;366(20):1938-1939.

Greenberg BM, Khatri BO, Kramer JF. Current and emerging multiple sclerosis therapeutics. *Continuum Lifelong Learning Neurol*. 2010 Dec;16(5):58-77.

106 NO SPECIFIED PATIENT AGE

Treatment/Management

Dimethyl fumarate may decrease lymphocyte counts; therefore, baseline and serial CBC testing is required to monitor for lymphopenia. Dimethyl fumarate has also been associated with liver injury, so liver function should be tested frequently as well.

Ongoing monitoring of laboratory values is required for other disease-modifying therapies, including creatinine while on cladribine, thyroid function while on interferons, urinalysis while on alemtuzumab, and immunoglobulin while on rituximab, ocrelizumab, or ofatumumab.

Dello Russo C, Scott KA, Pirmohamed M. Dimethyl fumarate induced lymphopenia in multiple sclerosis: a review of the literature. *Pharmacol Ther*. 2021 Mar;219:107710.

Rae-Grant A, Day GS, Marrie RA, et al. Comprehensive systematic review summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018 Apr;90(17):789-800. Reaffirmed September 2021. Endorsed by the Consortium of Multiple Sclerosis Centers, the Multiple Sclerosis Association of America, and the National Multiple Sclerosis Society.

Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018 Apr;90(17):777-788. Reaffirmed September 2021. Endorsed by the Consortium of Multiple Sclerosis Centers, the Multiple Sclerosis Association of America, and the National Multiple Sclerosis Society.

Question

123 ADULT NEUROLOGY**Treatment/Management**

Teriflunomide is an oral medication used for treatment of multiple sclerosis (MS). Cyclophosphamide, mycophenolate, and azathioprine are conventional immunosuppressants traditionally used for MS and neuromyelitis optica (NMO). However, monoclonal antibodies such as inebilizumab (B-cell depleting agent), eculizumab (complement blocking agent), and tocilizumab and satralizumab (interleukin-6 signaling blocking agents) have been shown to reduce relapse rates in aquaporin-4-positive NMO.

Chan KH, Lee CY. Treatment of neuromyelitis optica syndrome. *Int J Mol Sci*. 2021 Aug;22(16):8638.

Kessler RA, Mealy MA, Levy M. Treatment of neuromyelitis optica spectrum disorder: acute, preventive, and symptomatic. *Curr Treat Options Neurol*. 2016 Jan;18(1):2.

127 ADULT NEUROLOGY**CORE KNOWLEDGE****Diagnostic Procedures**

Treatment with natalizumab is associated with an increased risk of progressive multifocal leukoencephalopathy (PML), as inhibition of lymphocyte entry into the CNS results in loss of immune surveillance and potential active replication of the JC virus.

Symptoms of PML are typically more insidious and often include cognitive, motor, and language impairment. MRI scans typically demonstrate an area of abnormal confluent white matter signal with sparing of the cortex. In the setting of the appropriate clinical symptoms and MRI findings, CSF analysis with JC virus PCR identifies activating replicating JC virus that results in PML and is the least invasive method to confirm diagnostic criteria for definite PML.

Biopsy may be considered if CSF sampling is unrevealing. Antibody testing for JC virus in the CSF or serum can support exposure to JC virus but does not identify active replicating JC virus infection. As PML is restricted to the CNS, serum JC virus PCR testing is not indicated.

Berger JR, Aksamit AJ, Clifford DB, et al. PML diagnostic criteria. Consensus statement for the AAN Neuroinfectious Disease Section. *Neurology*. 2013 April 8;80(15):1430-1438.

Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018 Apr;90(17):777-788. Reaffirmed September 2021. Endorsed by the Consortium of Multiple Sclerosis Centers, the Multiple Sclerosis Association of America, and the National Multiple Sclerosis Society.

Rae-Grant A, Day GS, Marrie RA, et al. Comprehensive systematic review summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018 Apr;90(17):789-800. Reaffirmed September 2021. Endorsed by the Consortium of Multiple Sclerosis Centers, the Multiple Sclerosis Association of America, and the National Multiple Sclerosis Society.

Question

137 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

This patient has symptoms associated with parkinsonism after CAR-T therapy. Recent studies report that BCMA-directed CAR-T therapy can result in selective basal ganglia injury, presenting with movement and neurocognitive treatment-emergent adverse events, which can be more delayed than classic CAR-T associated neurotoxicity.

Urinary tract infection usually does not cause new focal neurologic findings. Herpes simplex virus encephalitis usually causes fever and altered mental status. Multiple myeloma only rarely invades the CNS and usually does not present with parkinsonism. Hydrocephalus would not typically cause parkinsonism.

Karschnia P, Dietrich J. Neurological complications of CAR T cell therapy for cancers. *Nat Rev Neurol*. 2025 Aug;21(8):422-431.

147 ADULT NEUROLOGY**Neuropathology**

Giant cell (temporal) arteritis is a granulomatous vasculitis chiefly affecting the extracranial arteries of the head (superficial temporal, ophthalmic, carotid and vertebral), usually sparing intracranial vessels. It may also affect the aorta and its branches. Patients are usually over 55 years of age, with a mean age of 75 years.

The central symptom is frequently headache. Other signs and symptoms include fever, visual impairment, scalp tenderness, malaise, myalgia, weight loss, anemia, jaw claudication, neck pain, and tenderness of the temporal artery to palpation with decreased arterial pulsation.

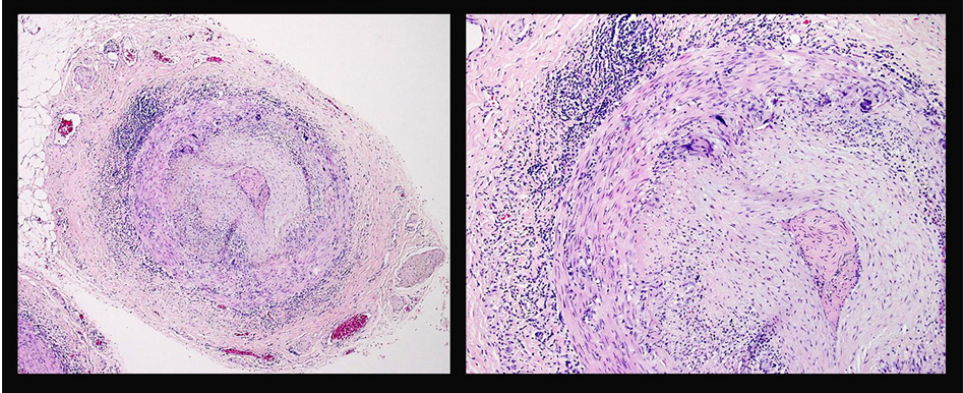
The etiology is not clear, although apparently cell mediated. Inflammatory cells are generally present in the media. Multinucleate giant cells are the hallmark (hence the name), but are not obligatory for the diagnosis. If present, they are usually seen along the internal elastic membrane and may engulf fragments of elastica. Fibrinoid necrosis also may be present.

(continues)

Question

Treatment with high-dose steroids prior to biopsy may result in a lack of inflammation and only scar formation to serve as proof of injury.

Smith C, Perry A, Kovacs G, et al (eds). Greenfield's Neuropathology. 10th ed. Boca Raton, FL: CRC Press; 2024.



157 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient presents with subacute cognitive decline and faciobrachial dystonic seizures, consistent with anti-LGI1 encephalitis. MRI scans and CSF analysis may be normal. Patients may have accompanying hyponatremia.

Day GS. Rapidly progressive dementia. Continuum Lifelong Learning Neurol. 2022 Jun;28(3):901-936.

Video credit: Day GS. Rapidly progressive dementia. Continuum Lifelong Learning Neurol. 2022 Jun;28(3):901-936.

Question

165 NO SPECIFIED PATIENT AGE**Treatment/Management**

This patient has neuromyelitis optica with an extensive longitudinally transverse myelitis refractory to IV steroids. The next treatment indicated is plasmapheresis, which is best supported by the available evidence over other therapies. Although maintenance immunosuppression may be necessary, improving the patient's acute symptoms with plasmapheresis takes precedence.

Flanagan EP. Neuromyelitis optica spectrum disorder and other non-multiple sclerosis central nervous system inflammatory diseases. *Continuum Lifelong Learning Neurol.* 2019 Jun;25(3):815-844.

Image credit: Flanagan EP. Neuromyelitis optica spectrum disorder and other non-multiple sclerosis central nervous system inflammatory diseases. *Continuum Lifelong Learning Neurol.* 2019 Jun;25(3):815-844.



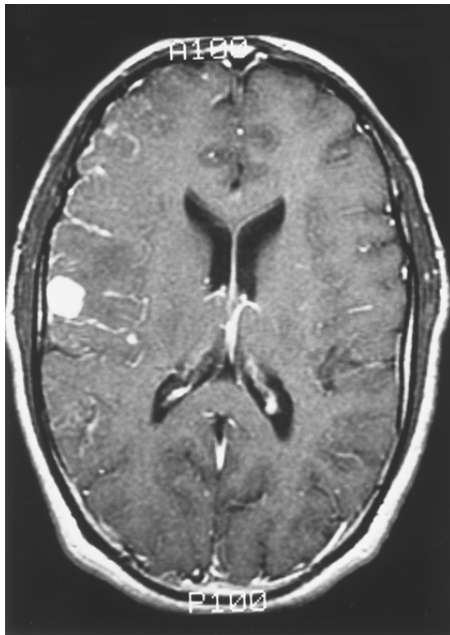
Question

174 ADULT NEUROLOGY**Neuroimaging**

Leptomeningeal enhancement, parenchymal enhancement, and especially pituitary stalk/hypothalamic involvement in a patient with cranial nerve symptoms is characteristic of neurosarcoidosis. Up to 10% of patients with sarcoidosis develop CNS involvement.

Lack of hemiatrophy and prominent (asymmetrical) choroid plexus enhancement make Sturge–Weber syndrome less likely. No gyral enhancement is seen in the imaging study. Low CSF pressure would not be limited to one hemisphere and would not have the mass-like and leptomeningeal enhancement seen here. The enhancing lesion is intra-axial and therefore is not a meningioma.

Salzman KL, Jhaveri MD, Osborn AG (eds). Diagnostic Imaging: Brain. 5th ed. Philadelphia: Elsevier; 2025.



Question

185 NO SPECIFIED PATIENT AGE**Treatment/Management**

Fingolimod is a sphingosine 1-phosphate receptor inhibitor used for relapsing–remitting multiple sclerosis (RRMS). Its putative mechanism of action in MS is sequestration of lymphocytes in lymph nodes. Natalizumab prevents adhesion of activated T cells at the blood–brain barrier, teriflunomide reduces lymphocyte proliferation, interferons suppress TH2 cells, and fumarates upregulate antioxidant pathways.

Cross A, Riley C. Treatment of multiple sclerosis. *Continuum Lifelong Learning Neurol.* 2022 Aug 1;28(4):1025-1051.

197 NO SPECIFIED PATIENT AGE**Treatment/Management**

West Nile virus is the most common neurotropic flavivirus in the continental United States and can cause meningitis, encephalitis, and myelitis. Detection of IgM antibodies against West Nile virus in CSF is diagnostic of CNS infection.

Opsoclonus–myoclonus–ataxia syndrome (OMAS) can occur as a parainfectious immune-mediated phenomena, including in the setting of CNS flavivirus infections. Although up to 50% of children with OMAS have a neuroblastoma, paraneoplastic associations in adults are rare.

While there is little evidence to support immunotherapies for treatment of flavivirus-associated CNS infection, immunotherapies may be useful in treating parainfectious syndromes associated with these viruses. A limited course of immunotherapy is sufficient in most cases of idiopathic or parainfectious OMAS without second-line maintenance immunotherapies such as rituximab. There are currently no effective antivirals against flaviviruses.

In immunocompetent patients, serology is more sensitive than nucleic acid amplification tests, and CSF PCR is frequently negative, so this additional analysis is not indicated.

Hass RM, Toledano M. Powassan and other emerging neuroinvasive arboviruses in North America. *Curr Opin Infect Dis.* 2025 Jun 1;38(3):242-251.

Margolin E, Kaur K, Jeeva-Patel T. Opsoclonus. [Updated 2025 May 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-.

Wallace A, Thomas J, Boren J, et al. Opsoclonus-myoclonus-ataxia syndrome in a patient with West Nile virus: Case report and a patient's experience. *Neurohospitalist.* 2025 Jul 15;19418744251361303.

Question

200 ADULT NEUROLOGY**Clinical Aspects of Disease**

Most patients with multiple sclerosis experience cognitive symptoms over the course of their disease. Episodic memory is often affected, but long-term memory is most often preserved. Although executive function, verbal fluency, and visuospatial analysis can be affected, processing speed is the most commonly affected domain.

Sumowski JF, Benedict R, Enzinger C, et al. Cognition in multiple sclerosis. *Neurology*. 2018 Feb 6;90(6):278-288.

202 NO SPECIFIED PATIENT AGE**Treatment/Management**

CAR-T therapy, a treatment that uses a patient's own genetically engineered T cells to attack cancer cells, has several potential adverse effects. This patient has symptoms of immune effector cell-associated neurotoxicity syndrome (ICANS). Onset typically occurs more than 1 week after treatment and is characterized by several neurologic symptoms, including altered mental status, language difficulties, and tremors. The most appropriate treatment for ICANS is methylprednisolone.

Tocilizumab is a treatment for cytokine release syndrome, another adverse effect of CAR-T therapy. Symptoms typically develop within a week after infusion and are more systemic, including fever and myalgias. Tocilizumab is not used for ICANS, as the protein cannot cross the blood-brain barrier.

Anakinra is used for hemophagocytic lymphohistiocytosis and rasbicurase for tumor lysis syndrome. While patients receiving oncologic therapy are at risk for infection, this patient has no specific signs to suggest the need for broad-spectrum antibiotics.

Sheth VS, Gauthier J. Taming the beast: CRS and ICANS after CAR T-cell therapy for ALL. *Bone Marrow Transplant*. 2021 Mar;56(3):552-566.

Rees JH. Management of immune effector cell-associated neurotoxicity syndrome (ICANS). In: Kröger N, Gribben J, Chabannon C, et al. (eds) *The EBMT/EHA CAR-T Cell Handbook* [Internet]. Cham, Switzerland: Springer; 2022, pp 141-146.

Question

214 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Treatment/Management

MOG antibody-associated disorder (MOGAD) is increasingly recognized as a cause of acute disseminated encephalomyelitis (ADEM) in pediatric patients. Patients often respond to IV steroids in the acute period, with IVIg or plasma exchange as second-line options in the acute phase. Consensus guidelines for MOGAD published in 2020 recommend close observation after initial presentation, with maintenance therapy recommended after a first relapse. Azathioprine, rituximab, and mycophenolate mofetil (MMF) are considered first-line options after the first relapse.

Bruijstens AL, Wendel EM, Lechner C, et al. E.U. Paediatric MOG Consortium Consensus: Part 5 - Treatment of paediatric myelin oligodendrocyte glycoprotein antibody-associated disorders. *Eur J Paediatr Neurol*. 2020 Nov;29:41-53.

224 ADULT NEUROLOGY

CORE KNOWLEDGE

Diagnostic Procedures

Brain MRI is the most important test to order in patients with suspected acute optic neuritis to determine the likelihood of progression from a clinically isolated syndrome to multiple sclerosis. Results can determine if initiating disease-modifying therapy is appropriate after treatment with IV steroids.

Oh J. Diagnosis of multiple sclerosis. *Continuum Lifelong Learning Neurol*. 2022 Aug;28(4):1006-1024.

235 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

Neuromyelitis optica spectrum disorder (NMOSD) is similar to myelin oligodendrocyte antibody-associated disease (MOGAD), with NMOSD associated with a relapsing course and MOGAD with either monophasic or relapsing courses. Optic neuritis and myelitis occur in both disorders. Area postrema syndrome, with nausea, vomiting or hiccups, is common in NMOSD, while seizures, encephalopathy, hypotension, and narcolepsy are more common in MOGAD.

Sechi E. NMOSD and MOGAD. *Continuum Lifelong Learning Neurol*. 2024 Aug;30(4):1052-1087.

Question

248 NO SPECIFIED PATIENT AGE**Neuropathology**

Progressive multifocal leukoencephalopathy (PML) is an opportunistic viral infection with tropism for oligodendrocytes. In addition to general characteristics of a demyelinating disease shared with active multiple sclerosis (such as abundant foamy macrophages, astrocytic atypia, and relative sparing of glial cell bodies), intranuclear oligodendrocytic viral inclusions are only seen in PML. Perivascular inflammatory infiltrates are not typically a feature of PML.

Smith C, Perry A, Kovacs G, et al (eds). Greenfield's Neuropathology. 10th ed. Boca Raton, FL:CRC Press; 2024.

251 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Bone lesions are the strongest red flag against a diagnosis of multiple sclerosis (MS), or at least as a single disease explanation. Bone lesions should prompt consideration of the histiocytoses, especially Erdheim-Chester disease, a non-Langerhans cell histiocytosis. Sarcoidosis, systemic lupus erythematosus, and thrombotic thrombocytopenic purpura are systemic diseases that can mimic MS, but bone lesions are not a feature. Multiple myeloma features bone lesions but very rarely affects the CNS.

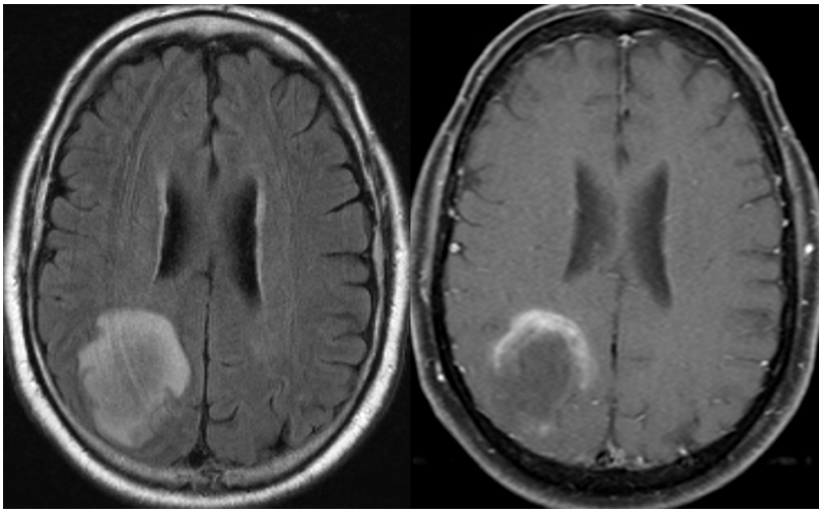
Garg N, Lavi ES. Clinical and neuroimaging manifestations of Erdheim-Chester disease: a review. J Neuroimaging 2021 Jan;31(1):35-44.

Question

270 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

This patient's MRI findings are typical of a tumefactive multiple sclerosis lesion. Demyelinating lesions typically show incomplete ring enhancement. Tumefactive lesions are generally >2 cm and show low cerebral blood volume on MR perfusion studies. Other features highly suggesting tumefactive demyelination instead of tumor are minimal or absent of mass effect for the size of the lesion.

Suh CH, Kim HS, Jung SC, et al. MRI findings in tumefactive demyelinating lesions: a systematic review and meta-analysis. *AJNR Am J Neuroradiol.* 2018 Sep; 39(9):1643-1649.



Question

281 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroscience and Mechanism of Disease

The presence of anti-MOG antibodies is associated with MOG-IgG associated disease (MOGAD). Diagnostic criteria also require one of the following six core clinical syndromes: optic neuritis, myelitis, acute disseminated encephalomyelitis, cerebral monofocal or polyfocal deficits, and brainstem or cerebellar deficits.

More recently, aseptic meningitis without definitive radiographic evidence of cortical encephalitis has been identified as a probable MOGAD attack phenotype. As in this patient, nearly 50% of patients experience a core demyelinating event in close association with meningitis. Optic neuritis in MOGAD is frequently bilateral, associated with long lesions (>50% length of the optic nerve) and papilledema (due to its proximity to the globe).

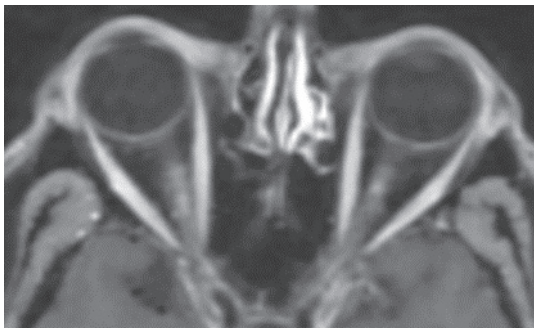
Aquaporin-4 antibodies are associated with neuromyelitis optica spectrum disorder (NMOSD). Optic neuritis in NMOSD can be bilateral or sequentially bilateral. However, lesions are retrobulbar or chiasmatic and usually not associated with papilledema. Meningitis is not a known presenting phenotype of NMOSD.

CASPR2 antibodies are associated with peripheral nerve hyperexcitability, neuromyotonia, Morvan and Isaacs syndromes, and most frequently limbic encephalitis. CRMP5 can cause paraneoplastic bilateral optic neuritis and associated papilledema. However, onset is subacute (weeks to months) and imaging studies negative. Optic neuritis is usually associated with retinitis and vitritis. Other neurologic manifestations include cerebellar ataxia, myelitis, and encephalitis. Meningitis is not a known manifestation. Anti-recoverin antibodies are associated with paraneoplastic retinitis.

Aboseif A, Kim NN, Bou G, et al. Meningitis as an attack phenotype of myelin oligodendrocyte glycoprotein antibody-associated disease. *JAMA Neurol.* 2025 Jun 16.

Banwell B, Bennett JL, Marignier R, et al. Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria. *Lancet Neurol.* 2023 Mar;22(3):268-282.

Cohen DA, Bhatti MT, Pulido JS, et al. Collapsin response-mediator protein 5-associated retinitis, vitritis, and optic disc edema. *Ophthalmology.* 2020 Feb;127(2):221-229.



Question

292 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

Intravenous methylprednisolone accelerated the recovery of vision in the Optic Neuritis Treatment Trial, but there was no significant difference in visual acuity, visual fields, color vision, or contrast sensitivity.

Volpe NJ. The Optic Neuritis Treatment Trial: a definitive answer and profound impact with unexpected results. *Arch Ophthalmol*. 2008 Jul;126(7):996-999.

302 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Clinical Aspects of Disease

Clinically isolated syndrome (CIS) is defined as a first demyelinating episode. This patient has only one lesion and therefore does not meet dissemination in space for multiple sclerosis (MS). However, the presence of oligoclonal bands or elevated kappa light free chains is suggestive of a chronic inflammatory process.

The significance of CIS has been borne out in clinical trials, which indicate that initiating disease-modifying therapy after CIS delays the time until a second clinical episode and a definitive diagnosis of MS.

Radiologically isolated syndrome refers to the finding of MRI lesions typical in location and character for MS in the absence of symptoms suggestive of MS. Neuromyelitis optica is characterized by longitudinally extensive spinal cord lesions (three or more vertebral segments).

Montalban X, Lebrun-Fréney C, Oh J, et al. Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria. *Lancet Neurol*. 2025 Oct;24(10):850-865.

Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018 Apr;90(17):777-788. Reaffirmed October 2024. Endorsed by the Consortium of Multiple Sclerosis Centers, the Multiple Sclerosis Association of America, and the National Multiple Sclerosis Society.

Rae-Grant A, Day GS, Marrie RA, et al. Comprehensive systematic review summary: disease-modifying therapies for adults with multiple sclerosis: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018 Apr;90(17):789-800. Reaffirmed September 2021. Endorsed by the Consortium of Multiple Sclerosis Centers, the Multiple Sclerosis Association of America, and the National Multiple Sclerosis Society.

Question

307 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Macular edema may develop in patients treated with siponimod; therefore, patients must be screened before initiation of treatment.

Gross RH, Corboy JR. Monitoring, switching, and stopping multiple sclerosis disease-modifying therapies. *Continuum Lifelong Learning Neurol.* 2019 Jun;25(3):715-735.

320 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

Regardless of patient age, NMDA–receptor autoimmune encephalitis has a similar presentation as subacute severe encephalopathy, characterized by neuropsychiatric symptoms, seizures, abnormal movements, and dysautonomia. Neoplastic process is rare in prepubertal children (as in this 5 year–old patient). MRI scans are typically normal. EEG can be nonspecific, but extreme delta brush is a common finding in NMDA encephalitis.

Neuromyelitis optica spectrum disorder (NMOSD) (AQP4) and myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) often present with acute demyelination syndromes, including optic neuritis and transverse myelitis.

Glial fibrillary acidic protein (GFAP) astrocytopathy also presents as a meningoencephalitis, often with T2 hyperintensities in the basal ganglia and thalamus on MRI. LGI1–antibodies present with an autoimmune encephalitis with characteristic faciobrachial dystonic seizures.

Hacohen Y. Pediatric autoimmune neurologic disorders. *Continuum Lifelong Learning Neurol.* 2024 Aug;30(4):1160-1188.

Question

325 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

Optic neuritis is a common presenting symptom in relapsing–remitting multiple sclerosis. Optical coherence tomography (OCT) provides a method to quantify retinal neuroaxonal loss following optic neuritis. After a period of inflammation (optic nerve edema, [94 μm right eye, 98 μm left eye]), subsequent thinning of the retinal nerve fiber layer often occurs weeks to months later. Therefore, it is most likely that the retinal nerve fiber layer in the left eye would be abnormally thin (88 μm right eye, 66 μm left eye). Inter–eye differences in retinal nerve fiber layer thickness of $<6 \mu\text{m}$ are unlikely to reflect optic neuritis.

Toosy AT, Naismith NT, Villoslada P. OCT as a window to the MS brain: The view becomes slightly clearer. *Neurology*. 2017 Dec 12;8(24):2404–2405.

333 Adult Neurology**Core Knowledge****Treatment/Management**

Eculizumab, a monoclonal antibody that inhibits the complement protein C5, is FDA approved for aquaporin–4 IgG–positive neuromyelitis optica spectrum disorder. Contraindications include unresolved *Neisseria meningitidis* infection and lack of meningococcal vaccination. Prophylactic antibiotics are recommended during treatment to mitigate the risk of meningococcal infection.

Romeo AR. Recent advances in the treatment of neuromyelitis optica spectrum disorders. *Current Opin Rheumatol*. 2021 May 1;33(3):233–239.

349 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Diagnostic Procedures**

Susac syndrome is an immune–mediated, pauci–inflammatory, occlusive microvascular endotheliopathy/basement membranopathy that affects the brain, retina, and inner ear. Features include a clinical triad consisting of encephalopathy, branch retinal artery occlusion (BRAO), and low–frequency sensorineural hearing loss. Many patients present with encephalopathy, but visual and hearing changes may not be readily apparent on examination or history.

Distinctive “snowball” lesions in the corpus callosum are seen on T2–weighted FLAIR sequence MRI scans, characteristically appearing as punched out hypointensities in T1–weighted sequences. Fluorescein

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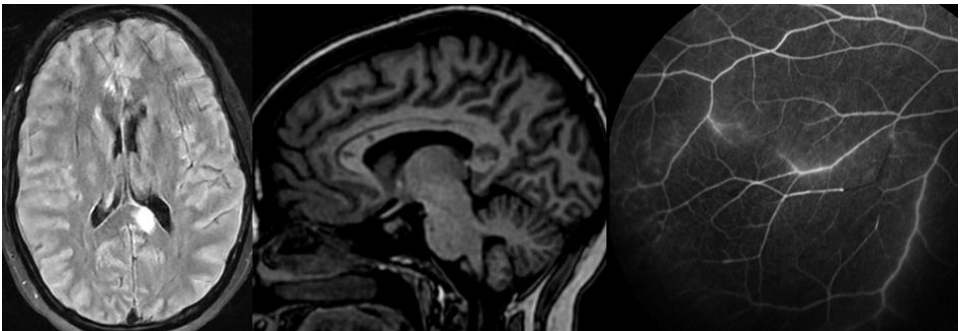
Question

angiogram shows BRAO and segmental hyperfluorescence and leakage. Pure tone audiometry showing low- to midfrequency sensorineural hearing loss can help establish the diagnosis. CSF is abnormal in almost 50% of patients, but findings are nonspecific.

Thinning of the retinal nerve fiber on OCT indicates prior optic neuritis, but these are not cardinal features of Susac syndrome. Dipeptidyl-peptidase-like protein 6 (DPPX) antibodies are usually associated with progressive encephalomyelitis with rigidity and myoclonus (PERM), along with gastrointestinal dysmotility manifesting as severe diarrhea. C-reactive protein usually is not elevated in Susac syndrome.

Rennebohm RM, Asdaghi N, Srivastava S, et al. Guidelines for treatment of Susac syndrome - An update. *Int J Stroke*. 2020 Jul;15(5):484-494.

Tobin WO, Lennon VA, Komorowski L, et al. DPPX potassium channel antibody: frequency, clinical accompaniments, and outcomes in 20 patients. *Neurology*. 2014 Nov 11;83(20):1797-1780.



Question

357 ADULT NEUROLOGY**Treatment/Management**

This patient has classic features of stiff-person syndrome (SPS), specifically truncal hypertonia and hyperlordosis. GAD65 antibodies are most commonly associated with SPS. Benzodiazepines such as diazepam, usually in relatively large doses, are generally considered first-line therapy for both seropositive and seronegative SPS.

Baclofen is typically reserved as second-line therapy for patients who cannot tolerate or have a poor response to benzodiazepines. Immunotherapy should be started as soon as GABA-enhancing medications are not fully effective or incompletely tolerated. The efficacy of IVIg was best shown in the randomized blinded crossover trial comparing IVIg with placebo in patients with GAD65-positive SPS. Rituximab is usually considered a second-line immunotherapy in patients with incomplete response to IVIg.

Dalakas MC. Therapies in stiff-person syndrome: advances and future prospects based on disease pathophysiology. *Neurol Neuroimmunol Neuroinflamm*. 2023 Apr 14;10(3):e200109.

Tobin WO, Pittock SJ. Autoimmune neurology of the central nervous system. *Continuum Lifelong Learning Neurol*. 2017 Jun;23(3):627-653.

Question

365 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

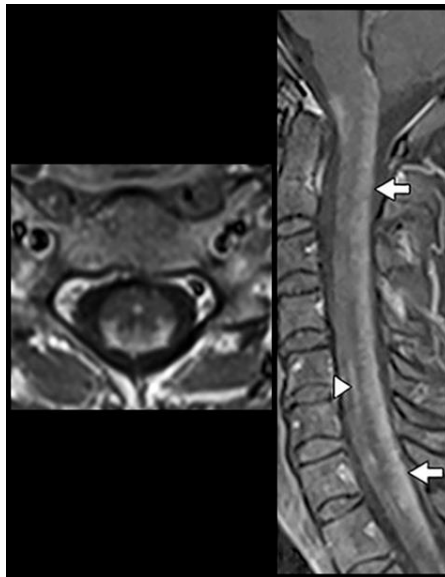
Diagnostic Procedures

This patient presents with extensive longitudinal transverse myelitis. Central cord involvement and subpial enhancement on MRI scan are features of the trident sign, a finding associated with neurosarcoidosis. Chest CT should be ordered next to assess for lymphadenopathy, as lymph node biopsy is the gold standard for establishing the diagnosis.

Brain MRI would likely be ordered to gauge the extent of involvement but would not provide as much diagnostic clarity. Serum calcium and interleukin-2 receptor (IL-2R) may be elevated, but neither is a specific measure. Angiotensin-converting enzyme on CSF analysis has low sensitivity and specificity for neurosarcoidosis.

Berntsson SG, Elmgren A, Gudjonsson O, et al. A comprehensive diagnostic approach in suspected neurosarcoidosis. *Sci Rep.* 2023 Apr 21;13(1):6539.

Zalewski NL, Krecke KN, Weinshenker BG, et al. Central canal enhancement and the trident sign in spinal cord sarcoidosis. *Neurology.* 2016 Aug;87(7):743-744.



Question

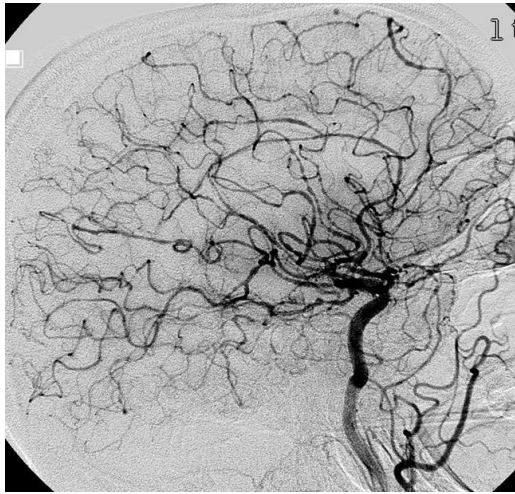
374 ADULT NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

The small- and medium-sized vessels are ragged and demonstrate the segmented pattern of vasculitis. Though vasospasm is possible, this typically affects larger vessels than those affected in this case. This appearance is known as "beads on a string."

Weinrich JM, Lenz A, Adam G, et al. Radiologic imaging in large and medium vessel vasculitis. *Radiol Clin North Am.* 2020 Jul;58(4):765-779.

**385** PEDIATRIC NEUROLOGY**Diagnostic Procedures**

Opsoclonus-myoclonus-ataxia syndrome (OMAS) clinically presents in children ages 12 to 36 months, with subacute onset of opsoclonus, trunk and limb myoclonus and ataxia, and often presenting with truncal ataxia or gait instability. Behavioral symptoms, including irritability, sleep disturbances, and developmental plateau or regression (particularly in social and language domains) are also seen. Half of children with OMAS have an underlying neuroblastoma. Both urine catecholamine testing and whole body imaging are recommended in the initial evaluation.

EEG and EMG are of limited diagnostic use in the context of OMAS. While there is some overlap in the clinical presentations of NMDA autoimmune encephalitis and MOGAD, opsoclonus is not a rare feature.

Rossor T, E AY, Khakoo Y, et al; OMS Study Group. Diagnosis and management of opsoclonus-myoclonus-ataxia syndrome in children. *Neurol Neuroimmunol Neuroinflamm.* 2022 Mar 8;9(3):e1153.

Question

396 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Neuroimaging

Both neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein-associated disease (MOGAD) can present with severe bilateral optic neuritis. Both also generally demonstrate longitudinally extensive optic nerve involvement on MRI. The presence of oligoclonal bands on CSF analysis is relatively low in both disorders. Optic nerve sheath enhancement on MRI can be seen in MOGAD but is not typically seen in NMOSD.

Eggenberger E. Optic neuritis. Continuum Lifelong Learning Neurol. 2025 Apr;31(2):407-435.

Question

15 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

This patient has signs and symptoms consistent with idiopathic (Bell) facial palsy. A 2001 AAN Practice Parameter on treatment of Bell palsy concluded that, based on the available evidence, steroids are probably effective in improving outcome.

Subsequent class I and II studies have not shown clear additional benefit from either acyclovir or valacyclovir for this condition, as underscored by the updated 2012 AAN Practice Parameter on the treatment of Bell palsy. Some experts, however, believe the addition of antivirals to steroids provides only a marginal increased benefit. This updated 2012 AAN Practice Parameter has been reaffirmed multiple times, most recently in 2023.

Even in Lyme–endemic regions, idiopathic facial palsy is more common than Lyme–related facial palsy. In the absence of a tick bite, erythema migrans rash, or meningitis–like prodrome, Lyme neuroborreliosis is unlikely; thus, doxycycline is not warranted unless Lyme serologies are positive.

Gronseth GS, Paduga R. Evidence-based guideline update: Steroids and antivirals for Bell palsy: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology* 2012 Nov;79(22):2209-2213. Reaffirmed February 2023.

Question

74 NO SPECIFIED PATIENT AGE

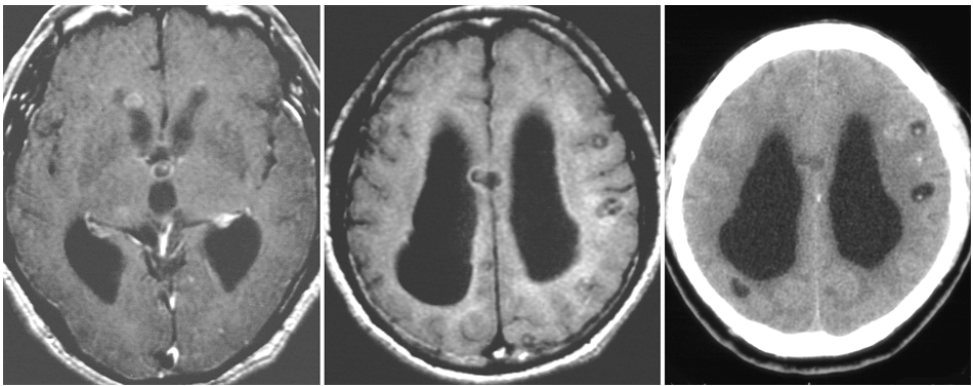
CORE KNOWLEDGE

Neuroimaging

This patient's MRI scans show multifocal cystic lesions with a central high-intensity/density punctate focus, findings consistent with neurocysticercosis caused by *Taenia solium*. Neurocysticercosis can cause seizures, and with subarachnoid or intraventricular cysts seen on imaging, hydrocephalus. *Taenia solium*, also known as pork tapeworm, is transmitted through ingestion of undercooked pork. This infection is widely endemic across Central America, South America, sub-Saharan Africa, and Asia.

Streptococcus pneumoniae can cause meningitis or bacterial abscess but would not appear on MRI scans as cystic lesions within the central scolex. Metastases from ovarian cancer would appear as ring-enhancing lesions, not these findings. Herpes virus simplex encephalitis would appear as limbic hyperintensity. Schistomiasis of the brain is rare but shows arborized enhancement rather than cystic lesions.

Garcia HH. Parasitic infections of the nervous system. *Continuum Lifelong Learning Neurol*. 2021 Aug;27(4):943-962.



Question

93 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroimaging

Sarcoidosis is associated with T-cell anergy and varying degrees of CD4 lymphopenia, resulting in an immunocompromised state. Patients with sarcoidosis can develop progressive multifocal leukoencephalopathy (PML) in the absence of therapeutic immune suppression.

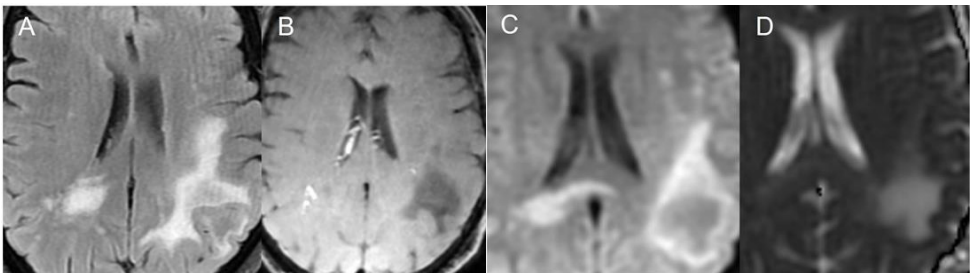
While contrast enhancement is rarely seen in classic PML, up to 25% of patients with sarcoidosis-associated PML demonstrate some degree of contrast enhancement within or bordering the characteristic T2 FLAIR hyperintense white matter lesions. Similarly, CSF can be mildly inflammatory in these patients, most likely due to their relatively preserved immune function. As in this patient, PML lesions can demonstrate restricted diffusion at the edge of the lesion (likely cytotoxic edema from oligodendrocyte cytopathy), which can be helpful diagnostically.

Patients with sarcoidosis and PML are at risk of being misdiagnosed with neurosarcoidosis. The latter commonly presents with chronic meningitis, and while it rarely presents with parenchymal lesions, these are invariably associated with leptomeningeal disease.

CSF JC virus PCR is both sensitive and specific for PML and should be obtained in these patients. Brain biopsy could be diagnostic of PML and should be considered if CSF JC virus PCR is negative. This patient's presentation is not consistent with neurosyphilis; thus, CSF VDRL testing is not indicated. CSF ACE has low sensitivity and specificity and is not additive in the evaluation of neurosarcoidosis.

McEntire CRS, Fletcher A, Toledano M, et al. Characteristics of progressive multifocal leukoencephalopathy associated with sarcoidosis without therapeutic immune suppression. *JAMA Neurol.* 2023 Jun 1;80(6):624-633.

Radswiki T, Ryan P, Sharma R, et al. Progressive multifocal leukoencephalopathy. Reference article, Radiopaedia.org (Accessed Aug 2025) <https://doi.org/10.53347/rID-12098>.



Question

101 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient has herpes zoster infection in a V1 distribution. The virus is dormant in the trigeminal ganglion and can reactivate in the setting of immunosuppression. Often, the skin in a V1 distribution becomes intensely erythematous before the vesicular rash appears. Keratitis is a common complication and may result in corneal scarring. The other disorders listed (rhinocerebral mucormycosis, orbital lymphoma, chemotherapy-related neuropathy, carotid cavernous fistula) would not exclusively involve the V1 branch of the trigeminal nerve nor manifest with the erythematous rash as shown.

Boegle A, Narayanaswami P. Infectious neuropathies. *Continuum Lifelong Learning Neurol.* 2023 Oct;29(5):1418-1443.



144 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

This patient most likely has postherpetic neuralgia. The herpes zoster infection most likely developed because of her immunocompromised state. There is no indication to use steroids or acyclovir after the vesicular rash has healed. Medication for neuropathic pain, such as gabapentin, would be most useful at this time. Doxycycline is typically used for Lyme disease. There is no evidence for the use of naproxen to treat neuropathic pain.

Hehir MK, Logigian EL. Infectious neuropathies. *Continuum Lifelong Learning Neurol.* 2014 Oct;20(5):1274-1292.

Question

181 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

Early treatment with dexamethasone improves outcomes in adults with acute bacterial meningitis (particularly pneumococcal meningitis) and does not increase the risk of gastrointestinal bleeding. There is no evidence that any of the other medications listed (mannitol, fosphenytoin, acetazolamide) are indicated in the acute treatment of bacterial meningitis in adults, nor is hyperbaric oxygen indicated.

Aksamit AJ, Berkowitz AL. Meningitis. Continuum Lifelong Learning Neuro. 2021 Aug;27(4):836-854.

220 PEDIATRIC NEUROLOGY

Clinical Aspects of Disease

This patient's presentation is classic for measles, including Koplik spots on the oral mucosa. Subacute sclerosing panencephalitis is a late complication of measles, developing 7 to 10 years later. Features include cognitive decline followed by myoclonic jerks, additional neurologic deterioration, and eventual death. Guillain-Barré syndrome follows viral or bacterial infections. Lyme disease can cause cranial neuropathies. Herpes simplex encephalitis is a trigger for NMDA receptor encephalitis. Sydenham chorea follows group A streptococcal infections.

Do LAH, Mulholland K. Measles 2025. N Engl J Med. 2025 Dec 18;393(24):2447-2458.

Sulaiman SA, Vora NM, Chhabra K, et al. Pediatric subacute sclerosing panencephalitis: a narrative review on measles and the future of vaccination. J Child Neurol. 2024 Mar;39(3-4):89-97.

Ropper AH, Samuels MA, Klein JP, Prasad S (eds). Adams and Victor's Principles of Neurology. 12th ed. New York: McGraw Hill; 2023.

Committee on Infectious Diseases, American Academy of Pediatrics. Group A streptococcal diseases. In: Kimerlin DW, Banerjee R, Barnett ED, et al (eds). Red Book: 2024-2027 Reports of Committee Infectious Diseases. 33rd ed. Itasca, IL: American Academy of Pediatrics; 2024, pp 785-798.

Question

253 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Decreased level of consciousness in patients with cryptococcal meningitis is most commonly due to elevated intracranial pressure, requiring therapeutic lumbar puncture before changes are made to a medication regimen.

Grill MF. Neurologic complications of human immunodeficiency virus. *Continuum Lifelong Learning Neurol.* 2021 Aug;27(4):963-991.

321 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

This patient is immunocompromised with signs and symptoms suggesting herpes zoster oticus (Ramsay Hunt syndrome). This syndrome occurs with activation of herpes zoster virus in the geniculate ganglion. Patients typically present with right-sided ear pain and redness, followed by facial weakness. Ulcerations are often present within the external acoustic meatus or lateral aspect of the tongue. Imaging and CSF examination are usually normal. Treatment is acyclovir. Steroids should be avoided in immunocompromised patients as they may cause systemic spread of viral infection.

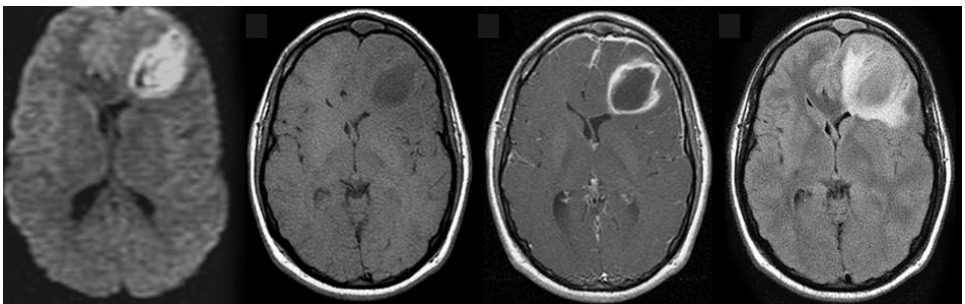
Ishiyama G. Selected otologic disorders causing dizziness. *Continuum Lifelong Learning Neurol.* 2021 Apr;27(2):468-490.

De Ru JA, van Benthem PPG. Combination therapy is preferable for patients with Ramsay Hunt syndrome. *Otol Neurotol.* 2011 Jul;32(5):852-855.

367 NO SPECIFIED PATIENT AGE**Neuroimaging**

This patient has acute neurologic symptoms correlating with a diffusion restricting, ring-enhancing lesion with surrounding edema, suggestive of cerebral abscess.

Venkatesan A. Encephalitis and brain abscess. *Continuum Lifelong Learning Neurol.* 2021 Aug;27(4):855-886.



Question

381 NO SPECIFIED PATIENT AGE

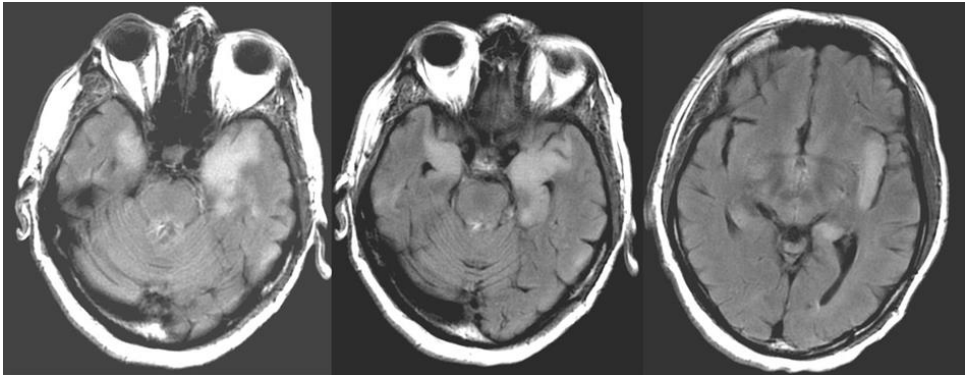
CORE KNOWLEDGE

Diagnostic Procedures|Neuroimaging

This patient's MRI scans show bilateral T2 hyperintensity in the limbic regions (medial temporal lobes and insula), consistent with limbic encephalitis. In the context of an acute presentation in an immunocompetent patient, herpes simplex virus (HSV) encephalitis is the most likely diagnosis.

West Nile virus encephalitis typically demonstrates signal change in the deep gray matter on imaging studies. Bacterial meningitis would not cause limbic signal change on imaging studies. Progressive multifocal leukoencephalopathy (PML) causes juxtacortical and middle cerebellar peduncle hyperintensity. Toxoplasmosis appears as ring-enhancing lesions with surrounding edema. PML and toxoplasmosis are only seen in the setting of immunocompromise; the patient's history has no record of immunocompromise.

Venktasen A. Encephalitis and brain abscess. *Continuum Lifelong Learning Neurol.* 2021 Aug;27(4):855-886.



Question

2 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

This patient has refractory myasthenia gravis. Eculizumab, currently the only FDA approved treatment for refractory myasthenia gravis, is a humanized monoclonal antibody that specifically binds with high affinity to human terminal complement protein C5. This inhibits enzymatic cleavage of C5 to C5a and C5b, thereby preventing C5a-induced chemotaxis of proinflammatory cells and formation of the C5b-induced membrane attack complex. Ravulizumab is another monoclonal antibody to the terminal complement protein C5. Efgartigimod is a monoclonal antibody that blocks the neonatal FC receptor on immune cells. These medications may also be used in the treatment of myasthenia gravis.

Howard JF Jr, Utsugisawa K, Benatar M, et al. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalised myasthenia gravis (REGAIN): a phase 3, randomised, double-blind, placebo-controlled, multicentre study. *Lancet Neurol*. 2017 Dec;16(12):976-986.

9 PEDIATRIC NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

This neonate's presentation is consistent with congenital myotonic dystrophy, a disorder characterized by generalized hypotonia, facial diplegia, and contractures (such as clubfeet or hip deformities). Polyhydramnios and reduced fetal movement are also common features. Congenital myotonic dystrophy has a maternal inheritance pattern; mothers may have mild/subclinical symptoms due to anticipation, with a CTG repeat expansion in *DMPK*.

None of the other disorders listed have a maternal inheritance pattern. Duchenne muscular dystrophy and spinal muscular atrophy type II do not present at birth or cause facial diplegia. Congenital muscular dystrophy, Fukuyama type, is associated with brain malformations (classically cobblestone lissencephaly) and eye abnormalities. Benign congenital hypotonia describes nonprogressive hypotonia and weakness without multiple-system involvement.

Volpe JJ, Inder TE (eds). *Volpe's Neurology of the Newborn*. 7th ed. Philadelphia, PA: Elsevier; 2024.

Question

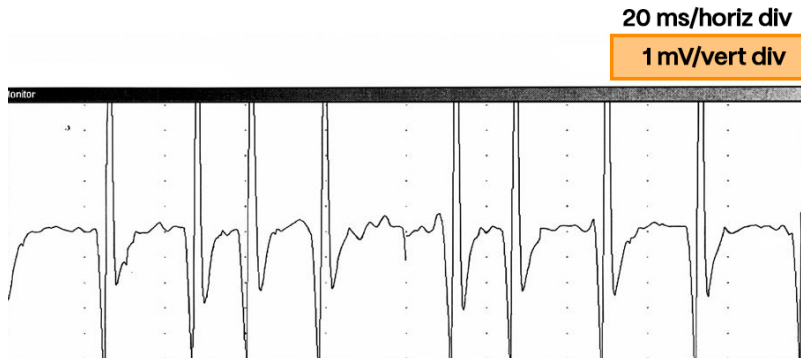
14 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Diagnostic Procedures

In cases of partial or gradual denervation, reinnervation usually occurs through collateral sprouting by adjacent surviving motor units. As the number of muscle fibers per motor unit increases, motor unit action potentials (MUAPs) become prolonged, high amplitude, and polyphasic. These MUAP changes, in conjunction with decreased recruitment, are the hallmarks of reinnervated motor units and nearly always imply chronic neuropathic disease (eg, disorders of the anterior horn cell, nerve root, or peripheral nerve). Long-duration, high-amplitude, polyphasic MUAPs are never seen in acute conditions. When present, they always imply a process has been present for at least several weeks, more often months or years.

Preston DC, Shapiro BE. *Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations*. 4th ed. Philadelphia: Elsevier Saunders; 2020.



26 NO SPECIFIED PATIENT AGE

Neuroanatomy

The tibial nerve innervates the tibialis posterior muscle, which inverts the foot. It also innervates the gastrocnemius, soleus, flexor digitorum longus, and flexor hallucis longus.

The deep peroneal nerve controls the tibialis anterior, extensor digitorum longus, extensor hallucis longus, and extensor digitorum brevis. The femoral nerve innervates the iliopsoas and quadriceps femoris. The medial plantar nerves innervate the small muscles of the foot, tested by observing the patient cupping the sole of the foot. The obturator nerve innervates the hip adductors.

Preston DC and Shapiro BE (eds). *Electromyography and Neuromuscular Disorders*. 4th ed. Philadelphia: Elsevier; 2020.

Question

52 NO SPECIFIED PATIENT AGE**Neurophysiology**

Paralysis develops in association with demyelinating neuropathies primarily because of conduction block, rather than slowed conduction velocity. Conduction block causes failure of nerve transmission, leading to inability of the nerve to cause muscle contraction and, thereby, loss of power.

Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

61 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

This patient with Sjögren syndrome presents with severe loss of vibratory and proprioceptive sensation, areflexia, and a sensory ataxia. The predominantly sensory nature and patchy pattern of this syndrome is most consistent with a sensory ataxic neuronopathy, primarily affecting the dorsal root ganglion.

The differential diagnosis of dorsal root ganglionopathy is limited and includes Sjögren syndrome, cisplatin and pyridoxine toxicity, and paraneoplastic sensory neuronopathy associated with anti-Hu antibodies.

In addition to sensory ataxic neuronopathy from dorsal root ganglionitis, Sjögren syndrome is associated with other forms of neuropathy, including painful distal sensory neuropathy, trigeminal neuropathy, autonomic neuropathy, and multiple mononeuropathy. The absence of long tract signs, a spinal level, a stocking-glove pattern, and relatively rapid onset of symptoms make the other conditions listed (cervical spine cord demyelinating disease, distal symmetric sensory polyneuropathy, bilateral thalamic mass, cervical compressive myelopathy) unlikely.

Pavlakakis PP. Rheumatologic disorders and the nervous system. Continuum Lifelong Learning Neurol. 2020 Jun;26(3):591-610.

Question

70 ADULT NEUROLOGY

CORE KNOWLEDGE

Neurophysiology

Carpal tunnel syndrome (median neuropathy at the wrist) is commonly bilateral, worse in the dominant hand, and characterized by numbness involving the thumb, index, middle, and frequently the radial half of the ring finger, with sparing over the thenar eminence. Weakness of the abductor pollicis brevis with denervation is seen in more severe cases. The other muscles listed (pronator teres, flexor carpi ulnaris, first dorsal interosseus, extensor digitorum communis) are not supplied by the median nerve. The pronator teres is supplied by the median nerve in the forearm.

Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders. 4th ed. Elsevier, Inc, 2020.

82 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

This patient presents with a Guillain-Barré syndrome (GBS)-like picture of rapidly ascending numbness, weakness, and areflexia. However, the history of gastrectomy raises the possibility of thiamine deficiency, which can mimic GBS. While it is reasonable to treat presumptively with IVIg, as in this case, thiamine should also be administered after obtaining whole blood thiamine and serum thiamine pyrophosphate levels.

Corticosteroids are not indicated in patients with GBS as they have not been shown to improve outcomes. Hemin is used for acute intermittent porphyria, which is in the differential but presents with acute abdominal pain. Cytomegalovirus-related polyradiculitis can also mimic GBS and is treated with ganciclovir. However, this patient was not immunocompromised, and CSF analysis usually demonstrates a polymorphonuclear pleocytosis, which was absent in this case. Likewise, Lyme infection can mimic GBS, but the CSF results would be abnormal.

Staff NP. Peripheral neuropathies due to vitamin and mineral deficiencies, toxins, and medications. Continuum Lifelong Learning Neurol. 2020 Oct;26(5):1280-1298.

Question

90 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neurophysiology

The quantitative sudomotor axon reflex test (QSART) is abnormal in 80% of patients with distal small fiber neuropathy. The EMG/nerve conduction studies and somatosensory evoked potentials are normal.

Low PA, Benarroch EE. Clinical Autonomic Disorders. 3rd ed. Baltimore: Lippincott-Raven, 2008.

99 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroscience and Mechanism of Disease

This patient's clinical presentation is consistent with subacute sensory neuronopathy/ganglionopathy, a paraneoplastic disorder closely associated with anti-Hu antibodies. GM1 antibodies accompany motor neuropathies, especially multifocal motor neuropathy with conduction block. Yo antibodies are commonly seen in paraneoplastic cerebellar degeneration. GQ1b antibodies are characteristic of the Miller Fisher variant of Guillain-Barré syndrome, and calcium channel antibodies are associated with Lambert-Eaton myasthenic syndrome.

Gwathmey KG. Sensory neuronopathies. Muscle Nerve. 2016 Jan;53(1):8-19.

Question

108 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Treatment/Management

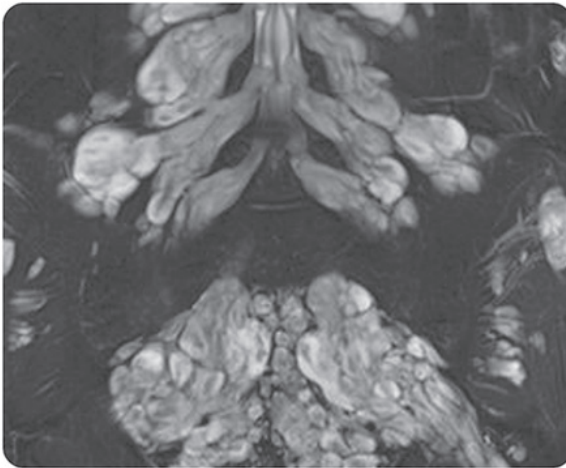
This patient meets the clinical criteria for neurofibromatosis type 1 (NF1), with his coronal MRI scan showing plexiform neurofibromas. Surgical resection is not feasible for deep plexiform neurofibroma lesions due both to the depth of the lesions and the interweaving of the plexiform neurofibroma around other adjacent structures. The standard of care for these symptomatic lesions is a mitogen-activated protein kinase kinase (MAP2K, or MEK) inhibitor, such as selumetinib for children or mirdametinib for children or adults.

mTOR inhibitors are used to treat the renal and intracerebral tumors of tuberous sclerosis. A course of anti-inflammatory medications would, at best, reduce pain temporarily but is unlikely to provide significant relief and is thus not an appropriate long-term option.

Cacchione A, Fabozzi F, Carai A, et al. Safety and efficacy of MEK inhibitors in the treatment of plexiform neurofibromas: a retrospective study. *Cancer Control*. 2023 Jan-Dec;30:10732748221144930.

Legius E, Messiaen L, Wolkenstein P, et al. Revised diagnostic criteria for neurofibromatosis type 1 and Legius syndrome: an international consensus recommendation. *Genet Med*. 2021 Aug;23(8):1506-1513.

Image credit: Grimsrud KW, Porter AB. Mystery case: Widespread plexiform neurofibromas in neurofibromatosis type 1: an uncommon cause of back pain. *Neurology*. 2017 Oct 31;89(18):e218-e219.



Question

115 NO SPECIFIED PATIENT AGE**Treatment/Management**

This patient has stiff-person syndrome (SPS), a disorder characterized by insidious onset of stiffness of the proximal lower limbs, back, and abdominal muscles. Symptoms worsen with certain stimuli such as touch, loud noises, or stress. Hyperlordosis is a characteristic finding. The head retraction reflex, in which the head or trunk pulls back with tapping of the nasal bridge, is also characteristic. About one third of patients with SPS have type 1 diabetes mellitus.

Elevated antibodies to the glutamic acid decarboxylase 65-kilodalton isoform (GAD65) are diagnostic, particularly if levels are >10,000 IU/mL by ELISA. If antibodies are <10,000, additional diagnostic testing may be ordered, including EMG (shows continuous firing of the motor units in agonist and antagonist muscles, even at rest) or lumbar puncture (about two thirds of patients have anti-GAD65 antibodies in the CSF). Treatment is both symptomatic, with GABA-ergic agonists (often high doses of diazepam), and immunologic, such as with IVIg.

Trihexyphenidyl, carbidopa/levodopa, and deep brain stimulation are both useful treatments for dystonia. While dystonia can present in the trunk such as with dystonia type 1, it is more likely to fluctuate and would not have the head retraction reflex.

Physical therapy and cognitive behavioral therapy would be appropriate for functional neurologic disorder, which should be considered in the differential diagnosis; however, SPS is a better clinical fit. Orthopedic referral may be considered, though surgical correction of scoliosis will not fix the underlying problem.

Bose S, Jacob. Stiff-person syndrome. *Pract Neurol*. 2025 Jan 16;25(1):6-17.

Question

118 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Benign fasciculation syndromes present with fasciculations in multiple muscles without associated cramps or weakness. Neurologic examination and electrodiagnostic testing are necessary to rule out motor neuron disease or cramp–fasciculation syndrome. Patients can improve with withdrawal of caffeinated substances or reduced life stressors.

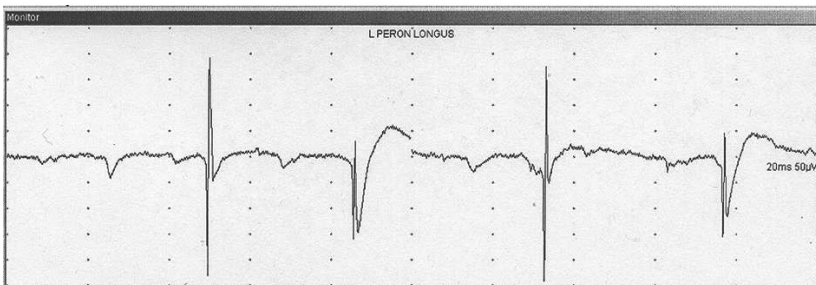
Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

126 NO SPECIFIED PATIENT AGE

Neurophysiology

Positive sharp waves and fibrillation potentials recorded during EMG indicate active denervation of the muscle under study or functionally equivalent denervation by dividing the muscle cell into two parts, one still connected to the motor nerve and the other part not connected to the motor nerve as seen in inflammatory myopathies. Small, polyphasic motor units (nascent motor units) indicate early reinnervation. Enlarged motor units indicate well-established or chronic reinnervation. Demyelination does not typically cause positive sharp waves and is best demonstrated by slowing or conduction block on nerve conduction studies.

Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

20ms 50 μ V

Question

135 ADULT NEUROLOGY**Clinical Aspects of Disease**

Inclusion body myositis (IBM) is the most common subtype of inflammatory myopathy in patients older than age 45 years. Clinical hallmarks include the characteristic inability to flex the deep finger flexors and weakness of the knee extensors. The 2024 European Neuromuscular Centre (ENMC) guidelines provide guidance in making an accurate diagnosis.

The diagnosis depends on clinical symptoms and histopathologic features, including the following: endomysial inflammation and lymphocytic invasion of non-necrotic fibers, rimmed vacuoles, and tubulofilamentous inclusions. The presence of the anti-cN1a antibody can also support the diagnosis.

Other inflammatory myopathies in the differential diagnosis include antisynthetase syndrome, overlap myositis, immune-mediated necrotizing myopathy, and dermatomyositis. These myopathies, however, do not present with deep finger flexor weakness on clinical examination or predominant knee extension weakness. These other disorders more typically have symmetric proximal upper and lower extremity weakness in shoulder abduction and hip flexion.

Other inflammatory myopathies have treatments available; however, no treatment is currently available for IBM. Making the correct diagnosis is important so patients are not treated inappropriately with immune suppression.

Lilleker JB, Naddaf E, Saris CGJ, et al; 272nd ENMC workshop participants. 272nd ENMC International Workshop: 10 Years of progress - revision of the ENMC 2013 diagnostic criteria for inclusion body myositis and clinical trial readiness. 16-18 June 2023, Hoofddorp, The Netherlands. *Neuromuscul Disord.* 2024 Apr;37:36-51.



Question

142 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

The pain that occurs with meralgia paresthetica, defined as damage to the lateral femoral cutaneous nerve, is often widely distributed and can include the low back, buttock, anterolateral thigh, and lateral knee. It is often aggravated by standing and relieved by sitting. Paresthesias and hypesthesia usually involve a much more limited area within the anterolateral thigh. This syndrome is often associated with obesity or pregnancy, and symptoms disappear with weight loss or delivery.

Waters JF. Neurologic complications of obstetric anesthesia. *Continuum Lifelong Learning Neurol.* 2022 Feb;28(1):162-179.

Massey EW, Guidon AC. Peripheral neuropathies in pregnancy. *Continuum Lifelong Learning Neurol.* 2014 Feb;20(1):100-114.

152 NO SPECIFIED PATIENT AGE

Neuropathology

Dermatomyositis is an idiopathic inflammatory myopathy. The typical skin manifestations include violaceous macular erythema with a symmetric distribution. Other typical skin findings include Gottron papules and violaceous papules overlying the dorsal interphalangeal or metacarpophalangeal areas, elbow, or knee joints. Skin lesions occur in about 70% of patients with dermatomyositis. Other signs and symptoms include proximal muscle weakness, dysphonia, and dysphagia. Muscle biopsy findings typically show perifascicular atrophy.

Ashwal S, Pearl PL, et al (eds). *Swaiman's Pediatric Neurology. Principles and Practice.* 7th ed. Philadelphia: Elsevier, 2025.



Question

162 ADULT NEUROLOGY

CORE KNOWLEDGE

Contemporary Issues

The 2009 AAN Practice Parameter The Care of the Patient with Amyotrophic Lateral Sclerosis: Drug, Nutritional, and Respiratory Therapies (which was reaffirmed in February 2023) recommends frequent discussions of the goals of care because decision making may be subject to change as the disease becomes more severe.

Miller RG, Jackson CE, Kasarskis EJ, et al. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: multidisciplinary care, symptom management, and cognitive/behavioral impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2009 Oct;73(15):1227-1233. Reaffirmed Feb 2023.

163 NO SPECIFIED PATIENT AGE

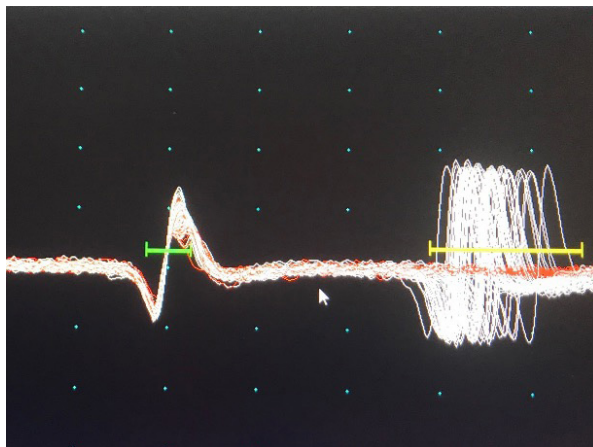
SUBSPECIALTY KNOWLEDGE

Neuroscience and Mechanism of Disease

The image shown demonstrates abnormal jitter and blocking on single fiber EMG. In single fiber EMG, two muscle fibers in the same motor unit are recorded as they fire in a time-locked manner. Excess variability of transmission time at their respective neuromuscular junctions is called abnormal jitter.

Demyelination of the terminal motor nerves might show prolonged and polyphasic motor units on conventional EMG. Reduced activation would appear on conventional needle EMG as sparse and slow firing motor units. Reduced recruitment would appear on conventional needle EMG as abnormally fast firing of a reduced number of motor units. Denervation of muscle fibers manifests as fibrillations or positive sharp waves in the resting muscle.

Juel VC. Single fiber electromyography. Handb Clin Neurol. 2019;160:303-310.



Question

172 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Neuralgic amyotrophy frequently affects the upper extremity nerves or the brachial plexus. This disorder is known by various names, including Parsonage–Turner syndrome, brachial plexitis, idiopathic brachial plexopathy, and brachial amyotrophy.

The syndrome is preceded by an event that triggers the immune system, usually a viral illness, immunization, or occasionally surgery. The onset of shoulder pain typically follows within several days to a few weeks. The pain is severe, often awakening the patient from sleep. As the pain subsides, significant underlying weakness becomes apparent. Certain nerves, especially the long thoracic and anterior interosseous nerves, are frequently involved.

Normal MRI scans exclude acute radiculopathies. The pattern of muscle weakness seen in this patient does not support isolated axillary neuropathy. Monomelic amyotrophy is a rare variant of motor neuron disease and does not present with pain.

Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

180 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

Spinal muscular atrophy (SMA) is caused by loss or mutation of the survival motor neuron 1 (*SMN1*) gene, leading to reduced SMN protein levels and a selective dysfunction of motor neurons. Individuals have either a homozygous deletion of *SMN1* or are compound heterozygous for an *SMN1* deletion and a pathogenic variation. The *SMN2* gene creates a less stable SMN protein. Individuals with milder forms of SMA (types II and III) have multiple copies of *SMN2*, which compensates to some extent for the loss of *SMN1*.

Burghes AH, Beattie CE. Spinal muscular atrophy: why do low levels of survival motor neuron protein make motor neurons sick?. *Nat Rev Neurosci*. 2009 Aug;10(8):597-609.

Question

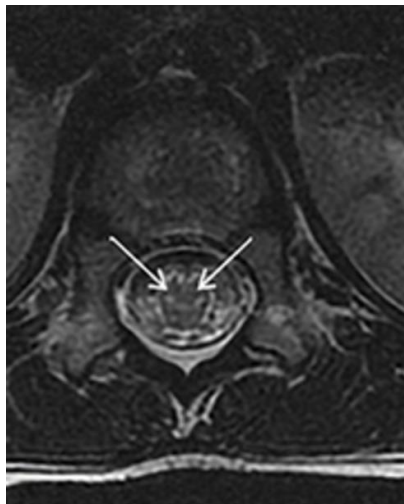
186 PEDIATRIC NEUROLOGY**Neuroimaging**

This patient's MRI scan shows hyperintense T2 signal in the central gray matter of the spinal cord, particularly the anterior horns. This finding is characteristic of acute flaccid myelitis compared with the other disorders listed (Guillain-Barré syndrome [GBS], Miller Fisher variant of GBS, transverse myelitis, neuromyelitis optica spectrum disorder). Anterior horn T2 hyperintensity can also be seen in spinal cord infarction. Clinically and radiographically, acute flaccid myelitis is similar to poliomyelitis. Enterovirus D68 is the most frequently associated virus with acute flaccid myelitis.

The classic MRI finding in transverse myelitis is a longitudinally extensive T2 hyperintense spinal cord lesion. Both ventral and dorsal aspects of the cord are involved, as opposed to only the anterior horns as seen here. In neuromyelitis optica, neuritis is seen in the optic nerves, and lesions consistent with transverse myelitis can be seen in the spinal cord. In patients with GBS, imaging of the lower spine may show enhancement of the nerve roots and/or the cauda equina. Spine MRI scans in patients with the Miller Fisher variant of GBS are typically normal, although thickening and enhancement of the nerve roots and/or the cauda equina, as well as lesions in the posterior columns, have been reported.

Wang C, Greenberg B. Clinical approach to pediatric transverse myelitis, neuromyelitis optica spectrum disorder and acute flaccid myelitis. *Children* (Basel). 2019 May 17;6(5):70.

Image credit : Al-Ghamdi F, Ghosh PS. Clinical reasoning: a 2-year-old child with acute flaccid paralysis. *Neurology*. 2016 Oct 4;87(14):e149-e154.



Question

196 ADULT NEUROLOGY**Treatment/Management**

A 2021 AAN practice guideline (reaffirmed in 2025) addressing treatment of painful diabetic polyneuropathy recommends screening for comorbidities, including depression and sleep apnea. Both disorders affect pain perception, and treatment may have a positive impact on quality of life and pain perception. Of the options presented, diagnosis (and treatment) of obstructive sleep apnea is the most likely to yield benefit.

Opioids should be avoided due to their addictive potential and lack of long-term efficacy in the treatment of neuropathic pain. Topiramate is not indicated for painful neuropathy. Ankle-foot orthoses may help with distal weakness, but this is not part of this patient's findings.

Price R, Smith D, Franklin G, et al. Oral and topical treatment of painful diabetic polyneuropathy: Practice guideline update summary. Report of the AAN Guideline Subcommittee. *Neurology*. 2022 Jan;98(1):31-43. Reaffirmed February 2025.

205 ADULT NEUROLOGY**Treatment/Management**

A clinical presentation including fluctuating ptosis, diplopia, proximal weakness, and shortness of breath is most consistent with myasthenia gravis (MG). Studies have suggested a link between susceptibility to MG and four single-nucleotide polymorphisms (SNPs) resulting from ineffective transcription of the *CTLA4* gene. Two case reports have linked MG with ipilimumab use for melanoma. There is an additional case report of a patient with small cell lung cancer who developed drug-induced MG shortly after induction with nivolumab and ipilimumab.

Santomasso BD. Anticancer drugs and the nervous system. *Continuum Lifelong Learning Neurol*. 2020 Jun;26(3):732-764.

Question

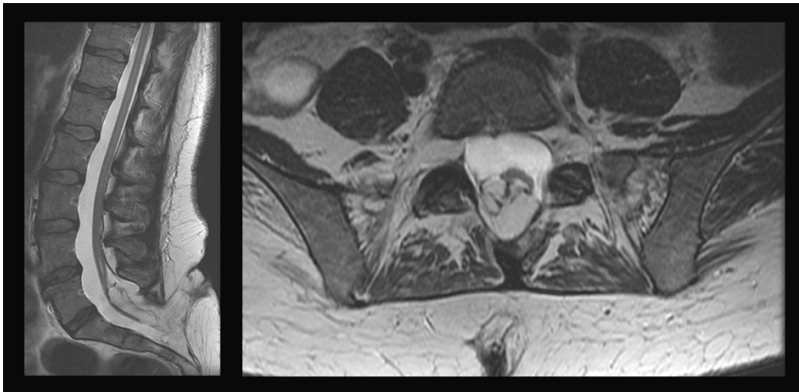
216 ADULT NEUROLOGY

Neuroimaging

This patient's MRI scans show that the spinal cord extends down to the sacral level and is attached to a large sacral lipoma, which has isointense signal to the patient's subcutaneous fat. A dysraphism of the sacrum is also seen.

A chordoma is a tumor mass that arises in the sacrum, not behind it. Spondylolisthesis is the displacement of one vertebra relative to the one adjacent to it. Chronic inflammatory polyneuropathy demonstrates thickened cauda equina nerve roots.

Salzman KL, Jhaveri MD, Osborn AG (eds). *Diagnostic Imaging: Brain*. 5th ed. Philadelphia: Elsevier; 2025.

**223** ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroscience and Mechanism of Disease

Belzutifan, a small molecule inhibitor of hypoxia-inducible factor 2 alpha (HIF-2 α), has demonstrated efficacy in treating CNS hemangioblastomas characteristic of von Hippel-Lindau disease (VHL). People with VHL lack the *VHL* gene that encodes a protein that breaks down HIF-2 α . Hemangioblastomas in VHL and other cancers may grow through manipulation of hypoxia-inducible factors, which promote angiogenesis. Belzutifan effectively reduces the size of hemangioblastomas by inhibiting this pathway and is commonly used to treat spinal cord tumors before proceeding with spinal surgery, which poses substantial risks.

(continues)

Question

Methotrexate inhibits cell division through disruption of folate synthesis but is not used for treatment of hemangioblastomas in VHL. Bevacizumab is a monoclonal antibody that binds VEGF. Though it also inhibits angiogenesis and is used for various tumors, it does not have demonstrated efficacy for CNS hemangioblastomas. Vincristine is a molecule that disrupts tubulin, thereby inhibiting cell division. Though it is a commonly used chemotherapeutic agent, it has not been used for CNS hemangioblastomas. Chimeric antigen receptor T (CAR-T) cells are immune cells that are engineered to attack tumor tissue. Though its use for treatment of cancer has expanded rapidly, CAR-T has not been used for treatment of hemangioblastomas.

McFaline-Figueroa JR. Spinal cord neoplasms. *Continuum Lifelong Learning Neurol.* 2024 Feb 1;30(1):99-118.

Toledo RA, Jimenez C, Armaiz-Pena G, et al. Hypoxia-inducible factor 2 alpha (HIF2 α) inhibitors: targeting genetically driven tumor hypoxia. *Endocr Rev.* 2023 Mar 4;44(2):312-322.

232 PEDIATRIC NEUROLOGY**Clinical Aspects of Disease**

Type II glycogen storage disease (Pompe disease) results in the lysosomal accumulation of glycogen as the result of a reduction in the activity of alpha-glucosidase (acid maltase). During infancy, the disorder usually presents at a median age of 2 months with hypotonia and weakness. Associated features include cardiac involvement, a large tongue with fasciculations, prominent rubbery muscles, and an enlarged liver.

Beckwith Wiedemann syndrome typically includes tongue enlargement, but it is not associated with an elevation in creatine kinase. Myotonic dystrophy and Prader-Willi syndrome are not associated with cardiomegaly. Spinal muscular atrophy type 1 would not be associated with an enlarged tongue or cardiomegaly.

Davison JE. Advances in diagnosis and management of Pompe disease. *J Mother Child.* 2020;24(2):3-8.

Reuser AJJ. Pompe disease. www.rarediseases.org/rare-diseases/pompe-disease/. Updated January 2024. Accessed September 2025.

Question

241 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient presents with classic features of acute inflammatory demyelinating polyradiculoneuropathy (AIDP)—rapidly progressive, symmetrical weakness, hyporeflexia, and CSF cytoalbuminologic dissociation. In porphyria, weakness begins in the upper extremities, and ongoing abdominal pain, autonomic dysfunction, and reddish-brown discoloration of the urine are typical. Normal pupillary function and elevated CSF protein make botulism unlikely. Herpes zoster radiculitis typically causes bladder dysfunction and CSF pleocytosis. Transverse myelitis usually manifests with bowel and bladder dysfunction, and a sensory level.

Bellanti R, Rinaldi S. Guillain-Barré syndrome: A comprehensive review. *Eur J Neurol*. 2024 Aug;31(8):e16365.

254 NO SPECIFIED PATIENT AGE**Neuroscience and Mechanism of Disease**

Charcot-Marie-Tooth disease type 1A is caused by a duplication of *PMP22* on chromosome 17, which leads to an overproduction of PMP22 protein, interfering with proper function of the myelin sheath. Characteristics include muscle atrophy in the feet, legs, and hands, high arches, foot drop, sensory loss in the feet, gait abnormalities, and scoliosis.

Klein CJ. Charcot-Marie-Tooth disease and other hereditary neuropathies. *Continuum Lifelong Learning Neurol*. 2020 Oct;26(5):1224-1256.

265 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Diagnostic Procedures

A clinical presentation characterized by diffuse weakness, areflexia, and distal numbness suggests a demyelinating polyneuropathy such as chronic inflammatory demyelinating polyneuropathy (CIDP). According to the 2021 European Academy of Neurology/Peripheral Nerve Society guidelines on diagnosis and treatment of CIDP, the best next best step in workup is EMG, not only to determine if diagnostic testing criteria are met but also to exclude CIDP mimics.

CSF analysis, nerve biopsy, and MRI are secondary tests to provide more evidence for the diagnosis. A serum paraneoplastic panel is rarely indicated in this type of presentation.

Van den Bergh PYK, van Doorn PA, Hadden RDM, et al. European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force-second revision. *Eur J Neurol*. 2021 Nov;28(11):3556-3583.

Question

272 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

This patient's repetitive stimulation testing demonstrated a decrement suggesting a neuromuscular junction disorder. After exercise, there was an increment with repetitive stimulation, consistent with a presynaptic disorder. In the context of progressive proximal weakness over 4 months and complaints of a dry mouth, these findings are most consistent with Lambert–Eaton myasthenic syndrome (LEMS).

3,4-Diaminopyridine has been shown in a double-blind randomized trial to improve strength and compound muscle action potential amplitude in patients with LEMS. In the same trial, pyridostigmine was also tested and shown to add no benefit. Edaravone, a free radical scavenger, and riluzole, an antiglutaminergic drug, are used to treat ALS. Eteplirsen, an antisense oligonucleotide, is designed to skip exon 51 of the *DMD* gene.

Randall DP. The recognition, physiology, and treatment of Lambert-Eaton myasthenic syndrome. *Dis Mon.* 2025 Aug;71(8):101967.

Keogh M, Sedehizadeh S, Maddison P. Treatment for Lambert-Eaton myasthenic syndrome. *Cochrane Database Syst Rev.* 2011 Feb 16;(2):CD003279.

278 PEDIATRIC NEUROLOGY

Diagnostic Procedures

This patient's presentation is consistent with spinal muscular atrophy (SMA), an autosomal recessive disorder caused by pathogenic variants in *SMN1*. Humans also carry a variable copy number of an *SMN2* gene that produces a smaller number of full-length transcripts. The number of copies of *SMN2* determines the severity of disease.

Since 2024, SMA is on the newborn screen (NBS) in all states. This screening evaluates for deletions of *SMN1*, the cause of SMA in 95% of patients. The other 5% of patients have point mutations (rather than deletions) and are missed on the NBS. Therefore, it is important to consider SMA as a diagnostic possibility even in the presence of a normal NBS.

Gene therapy is now available and most effective when performed early in the disease process. Whole exome sequencing would be diagnostic but takes longer and is more expensive. It is appropriate to start with SMA testing and reflex to broader testing as needed.

(continues)

Question

Needle EMG would show findings of a motor neuron disease; however, genetic testing is still needed to confirm the diagnosis and proceed with treatment. Lumbar puncture could be helpful in some conditions such as Guillain-Barré syndrome, although this syndrome is unusual in a patient this age (4 months) and less likely given the chronic clinical picture.

Mercuri E, Finkel RS, Muntoni F, et al; SMA Care Group. Diagnosis and management of spinal muscular atrophy: Part 1: recommendations for diagnosis, rehabilitation, orthopedic and nutritional care. *Neuromuscul Disord*. 2018 Feb;28(2):103-115.

283 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuropathology**

A clinical presentation characterized by peroneal, median, and radial neuropathies is consistent with mononeuropathy multiplex. The differential of mononeuropathy multiplex includes vasculitis, hereditary neuropathy with liability to pressure palsies (HNPP), amyloidosis, multifocal acquired demyelinating sensory and motor neuropathy (variant of CIDP), and multifocal motor neuropathy (if predominantly motor involvement).

Painful mononeuropathy multiplex in a patient with known rheumatoid arthritis, in conjunction with a rash and other systemic symptoms, makes vasculitis the most likely underlying pathology. Vasculitis can be primary, including polyarteritis nodosa or microscopic polyangiitis, or secondary to infection or connective tissue diseases.

When vasculitis is a concern, nerve and muscle biopsy is usually performed to maximize the number of blood vessels evaluated. The presence of inflammatory cells in the vessel wall and damage of the vessel wall such as fibrinoid necrosis is required to make a diagnosis of vasculitis histopathologically.

The inflammation in affected blood vessels is transmural, not granulomatous. There would be axonal loss with secondary demyelination with no onion bulbs. Amyloid deposition is not a part of the disease process of vasculitis.

Koike H, Nishi R, Ohyama K, et al. ANCA-associated vasculitic neuropathies: a review. *Neurol Ther*. 2022 Mar;11(1):21-38.

Question

289 ADULT NEUROLOGY**Clinical Aspects of Disease**

Diabetic lumbosacral radiculoplexus neuropathy or diabetic amyotrophy typically causes abrupt, severe unilateral thigh pain that may be associated with less severe hip or lower back pain. The pain persists for days to months and is followed shortly thereafter by progressive weakness and atrophy in the affected limb. Weight loss is often associated. Treatment is typically supportive, as the disorder stabilizes over weeks to months followed by slow recovery. There is no clear evidence that immunotherapy helps in the long-term neurologic outcome. Though this is a monophasic syndrome, significant residual weakness and incomplete recovery often result.

Inclusion body myositis presents initially with slowly progressive painless deep finger flexor, grip, and knee extension weakness, a pattern not seen in this patient. Motor neuron disease can present with asymmetric limb weakness but is more often painless and slowly progressive and can be accompanied by bulbar symptoms. Facioscapulohumeral muscular dystrophy (FSHD) can present with asymmetric weakness but is often slowly progressive and painless. Scapular winging can be seen in both FSHD and some types of limb girdle muscular dystrophy. An immune-mediated necrotizing myopathy typically causes symmetric subacute weakness with markedly elevated serum creatine kinase.

Glenn MD, Jabari D. Diabetic lumbosacral radiculoplexus neuropathy (diabetic amyotrophy). *Neurol Clin.* 2020 Aug;38(3):553-564.

Singleton JR, Smith AG, Russell J, et al. Polyneuropathy with impaired glucose tolerance: implications for diagnosis and therapy. *Curr Treat Options Neurol.* 2005 Jan;7(1):33-42.

Dyck PJ, Windebank AJ. Diabetic and nondiabetic lumbosacral radiculoplexus neuropathies: new insights into pathophysiology and treatment. *Muscle Nerve.* 2002 Apr;25(4):477-491.

Question

299 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroanatomy

The suprascapular nerve innervates the supraspinatus and infraspinatus muscles. The supraspinatus muscle is responsible for the first 15° of humeral abduction, and the infraspinatus muscle externally rotates the arm.

Brazis PW, Masdeu JC, Biller J (eds). Localization in Clinical Neurology. 8th ed. Philadelphia: Wolters Kluwer; 2022.

303 ADULT NEUROLOGY

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

Critical care myopathy is an under-recognized disorder characterized by selective loss of myosin from myofibers. Also known as myosin-losing myopathy, this disorder is most commonly seen in critically ill patients treated with corticosteroids and neuromuscular blockers. The other options listed (merosin, laminin, dystrophin, actin) are muscle proteins that are not selectively affected in critical illness myopathy.

Birch TB. Neurocritical care. Continuum Lifelong Learning Neurol. 2021 Oct;27(5):1344-1364.

309 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Atlantoaxial subluxation is a known complication of rheumatoid arthritis that occurs due to inflammatory destruction of the synovial joint around the odontoid process. Symptoms range from isolated neck pain to a severe progressive cervical myelopathy with upper and lower extremity weakness and sensory loss. Dural arteriovenous fistula, Chiari malformation, necrotizing vasculitis, and cervical spinal cord demyelination are not specifically associated with rheumatoid arthritis.

Pavlakis PP. Rheumatologic disorders and the nervous system. Continuum Lifelong Learning Neurol. 2020 Jun;26(3):591-610.

Question

313 ADULT NEUROLOGY**Clinical Aspects of Disease**

Symmetric proximal weakness that improves with repeated testing is most consistent with Lambert–Eaton myasthenic syndrome (LEMS), a disorder associated with malignancy in two thirds of patients, most commonly small cell lung cancer. Diabetic polyneuropathy or amyotrophy is in the differential diagnosis, but in neither case does strength improve with exercise, a diagnostic finding in LEMS.

Hypothyroidism may cause polyneuropathy and myopathy, which can manifest as proximal weakness, but the weakness does not improve with exercise. Monoclonal gammopathy is associated with polyneuropathies in which weakness is predominantly distal rather than proximal and does not improve with repetitive testing. Temporal arteritis presents with headache and vision loss along with myalgias, but true muscle weakness and reflex abnormalities do not occur.

Schoser B, Eymard B, Datt J, et al. Lambert-Eaton myasthenic syndrome (LEMS): a rare autoimmune presynaptic disorder often associated with cancer. *J Neurol*. 2017 Sep;264(9):1854-1863.

318 NO SPECIFIED PATIENT AGE**Neuroanatomy**

The most likely cause of anhidrosis (inability to sweat) following a viral illness is immune-mediated injury to the postganglionic sympathetic cholinergic fibers, which innervate the eccrine sweat glands and are responsible for thermoregulatory sweating. These fibers release acetylcholine, which acts on the muscarinic receptors in the sweat glands to stimulate sweating.

The other types of autonomic fiber listed (postganglionic parasympathetic cholinergic fibers, postganglionic sympathetic adrenergic fibers, preganglionic parasympathetic cholinergic fibers, and preganglionic sympathetic adrenergic fibers) do not directly innervate the sweat glands.

Vanderah TW, Gould DJ (eds). Nolte's *The Human Brain*. 8th ed. Philadelphia: Elsevier; 2021.

Question

327 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neurophysiology

In a postsynaptic disorder such as myasthenia gravis, rapid (50–Hz) repetitive stimulation results in no change in the compound muscle action potential. A >10% decrement is typically seen on slow (3–Hz) repetitive stimulation. A significant increment on rapid repetitive stimulation is typically seen in presynaptic disorders such as Lambert–Eaton myasthenic syndrome (LEMS) and botulism. This patient's age (36 years) and female sex make myasthenia gravis more likely than LEMS.

Katzberg HD, Abraham A. Electrodiagnostic assessment of neuromuscular junction disorders. *Neurol Clin.* 2021 Nov;39(4):1051-1070.

336 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

Acute onset of diplopia, ataxia, and areflexia is classic for the Miller Fisher variant of Guillain–Barré syndrome (GBS). Most patients with this syndrome or with oculomotor involvement of GBS have antibodies to GQ1b.

Acetylcholine receptor antibodies are associated with myasthenia gravis. GM1 antibodies are seen in multifocal motor neuropathy, a chronic disorder without cranial nerve abnormalities. Voltage-gated calcium channel antibodies occur in Lambert–Eaton myasthenic syndrome, a chronic disorder without ataxia. Aquaporin–4 antibodies are present in neuromyelitis optica, which may appear similar to Miller Fisher syndrome, but these are typically associated with hyperreflexia as it is a CNS disorder.

Habib AA. Guillain–Barré syndrome. *Continuum Lifelong Learning Neurol.* 2023 Oct;29(5):1327-1356.

Bril V. Neuromuscular complications of diabetes mellitus. *Continuum Lifelong Learning Neurol.* 2014 Jun;20(3):531-544.

Question

347 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neurophysiology**

Paramyotonia congenita is a hereditary disorder characterized by muscle stiffness that worsens with repetitive movements and is exacerbated by cold temperatures. The EMG shows myotonic discharges. Symptoms can last for hours but usually are so mild that treatment is not required.

Complex repetitive discharges occur in a variety of nerve and muscle disorders and, therefore, lack the diagnostic specificity of myotonic discharges. Fasciculations occur in disorders of the motor neuron or its axon, not in muscle disease. Myokymic discharges are rare and are most closely associated with radiation-induced plexopathy. They are attributed to hyperexcitability of peripheral motor axons and do not occur in muscle disease. Finally, neuromyotonia is a very rare phenomenon characterized by rapid repetitive firing of motor units and is due to hyperexcitability of motor nerve terminals.

Trivedi JR. Muscle channelopathies. Continuum Lifelong Learning Neurol. 2022 Dec 1;28(6):1778-1799.

Statland J, Barohn R. Muscle channelopathies: the nondystrophic myotonias and periodic paralyses. Continuum Lifelong Learning Neurol. 2013 Dec;19(6):1598-1614.

355 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Of the medications listed, corticosteroids are preferred for pregnant patients with myasthenia gravis, if immunosuppression is needed. Pyridostigmine, IVIg, and plasma exchange are also considered safe.

Mycophenolate mofetil and methotrexate are associated with a risk of fetal malformation and should be discontinued before and during pregnancy. There is an increased risk of prematurity with cyclosporine. Currently, only case reports are available that describe eculizumab being safely used in pregnancy; thus, there is insufficient evidence of the safety eculizumab in pregnancy to recommend its use.

Ciafaloni E. Myasthenia gravis and congenital myasthenic syndromes. Continuum Lifelong Learning Neurol. 2019 Dec;25(6):1767-1784.

Question

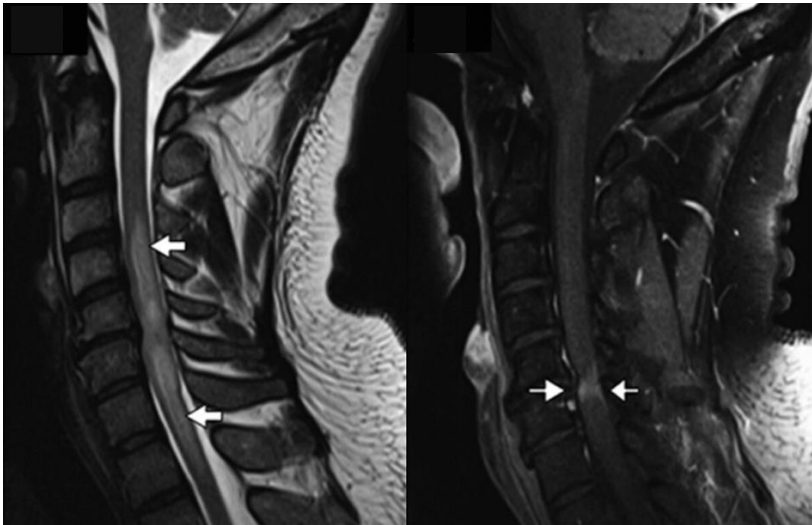
363 ADULT NEUROLOGY**Clinical Aspects of Disease**

This patient's history (chronic neck pain after a fall years ago, progressive weakness, gait imbalance) is suggestive of a cervical myelopathy. A normal jaw jerk localizes a corticospinal tract lesion caudal to the brainstem. MRI findings are characteristic of spondylotic cervical myelopathy with probable spinal cord ischemia (spinal canal stenosis, fusiform hyperintensity, and pancake-like enhancement).

Neither the neurologic examination nor MRI imaging findings are typical for ALS (no upper motor neuron signs above lower motor neuron signs, MRI enhancement); metastatic cancer (no pain, no edema, temporal profile, intramedullary location, lack of ring or homogenous enhancement pattern); neuromyelitis optica spectrum disorder (absence of area postrema, brainstem syndrome, longitudinally extensive transverse myelitis); or vitamin B12 deficiency (lack of posterior column and corticospinal tract T2 hyperintensity or atrophy).

Tavee JO, Levin K. Myelopathy due to degenerative and structural spine disease. *Continuum Lifelong Learning Neurol.* 2015 Feb;21(1):52-66.

Image credit: Flanagan EP, Marsh RW, Weinshenker BG. Teaching NeuroImages: "Pancake-like" gadolinium enhancement suggests compressive myelopathy due to spondylosis. *Neurology.* 2023 Apr;100(16_supplement_1):S229.



Question

373 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuropathology**

Chronic steroid myopathy may develop in Cushing disease or during chronic steroid treatment. Moderate to severe atrophy of type 2 fibers is a consistent finding in both iatrogenic steroid myopathy and in Cushing disease with myopathy. Perifascicular atrophy is characteristic of dermatomyositis. Ragged-red fibers are seen in mitochondrial myopathies. Tubular aggregates are seen in a variety of hereditary and acquired myopathies but are not characteristic of steroid myopathy. Rimmed vacuoles are seen in several myopathies, most notably in inclusion body myopathy.

Dubowitz V, Sewry CA, Oldfors A (eds). *Muscle Biopsy: A Practical Approach*. 5th ed. Philadelphia: Elsevier; 2021.

395 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Azathioprine is a purine analogue immunosuppressant metabolized through an enzyme called thiopurine methyltransferase (TPMT). Genetic variants of this enzyme can cause poor tolerability of azathioprine, leading to hepatotoxicity or myelosuppression. Azathioprine hypersensitivity syndrome (AHS), or an idiosyncratic reaction to azathioprine, can occur within the first 2 to 4 weeks of starting the medication and is independent of both *TPMT* genetic status and medication dose. AHS mimics infectious and cutaneous syndromes.

It is important to immediately stop this medication and provide supportive care. Continuation or re-introduction of the medication can lead to multiple organ failure and cardiovascular collapse and thus can be life threatening. Patients must be advised of these side effects when starting this medication. Often, this side effect of azathioprine is mistaken for sepsis or diabetic ketoacidosis. Diabetic ketoacidosis can present with nausea and vomiting and abdominal pain but also severely elevated blood glucose levels.

Pyridostigmine toxicity would present with bradycardia, diarrhea, excessive salivation, and vomiting as part of a cholinergic crisis. Myasthenic crisis would present with worsening symptoms of myasthenia gravis that could include diplopia, ptosis, dyspnea, dysphagia, dysarthria, and muscle weakness. There can be overlapping symptoms as noted; however, initiation of azathioprine is the most likely cause of the patient's new symptoms (ie, nausea and vomiting, rash, fever, abdominal pain).

Moya-Martínez C, Núñez-Hipólito L, Barrio-González S, et al. Azathioprine hypersensitivity syndrome: report of two cases with cutaneous manifestations. *Clin Exp Dermatol*. 2021 Aug;46(6):1097-1101.

Question

399 NO SPECIFIED PATIENT AGE**Neuroanatomy**

The baroreceptor reflex helps to regulate blood pressure by detecting changes via baroreceptors mostly located in the carotid sinus and aortic arch. Information from the carotid sinus travels via the glossopharyngeal nerve while that from the aortic arch is carried by the vagus nerve. All baroreceptor afferents terminate in the nucleus tractus solitarius, which then projects to the ventrolateral medulla. A decrease in blood pressure results in an increase in sympathetic tone and decrease in parasympathetic tone, with an increase in blood pressure producing the opposite effect.

Benarroch EE. Physiology and pathophysiology of the autonomic nervous system. *Continuum Lifelong Learning Neurol.* 2020 Feb;26(1):12-24.

Question

3 ADULT NEUROLOGY

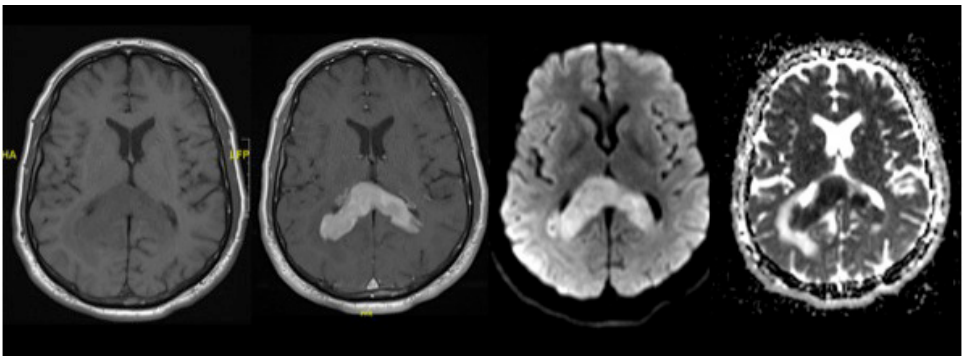
CORE KNOWLEDGE

Neuroimaging

The lesion involves the splenium and demonstrates homogenous enhancement and diffusion restriction. Abscess may demonstrate diffusion restriction but typically shows ring enhancement. Glioblastoma typically shows ring enhancement but not diffusion restriction.

The lesion shown does not fit a vascular territory to suggest ischemic stroke, and though ischemic stroke may demonstrate enhancement, this is a subacute finding, at which point ADC darkness would be unlikely to persist. The location is atypical for metastasis. Metronidazole toxicity can affect the splenium but does not cause this extent of enhancement.

Klein JP, Dietrich J. Neuroradiologic pearls for neuro-oncology. *Continuum Lifelong Learning Neurol.* 2017 Dec;23(6):1619-1634.



85 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

The clinical findings (recent onset of ataxia, nausea, and vomiting) and imaging studies (large isointense lesion within the cerebellar vermis, multiple small lesions coating the spinal cord) in this 6-year-old patient are consistent with a pediatric brain tumor, arising within the cerebellum and producing "drop metastases" along the spinal axis.

Hemangioblastoma often arises within the cerebellum but is more typically seen in adults. The other tumors listed (pilocytic astrocytoma, meningioma, hemangioblastoma, dysplastic gangliocytoma) may be seen in children; however, only medulloblastoma exhibits the biologically aggressive behavior (rapid growth and metastases) described here.

WHO Classification of Tumours Editorial Board. *WHO Classification of Tumours of the Central Nervous System*. 5th ed. Lyon, France: International Agency for Research on Cancer; 2021.

Question

124 ADULT NEUROLOGY

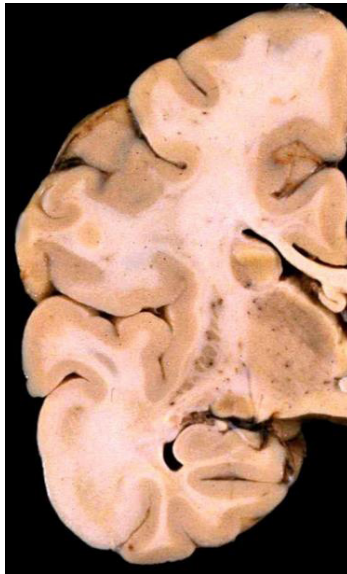
SUBSPECIALTY KNOWLEDGE

Neuropathology

The gross specimen shows multiple areas of focal cortical dysplasia (FCD), which can occur in the context of tuberous sclerosis complex (TSC), other mTOR-opathies, or as a result of somatic (not germline) mutations. In FCD type 2b, a type seen in TSC, the hallmark histopathology includes dysplastic neurons (enlarged and abnormally shaped neurons) and balloon cells (very large glassy eosinophilic cells with laterally displaced nuclei of mixed glial neuronal lineage).

Oligodendroglia hyperplasia has a different pathology and is associated with mild malformation of cortical development with oligodendroglial hyperplasia and epilepsy (MOGHE). Microglial nodules are clusters of activated brain macrophages seen in multiple disease contexts, including Rasmussen encephalitis. Meningeal angiomatosis is seen in Sturge Weber syndrome. Dysmyelination is a nonspecific finding seen in many brain development disorders.

Guerrini R, Barba C. Focal cortical dysplasia:an update on diagnosis and treatment. Expert Rev Neurother. 2021 Nov;21(11):1213-1224.



Question

156 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

Leptomeningeal metastases (LM) can occur in up to 10% of patients with metastatic breast cancer and presents with multifocal symptoms involving the brain, cranial nerves, and spinal roots. Neither CSF cytology nor MRI is adequately sensitive to be used in isolation. The first diagnostic test for suspected LM is brain and spinal cord MRI. With negative imaging findings, CSF evaluation is the next most helpful diagnostic study.

Kumthekar P, Le Rhun E. Brain metastases and leptomeningeal disease. *Continuum Lifelong Learning Neurol.* 2023 Dec;29(6):1727-1751.

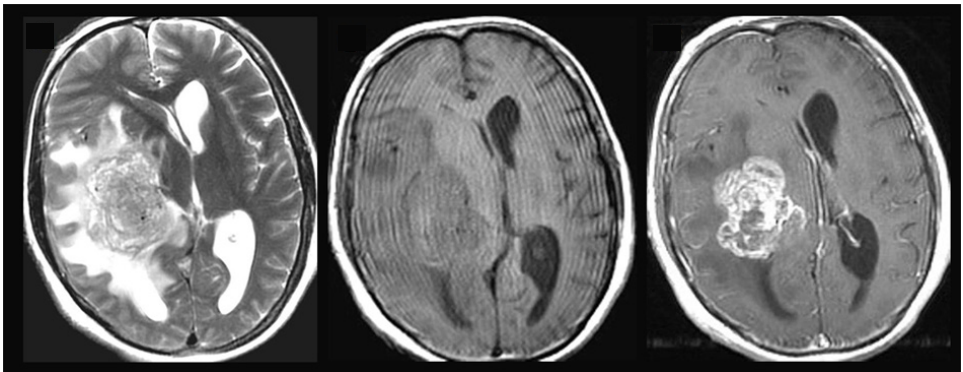
244 ADULT NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

This patient's imaging studies show a single, large infiltrative multicystic enhancing mass with vasogenic edema. This appearance is most frequently seen with a glioblastoma. No vascular structures are seen as expected in an arteriovenous malformation. An infectious process, such as toxoplasmosis and metastasis, would more likely have a ring pattern of enhancement and not the large complex multicystic pattern seen here.

Salzman KL, Jhaveri MD, Osborn AG (eds). *Diagnostic Imaging: Brain*. 5th ed. Philadelphia: Elsevier; 2025.



Question

274 PEDIATRIC NEUROLOGY

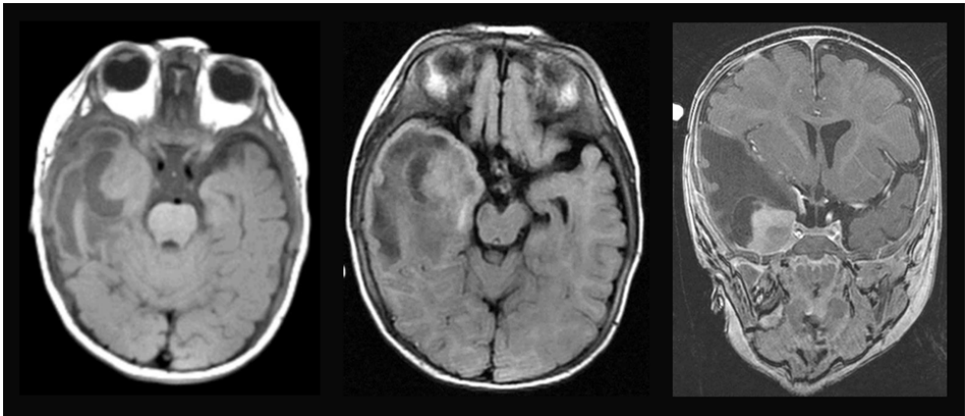
SUBSPECIALTY KNOWLEDGE

Neuroimaging

This patient's lesion is a cystic mass with a mural nodule in the temporal lobe. Classically, ganglioglioma is described as a cystic mass with a mural nodule in approximately 40% of diagnosed cases. Ganglioglioma is a member of the class of mixed neuronal-glial cell neoplasms, which as a class are less aggressive than pure glial cell neoplasms. Most gangliogliomas occur in children (as in this 6-year-old patient) and young adults and arise in the temporal lobe. Gangliogliomas in this location commonly present with drug-resistant focal epilepsy.

The imaging features shown here are not consistent with arteriovenous malformation or hematoma. Similarly, the findings do not fit well with abscess and most likely would have a different clinical presentation than chronic epilepsy. Mesial temporal sclerosis is manifested by tissue loss rather than a mass lesion.

Passaro EA. Neuroimaging in adults and children with epilepsy. Continuum Lifelong Learning. 2023 Feb;29(1):104-155.



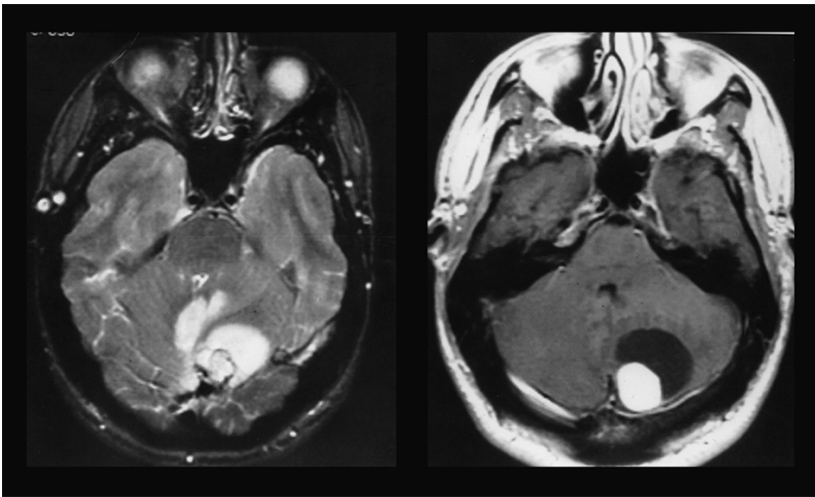
Question

342 ADULT NEUROLOGY

Neuroimaging

This patient's MRI scans show a cystic cerebellar hemispheric mass with an enhancing mural nodule. The T2-weighted image suggests the presence of small vessels within the mural nodule as hypointense flow voids. The mass is intra-axial and infratentorial. These findings are most consistent with a cerebellar cystic hemangioblastoma. The differential diagnosis includes ganglioglioma, medulloblastoma, cystic astrocytoma, and abscess. Demyelinating plaques may present as a mass lesion, but this is unusual and would present with ring enhancement, not this pattern.

Jordan J, Gerstner ER. Imaging of brain tumors. Continuum Lifelong Learning Neurol. 2023 Feb;29(1):171-193.



Question

389 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroimaging

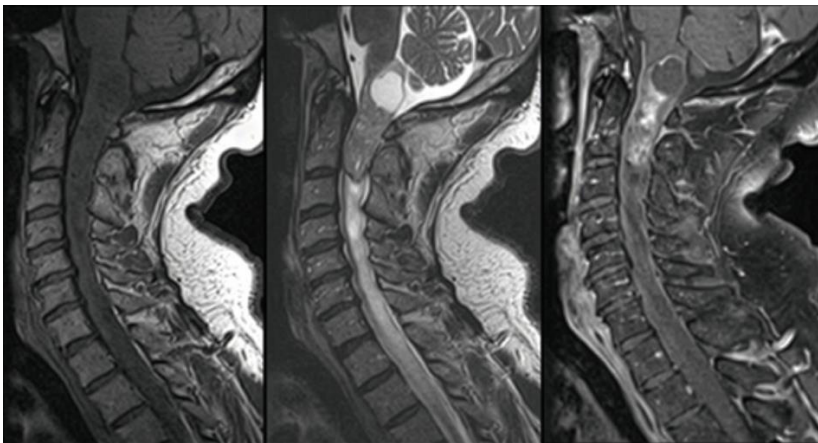
The presence of a well-defined intramedullary mass with contrast enhancement, T2 hyperintensity and T1 hypointensity in the cord, and cystic components adjacent to the solid enhancing portions of the tumor are typical of ependymoma. Also typical is subtle T2 hypointensity along the margins of the well-defined solid portion of the tumor.

Spinal cord abscesses have an acute onset, often with fever, and their course develops rapidly enough that they do not attain the massive size of the lesion shown. The very gradual onset (several years) of this patient's ataxia is not typical for cavernous hemangiomas, which typically present with acute or stepwise progression due to mass effect from bleeding.

Intramedullary metastases in the spinal cord are rare, occurring in only 1% to 3% of all patients with terminal cancer; if a melanoma metastasis had occurred in the spinal cord, the clinical decline would have been more rapid than this patient's slow (ie, several year) disease progression.

The degree of mass effect seen here is not typical for multiple sclerosis, and the bulky well-defined mass and the pattern of enhancement are not features seen in multiple sclerosis of the spinal cord.

McFaline-Figueroa JR. Spinal cord neoplasms. *Continuum Lifelong Learning Neurol.* 2024 Feb; 30(1):99-118.



Question

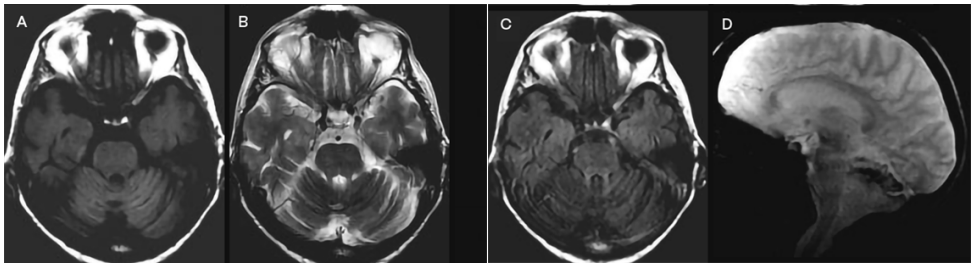
13 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroimaging

Typical features of superficial siderosis of the CNS are deafness and cerebellar ataxia, which are reported in 90% of patients. The MRI scans show hemosiderin deposition along the upper cerebellar folia with adjacent cerebellar atrophy. Hemosiderin deposition in the subpial layers of the brain and spinal cord causes parenchymal damage by chronic slow or repeated bleeding into the subarachnoid space.

Weidauer S, Neuhaus E, Hattingen E. Cerebral superficial siderosis: etiology, neuroradiological features and clinical findings. *Clin Neuroradiol*. 2023 Jun;33(2):293-306.



62 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Diagnostic Procedures

This patient has a left relative afferent pupillary defect (RAPD), as demonstrated in the video by the swinging flashlight test. In this case, both pupils constrict when the light is shined into the right eye, but each time the light is shined into the left eye, both pupils dilate. This finding indicates the left optic nerve is not functioning as well as the right optic nerve. An RAPD is an important indicator of an optic neuropathy.

The Edinger–Westphal nuclei and oculomotor nerves are working normally in this patient. With a deficit of the oculomotor nerve, there would be reduced constriction of the pupil on the affected side alone, producing anisocoria (unequal sized pupils) that is more pronounced in light.

Wilhelm H. Disorders of the pupil. *Handb Clin Neurol*. 2011;102:427-466.

Question

80 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

This patient has unidirectional nystagmus (right-beating in all directions of gaze) that diminishes when looking to the left, unilateral abnormal head impulse test, and no skew deviation. This pattern of findings denotes a unilateral peripheral vestibulopathy. The acute time course suggests vestibular neuritis, which can be treated with corticosteroids.

When the acute vestibular syndrome is caused by a posterior circulation stroke, the pattern of nystagmus is usually direction-changing rather than unidirectional, the horizontal head thrust test is usually normal, and there can be an accompanying skew deviation (ie, vertical misalignment of the eyes).

Steenerson KK. Acute vestibular syndrome. *Continuum Lifelong Learning Neurol.* 2021 Apr;27(2):402-419.

109 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Acute angle-closure glaucoma is a neurologic and ophthalmologic emergency characterized by a sudden elevation of intraocular pressure with impaired visual acuity and pupillary reactivity.

Internal carotid artery dissection may lead to an ipsilateral Horner syndrome. Cluster headache may also feature miosis and ptosis. Retinal migraine leads to a monocular visual aura in the context of a migraine attack. Tolosa-Hunt syndrome is idiopathic inflammation in the cavernous sinus that may lead to ophthalmoparesis and pupillary dilation with cranial nerve III involvement.

Filler L, Akhter M, Nimlos P. Evaluation and management of the emergency department headache. *Semin Neurol.* 2019 Feb;39(1):20-26.

Question

140 NO SPECIFIED PATIENT AGE**Diagnostic Procedures**

Ocular flutter, or involuntary conjugate horizontal back to back saccades, is often secondary to cerebellar disorders. Common etiologies include parainfectious, paraneoplastic, autoimmune, toxic/metabolic, and/or structural processes. Idiopathic ocular flutter is rare and a diagnosis of exclusion.

Opsoclonus are chaotic, multidirectional eye movements. Gaze-evoked nystagmus occurs when the eyes are held in a far right or left position, with the fast phase of the nystagmus beating in the direction of the gaze. Ocular neuromyotonia is a rare eye movement disorder characterized by brief, painful involuntary spasms of the eye muscles. Ocular bobbing is a pathologic finding of rapid downward jerk of both eyes with a slow return to a neutral position.

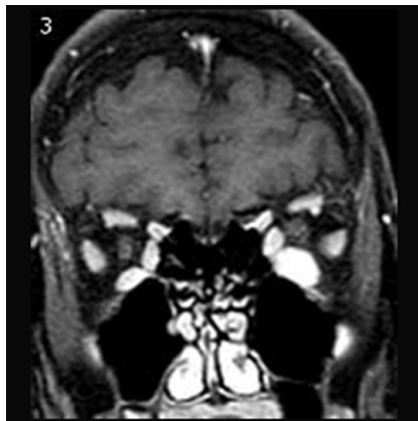
Gold D. Nystagmus and saccadic intrusions. *Continuum Lifelong Learning Neurol.* 2025 Apr;31(2):503-526.

Video credit: Gordon L, Dinkin M. Paraneoplastic syndromes in neuro-ophthalmology. *Continuum Lifelong Learning Neurol.* 2019 Oct;25(5):1401-1421.

167 ADULT NEUROLOGY**Neuroimaging**

This patient's MRI scan shows enlargement of the extraocular muscles, involving the left more than the right inferior and medial recti. Multiple extraocular muscle enlargement can also be seen with ocular myositis and orbital pseudotumor. In thyroid eye disease, typically the enlargement of the extraocular muscles, the tendinous insertions of the muscles are often spared. Evidence of increased orbital fat and crowding at the orbital apex may also be seen, which can contribute to optic nerve compression.

Johnson BT, Jameyfield E, Aakalu VK. Optic neuropathy and diplopia from thyroid eye disease: update on pathophysiology and treatment. *Curr Opin Neurol.* 2021 Feb;34(1):116-121.



Question

194 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

This patient's symptoms are most consistent with a right fourth nerve palsy. A patient with acquired fourth nerve palsy would use compensatory head positions to decrease the vertical diplopia that would include the following: 1) head tilt to opposite shoulder (head tilt is away from the side of the lesion), 2) head turn downward with chin depressed and eyes upward, and 3) face turn to the opposite side.

Brazis PW, Masdeu JC, Biller J (eds). *Localization in Clinical Neurology*. 8th ed. Philadelphia: Wolters Kluwer; 2022.

217 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Superior canal dehiscence syndrome can present with either acoustic or vestibular symptoms. The latter may be triggered by loud noises (Tulio phenomenon) or Valsalva maneuvers that last for seconds or minutes.

Cogan syndrome is an autoimmune-mediated cause of vestibuloauditory dysfunction and interstitial keratitis. Episodes consist of vertigo, ataxia, nausea, tinnitus, and hearing loss.

Ménière disease presents with episodic vertigo (lasting minutes to hours) accompanied by unilateral auditory symptoms, specifically tinnitus, hearing loss, and a sensation of fullness.

Vestibular neuronitis is believed to be a viral or postviral disorder affecting the vestibular segment of cranial nerve VIII, leading to acute, severe, and persistent vertigo, spontaneous nystagmus, and gait instability, but with preserved hearing function.

Ishiyama G. Selected otologic disorders causing dizziness. *Continuum Lifelong Learning Neurol*. 2021 Apr;27(2):468-490.

Question

242 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient has a presentation typical of Ménière disease, characterized by vertigo, tinnitus, hearing loss, and sudden falling spells (Tumarkan otolithic crisis). Ear fullness would also be a characteristic symptom.

Ishiyama F. Selected otologic disorders causing dizziness. *Continuum Lifelong Learning Neurol.* 2021 Apr;27(2):468-490.

Fife TD. Dizziness in the outpatient care setting. *Continuum Lifelong Learning Neurol.* 2017 Apr;23(2):359-395.

262 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

This patient has components of Parinaud syndrome (conjugate upgaze paresis, convergence-retraction nystagmus, and light-near dissociation of the pupils). A lesion producing these findings occurs in the midbrain tectal region and is often the result of extra-axial compression on the quadrigeminal plate (particularly the superior colliculi). Pineal region masses and obstructive hydrocephalus may also cause this syndrome.

Blumenfeld H. *Neuroanatomy Through Clinical Cases.* 3rd ed. Sunderland: Sinauer Associates/Oxford University Press; 2021.

286 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient has arteritic acute ischemic optic neuropathy, in which typical findings are a swollen disc and retinal pallor. The mechanism is likely to be giant cell arteritis based on his history of sudden vision loss, 3-week history of headache, 10-lb (4.5-kg) weight loss, and myalgias.

Biousse V, Newman NJ. Ischemic optic neuropathies. *N Engl J Med.* 2015 Jun 18;372(25):2428-2436.

Arnold AC. Pediatric ophthalmology, neuro-ophthalmology, genetics. In: Lorenz B, Borruat FX (eds). *Ischemic Optic Neuropathies.* Berlin Heidelberg: Springer; 2008, pp 19-35.

Question

343 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Clinical Aspects of Disease

This patient has bilateral internuclear ophthalmoplegia. There is slowed adduction of each eye with rapid horizontal eye movements. The slowed adduction occurs because of a lesion affecting the medial longitudinal fasciculus, which connects the abducens nucleus in the pons to the medial rectus subnucleus in the midbrain. The most likely diagnosis in this patient is multiple sclerosis.

Virgo JD, Plant GT. Internuclear ophthalmoplegia. *Pract Neurol*. 2017 Apr;17(2):149-153.

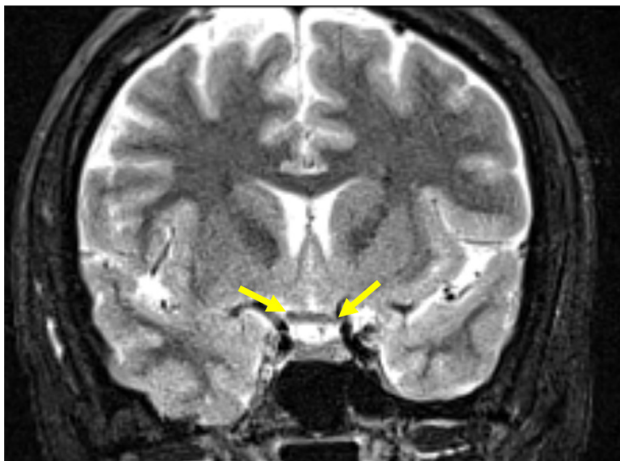
368 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroimaging

The optic chiasm is identified on MRI as situated above the pituitary sella. It is usually slightly hypointense compared to pituitary tumors on T2-weighted views.

Greenberg JO (ed). *Neuroimaging: A Companion to Adams and Victor's Principles of Neurology*. 2nd ed. New York: McGraw-Hill, 1999.



Question #

31 NO SPECIFIED PATIENT AGE

Neurophysiology

To calculate motor conduction velocity, subtract distal latency from proximal latency for the conduction time between stimulation sites. The distance between the two stimulation sites is then divided by the conduction time between the two sites to equal meters/sec (distance over time). Distal latencies are not converted to conduction velocities, as they include time for the impulse to traverse the nerve, cross the neuromuscular junction, and depolarize the muscle. Thus, distal latencies are left as raw latencies and compared to norms.

Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

86 NO SPECIFIED PATIENT AGE

Contemporary Issues

The Health Insurance Portability and Accountability Act (HIPAA) protects a patient's protected health information (PHI), except when allowed in writing to be shared with other individuals. One of the major purposes of the Privacy Rule is to define and limit the circumstances in which an individual's PHI may be used or disclosed by covered entities. A covered entity may not use or disclose PHI, except either: (1) as the Privacy Rule permits or requires; or (2) as the individual who is the subject of the information (or the individual's personal representative) authorizes it in writing.

Summary of the HIPPA Privacy Rule. U.S. Department of Health and Human Services. <http://www.hhs.gov/ocr/privacy/hipaa/understanding/summary/index.html>. Reviewed March 2025. Accessed February 24, 2026.

122 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Contemporary Issues

Patient-reported outcome measures are tools to assess patients' perspectives on their outcomes, such as health-related quality of life, symptoms, functional status, and their health behaviors. These assessments should be completed by patients or, when patients are unable to complete their assessments, by a proxy who is in close contact with the patient.

Cella D, Hahn EA, Jensen SE, et al. Patient-reported outcomes in performance measurement. Research Triangle Park (NC): RTI Press; 2015 Sep. <https://www.ncbi.nlm.nih.gov/books/NBK424381/>. Published September 2015. Accessed February 24, 2026.

Centers for Medicare & Medicaid Services. Patient-reported outcome measures. <https://mmshub.cms.gov/sites/default/files/Patient-Reported-Outcome-Measures.pdf>. Published May 2022. Updated November 2025. Accessed February 24, 2026.

Question

155 ADULT NEUROLOGY**Neurophysiology**

Subclinical rhythmic electrographic discharge is most commonly seen during wakefulness in adults older than age 50. It most commonly appears on EEG as sharply contoured theta activity in the temporoparietal regions and may appear to evolve. Despite its epileptiform appearance, it is a benign variant of undetermined significance that does not seem to be associated with epilepsy, encephalopathy, or medication use.

Husain AM (ed). Current Practice of Clinical Electroencephalography. 5th ed. Philadelphia: Wolters Kluwer Health; 2023.

182 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroimaging

Apparent diffusion coefficient imaging (ADC) is a measure of the ability of water molecules to randomly diffuse within the brain environment. In various disease states (eg, stroke, infection), diffusion is limited and is demonstrated as dark signal on ADC sequences. In other states (eg, encephalomalacia), there is increased diffusion of water and is demonstrated as bright signal.

Louis ED, Mayer SA, Noble JM (eds). Merritt's Neurology. 14th ed. Philadelphia: Wolters Kluwer; 2021.

206 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

Voltage-gated calcium channels in the presynaptic motor neuron are activated by change in membrane electrical potential when an action potential propagates via sodium channel depolarization to the nerve terminus. The influx of calcium causes primary vesicles containing acetylcholine anchored to the presynaptic cell membrane to fuse, releasing acetylcholine into the presynaptic cleft. The mechanism by which the calcium triggers vesicle fusion has not been clearly established.

Amato AA, Doughty CT, Paganoni S, et al. Amato and Russell's Neuromuscular Disorders. 3rd ed. New York: McGraw-Hill Medical; 2025.

Question

221 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Contemporary Issues

In a case-control study, participants with the outcome of interest (cases) and a comparison population without the outcome of interest (controls) are identified. The exposure histories of cases and controls are then compared. The case-control design is more efficient than the cohort study for studying rare diseases because study participants are sampled based on their disease status, and more readily enable the evaluation of multiple exposures of interest.

Randomized controlled trials are not well suited to the study of rare outcomes; rather, these are more appropriate for the study of potential treatments or preventive strategies. The stated interest in risk factors raises the question of equipoise.

The cohort study design is preferred when the exposure of interest is rare or when there are multiple potential outcomes of interest. Finally, cross-sectional studies examine the prevalence of a single exposure in relation to disease prevalence within a given time period.

Aschengrau A, Seage GR. *Essentials of Epidemiology in Public Health*. 4th ed. Burlington, MA: Jones & Bartlett Learning; 2020.

Hayden GF, Kramer MS, Horwitz RI. The case-control study: a practical review for the clinician. *JAMA*. 1982 Jan 15;247(3):326-331.

Question

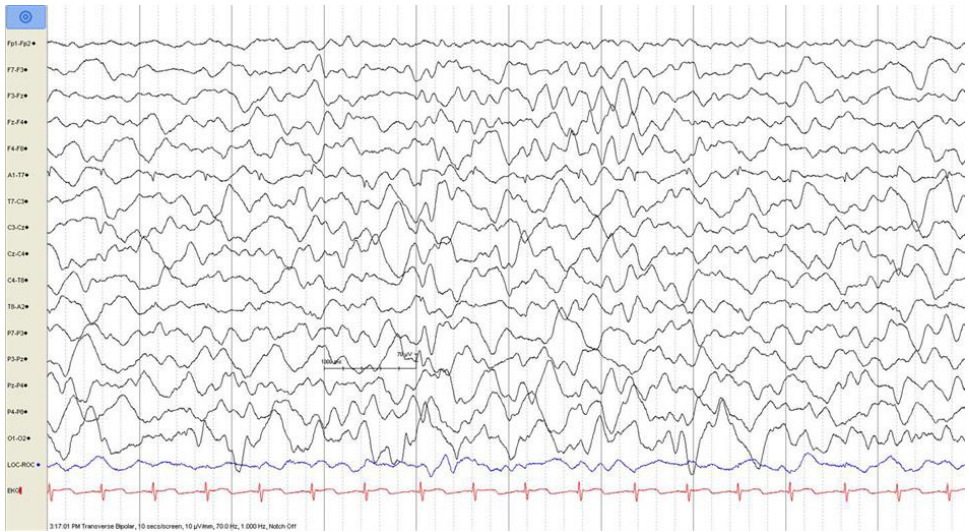
231 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neurophysiology

The rhythmic sharp transients seen in this EEG represent artifact—a common finding that is often particularly prominent in referential derivations.

Husain AM (ed). Current Practice of Clinical Electroencephalography. 5th ed. Philadelphia: Wolters Kluwer Health; 2023.

**234** NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Contemporary Issues

A near-miss or close call is an event or situation that does not produce patient injury—but only by chance. A never event is a serious, largely preventable incident that should not occur if the available preventive measures have been implemented.

Woodier N, Burnett C, Moppett I. The value of learning from near misses to improve patient safety: a scoping review. J Patient Saf. 2023 Jan;19(1):42-47.

Question

267 NO SPECIFIED PATIENT AGE**Contemporary Issues**

Randomization has two main goals in an experimental study or randomized controlled trial: it ensures that treatment assignment occurs in an unbiased fashion; and it produces treatment and comparison groups with similar baseline characteristics and therefore controls for both measured and unmeasured confounding characteristics.

Aschengrau A, Seage GR. Essentials of epidemiology in public health. 4th ed. Burlington, MA: Jones & Bartlett Learning; 2020.

Holmberg MJ, Andersen LW. Adjustment for baseline characteristics in randomized clinical trials. JAMA. 2022 Dec 6;328(21):2155-2156.

275 NO SPECIFIED PATIENT AGE**Neurophysiology**

Somatosensory evoked potentials assess the functional integrity of the dorsal columns. Transcranial motor evoked potentials may be used to assess functional integrity of the lateral corticospinal tract.

Husain AM (ed). Illustrated Manual of Clinical Evoked Potentials. New York: Demos Medical/Springer Publishing; 2017.

314 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Contemporary Issues**

Medication reconciliation is the process of identifying the most accurate list of all medications that a patient is taking, including name, dosage, frequency, and route, by comparing the medical record to an external list of medications obtained from the patient, hospital, or other provider.

Shenoy AM, Bennett A, Segal AZ. Tips and resources for medication reconciliation. Continuum Lifelong Learning Neurol. 2019 Apr;25(2):543-549.

Question

350 NO SPECIFIED PATIENT AGE**Contemporary Issues**

The FDA requires that a generic drug meet the same standards as the original innovator drug, including the following characteristics: the same active ingredients as the innovator drug, though inactive ingredients may vary; identical in strength, dosage form, and route of administration; the same use indications; bioequivalency; the same batch requirements for identity, strength, appearance, and quality; and manufactured with the same strict standards required for the innovator drug.

US Food and Drug Administration. Generic drugs: questions & answers. [https://www.fda.gov/drugs/frequently-asked-questions-popular-topics/generic-drugs-questions-answers#:~:text=Any%20generic%20medicine%20must%20perform,\(with%20certain%20limited%20exceptions\)](https://www.fda.gov/drugs/frequently-asked-questions-popular-topics/generic-drugs-questions-answers#:~:text=Any%20generic%20medicine%20must%20perform,(with%20certain%20limited%20exceptions).). Updated March 2021. Accessed February 24, 2026.

380 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Contemporary Issues

A 95% confidence interval (CI) provides information about statistical significance, precision, and the range of likely values for the true population parameter of interest: in this case, the hazard ratio [HR].

Statistical significance is indicated based on whether the CI includes the inferential null value. In this case, the results are statistically significant because the 95% CI does not include the null value of 1.00.

Precision is reflected in the width of the 95% CI. Wide confidence intervals reflect reduced precision or small sample size, whereas a narrow confidence interval is indicative of greater precision and often a larger sample size.

Finally, if multiple samples were drawn from the same study population and the same analysis was repeated in these samples, the CI would be expected to contain the true population parameter of interest 95% of the time.

Naimi AI, Whitcomb BW. Can confidence intervals be interpreted? *Am J Epidemiol*. 2020 Jul 1;189(7):631-633.

Elser H, Gottesman RF, Walter AE, et al. Head injury and long-term mortality risk in community-dwelling adults. *JAMA Neurol*. 2023 May 1;80(3):260-269.

Question

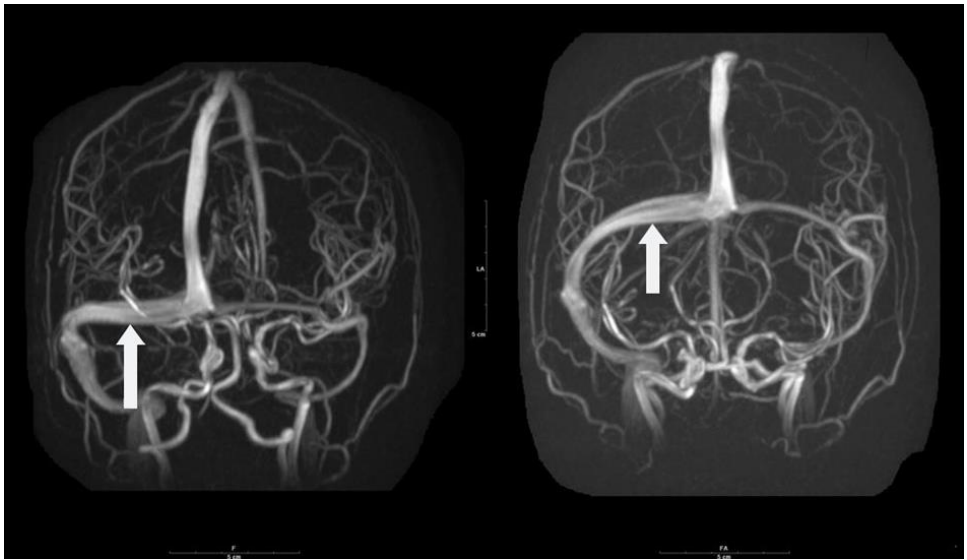
388 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroimaging

The arrow points to the right transverse sinus, which is dominant in this patient. The right transverse sinus is dominant in most individuals.

Dalley AF II, Agur AMR (eds). Moore's Clinically Oriented Anatomy. 9th ed. Philadelphia: Wolters Kluwer; 2022.



Question

18 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Diagnostic Procedures

This patient's presentation raises suspicion for attention-deficit/hyperactivity disorder (ADHD). Criteria for diagnosis include symptom onset before age 12 years and occurrence in two or more settings. A history of inattention, hyperactivity, distractibility, poor academic performance, and/or behavioral problems is characteristic. Emotional dysregulation can also be seen. Next steps in workup consist of clinical interviews with the patient and caregivers and supplemented by validated rating scales completed by both caregivers and teachers.

This patient could also be evaluated for possible seizures, which can present with "zoning out" and inattention, both of which are in the patient's history. However, his routine awake EEG was normal. Additionally, his clear distractibility and ability to easily "snap out" of spells when called significantly lowers the likelihood of an epileptic origin. Obtaining prolonged and sleep-deprived EEG as next steps in workup extend the investigation of an epileptic origin.

Absence seizures are clinically highest on the differential based on the history of brief events with immediate return to baseline. Routine EEG with hyperventilation is extremely high yield in identifying 3-Hz spike and wave absence seizures in an untreated child with childhood absence epilepsy. Given the low clinical concern that this patient's episodes are seizures, however, committing to a prolonged EEG study is considered low yield and thus not the most appropriate next step in workup.

A spell log would be helpful if it was felt that the need for spell capture via EEG would be high yield. However, in this situation, a spell log is not likely to be helpful in determining the cause. Finally, imaging studies are not indicated in this patient, as no focal neurologic deficits are reported during the spells, nor are there signs of neurologic regression. Brain MRI scan is likely to be normal and will not further the patient's evaluation.

Jerome D, Jerome L. Approach to diagnosis and management of childhood attention deficit hyperactivity disorder. *Can Fam Physician*. 2020 Oct;66(10):732-736.

Question

30 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

Functional seizures (psychogenic nonepileptic events) are a type of functional neurologic disorder characterized by paroxysmal events resembling epileptic seizures. These are thought to be correlated to biopsychosocial factors and do not have an electrographic correlate on EEG. Although ictal video-EEG demonstrating no electrographic changes consistent with epileptic seizure is the gold standard to confirm the diagnosis, video review and the ictal EEG are generally sufficient. Additional diagnostic testing is not needed, specifically additional routine EEG and imaging.

There is limited guidance on the assessment and management of functional seizures in the pediatric population. Early recognition is important as it may decrease unnecessary health care utilization and improve quality of life for children and their caregivers. While biopsychosocial factors may be involved in the development of functional seizures, pharmacologic therapy is not the first-line approach to treatment. Referral to a mental health team is preferred for psychological support through behavioral approaches and skills teaching in younger children and cognitive behavioral therapy in older children.

While essential tremor may be high amplitude and low voltage, it is neither episodic nor unilateral. Paroxysmal kinesigenic dyskinesia is episodic, triggered by voluntary movement, but appears dystonic or dyskinetic, not characterized by rhythmic or repetitive movements.

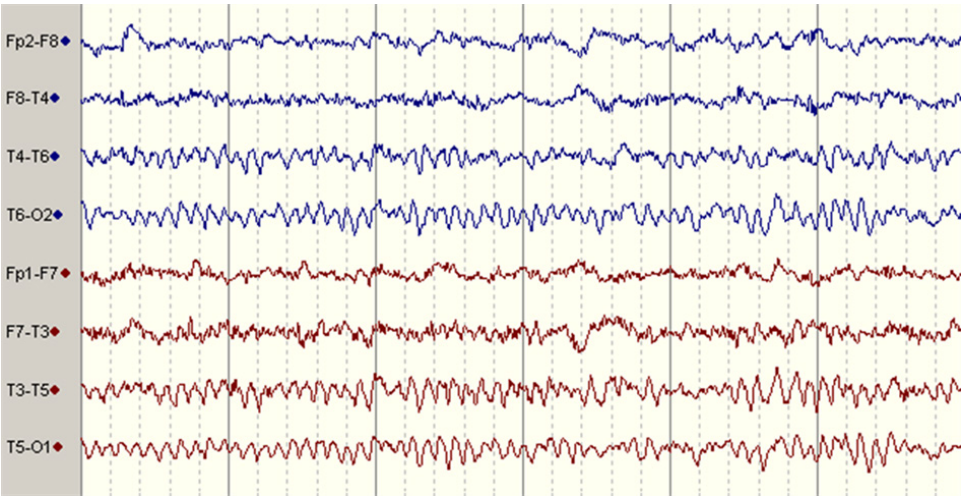
(continues)

Question #

Watson M, Kreuzman J, Zeribi K, et al. The current state of pediatric functional neurological disorder treatment in the United States. *Pediatr Neurol.* 2024 Sep;158:144-155.

Talai A, Freedman DA, Trott K, et al. Results of a national Delphi consensus on the outpatient management of pediatric psychogenic nonepileptic seizures in the United States. *Epil Behav.* 2024 Nov;160:110096.

Reilly C, Jette N, Johnson EC, et al. Scoping review and expert-based consensus recommendations for assessment and management of psychogenic non-epileptic (functional) seizures (PNES) in children: a report from the Pediatric Psychiatric Issues Task Force of the International League Against Epilepsy. *Epilepsia.* 2023 Dec;64(12):3160-3195.



71

NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

This patient with multiple sclerosis and neuropathic pain has steroid-induced psychosis, a disorder that can develop any time during treatment with corticosteroids and is not dose-dependent. People with a history of psychiatric disorders may be at a slightly higher risk for this disorder. The initial treatment of choice is discontinuing the corticosteroids. If this is not possible because of the necessity of ongoing corticosteroid treatment, antipsychotic medications can be used judiciously for short-term treatment. Discontinuation of other medications generally is not required unless the patient has a known risk of psychosis. Divalproex acid and electroconvulsive therapy do not play a role in treatment of this disorder.

Huynh G, Reinert JP. Pharmacological management of steroid-induced psychosis: a review of patient cases. *J Pharm Technol.* 2021 Apr;37(2):120-126.

Question

83 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

Psychiatric comorbidities are common in children and adolescents with epilepsy, the most common of which are anxiety disorders, depression, and attention-deficit/hyperactivity disorder (ADHD). For generalized anxiety disorder, excessive anxiety or worry that is difficult to control is seen over a period of 6 months, affecting a number of activities on most days. In addition, a child or adolescent should experience or report at least one of the following: restlessness, fatigue, inattention, irritability, muscle tension, rumination, or sleep disturbance.

Major depressive disorder, bipolar disorder, obsessive-compulsive disorder, and ADHD are psychiatric comorbidities in children and adolescents with epilepsy, but none of these presents with excessive worry. Obsessive-compulsive disorder describes a pattern of unwanted thoughts or fears (obsessions) that lead to repetitive behaviors (compulsions). Major depressive disorder and bipolar disorder are mood disorders. ADHD describes a condition characterized by inattention, impulsivity, and hyperactivity.

Kwon CS, Rafati A, Ottman R, et al. Psychiatric comorbidities in persons with epilepsy compared with persons without epilepsy: a systematic review and meta-analysis. *JAMA Neurol.* 2025 Jan;82(1):72-84.

119 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Apathy is the one behavioral symptom that predictably increases in a linear manner with disease progression in Huntington disease. Apathy, irritability, and depression are each associated with distinct longitudinal profiles. Apathy progresses over time and across disease stages. Irritability also increases significantly, but only in early stages of Huntington disease. Depression does not increase significantly at any stage of disease. Obsessive-compulsive behaviors are frequently reported in Huntington disease, including in otherwise asymptomatic patients.

Thompson JC, Harris J, Sollom AC, et al. Longitudinal evaluation of neuropsychiatric symptoms in Huntington's disease. *J Neuropsychiatry Clin Neurosci.* 2012 Winter;24(1):53-60.

van Duijn E, Craufurd D, Hubers AAM, et al; European Huntington's Disease Network Behavioural Phenotype Working Group. Neuropsychiatric symptoms in a European Huntington's disease cohort (REGISTRY). *J Neurol Neurosurg Psychiatry.* 2014 Dec;85(12):1411-1418.

Question

169 ADULT NEUROLOGY**Neuroscience and Mechanism of Disease**

A presentation of new-onset psychosis is concerning for schizophrenia in a 19-year-old patient, but NMDA receptor (NMDAR) encephalitis is also a consideration. Importantly, individuals who have psychiatric diagnoses are more likely to test positive for anti-NMDAR antibodies than healthy controls, suggesting that some individuals diagnosed with primary psychiatric disorders can have undiagnosed autoimmune encephalitis.

Individuals with schizophrenia or schizoaffective, bipolar, or major depressive disorders are collectively about three times more likely to have elevated NMDAR antibody titers compared with healthy controls. In one study, up to 10% of individuals with atypical schizophrenia had neuronal cell surface antibodies, including NMDAR antibodies. Patients who test positive for anti-NMDAR antibodies and respond to immunotherapy should be diagnosed with anti-NMDAR encephalitis, not schizophrenia. Testing for NMDAR antibodies is vital because the treatment approaches and prognosis differ dramatically. Anti-NMDAR encephalitis often responds to immunosuppression and has the potential for full recovery, whereas schizophrenia requires long-term psychiatric management.

The other antibodies listed do not typically result in a limbic encephalitis: CRMP5 is associated with optic neuropathy and chorea; GAD is associated with stiff-person syndrome; Ri is associated with opsoclonus-myoclonus syndrome; and Yo is associated with paraneoplastic cerebellar degeneration.

Pearlman DM, Najjar S. Meta-analysis of the association between N-methyl-D-aspartate receptor antibodies and schizophrenia, schizoaffective disorder, bipolar disorder, and major depressive disorder. *Schizophr Res.* 2014 Aug;157(1-3):249-258.

Ellul P, Groc L, Tamouze R, et al. The clinical challenge of autoimmune psychosis: Learning from anti-NMDA receptor autoantibodies. *Front Psychiatry.* 2017 Apr 19;8:54.

Lennox BR, Plamer-Cooper EC, Pollak T, et al. Prevalence and clinical characteristics of serum neuronal cell surface antibodies in the first-episode psychosis: a case-control study. *Lancet Psychiatry.* 2017 Jan;4(1):42-48.

Pollak TA, McCormack R, Peakman M, et al. Prevalence of anti-N-methyl-D-aspartate (NMDA) receptor [corrected] antibodies in patients with schizophrenia and related psychoses: a systematic review and meta-analysis. *Psychol. Med.* 2014 Sep;44(12):2475-2487.

Question

178 NO SPECIFIED PATIENT AGE**Treatment/Management**

Depression is a known side effect of and black box warning for tetrabenazine, an FDA-approved medication for management of chorea associated with Huntington disease. Tetrabenazine acts as a vesicular monoamine transporter 2 inhibitor, which impairs the packaging of monoamines (including dopamine, norepinephrine, and serotonin) into vesicles, thus depleting effective monoamine supply and increasing the risk of depression. The potential for this side effect should be carefully considered when choosing a medication for chorea in this psychiatrically vulnerable population.

Termsarasab P. Chorea. *Continuum Lifelong Learning Neurol.* 2019 Aug;25(4):1001-1035.

190 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Clinical Aspects of Disease**

Problems with interpersonal relationships, fear of abandonment, alternating between idealizing and devaluing people close to them, impulsive outbursts of anger, suicidal gestures, associated depression, and frequent dissociative states are all commonly seen in borderline personality disorder. The DSM-5 has maintained a similar conceptual framework for diagnosis.

People with histrionic personality disorder generally display flirtatious, seductive, or emotional behavior to gain the approval of others. Dependent personality disorder is characterized by being excessively needy or dependent. People with schizoid personality disorder exhibit aloof, blunted, isolated, disengaged, and distant behavior. An inability to relate or connect to others as a result of fantastical or imaginary beliefs, superstitions, or eccentric behaviors is characteristic of schizotypal personality disorder.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5th Edition. Arlington, VA: American Psychiatric Association; 2013.

Leichsenring F, Fonagy P, Heim N, et al. Borderline personality disorder: A comprehensive review of diagnosis and clinical presentation, etiology, treatment, and current controversies. *World Psychiatry.* 2024 Feb;23(1):4-25.

Question

218 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Catatonia is a complex neuropsychiatric syndrome characterized by immobility, behavioral disturbances, and autonomic dysfunction. This syndrome occurs in the context of many underlying psychiatric and medical disorders, including neurodegenerative disorders. Although catatonia can develop in association with any neurodegenerative dementia, it more commonly occurs in patients with frontotemporal dementia (FTD).

Once potential reversible medical conditions have been addressed, treatment with a benzodiazepine such as lorazepam should be initiated in all patients with nonmalignant catatonia. Electroconvulsive therapy (ECT) should be tried only if patients have a partial response or do not respond to a benzodiazepine challenge. Early initiation of ECT is recommended in malignant catatonia.

Antipsychotic medications generally should be avoided in patients with catatonia. While limited evidence supports a role for clozapine in catatonia associated with psychosis, it is not first-line therapy. Bromocriptine is a dopamine agonist sometimes used in the management of neuroleptic malignant syndrome but is not recommended in patients with nonmalignant catatonia. While SSRIs are used to manage behavioral symptoms in FTD, they are not effective in managing catatonia.

Câmara Pestana P, Estibeiro MJ, Côrte-Real B, et al. Catatonia in dementia: a systematic review of case reports and case series. *Am J Geriatr Psychiatry*. 2024 Nov;32(11):1297-1308.

Rogers JP, Oldham MA, Fricchione G, et al. Evidence-based consensus guidelines for the management of catatonia: recommendations from the British Association for Psychopharmacology. *J Psychopharmacol*. 2023 Apr;37(4):327-369.

247 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Clinical Aspects of Disease

Primary gain refers to internal rewards from a behavior. Secondary gain refers to external rewards such as avoiding employment or gaining financial compensation. Factitious disorder is a psychological condition in which a person assumes the role of a patient to receive internalized rewards without apparent external rewards. In contrast, malingering is defined as receiving benefits that are externalized, such as seeking shelter, financial compensation, or documents for legal action. Receiving sympathy from medical staff, undergoing unnecessary medical procedures, relief of anxiety from medical symptoms, and receiving attention and care by physicians are examples of primary, not secondary, gain.

Mason XL. Challenges to the diagnosis of functional neurological disorder: feigning, intentionality, and responsibility. *Neuroethics*. 2023;16(1):2.

Question

258 ADULT NEUROLOGY

CORE KNOWLEDGE

Neuroscience and Mechanism of Disease

The most likely diagnosis in this patient is serotonin syndrome, a potentially life-threatening disorder resulting from hyperstimulation of 5-hydroxytryptamine (5-HT) receptors. The diagnosis is based on the Hunter criteria in which a patient has a history of exposure to a serotonergic medication and at least one of the following symptoms: spontaneous clonus, inducible clonus with agitation and diaphoresis, ocular clonus with agitation and diaphoresis, tremor and hyperreflexia, hypertonia, temperature $>100.4^{\circ}\text{F}$ (38°C) with ocular and inducible clonus. Symptoms are seen within hours to days following administration of drugs that elevate serotonin concentration in combination or in overdose.

Management includes immediate discontinuation of serotonergic agents, hydration, and supportive care for respiratory and cardiac symptoms, fever, and hypertension. Medications and supplements that can contribute to this disorder include monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, tricyclics, serotonin modulators, St. John's wort, tryptophan, and levodopa. Drugs of abuse, including amphetamines, cocaine, and 3,4-methylenedioxy-methamphetamine (MDMA), can also cause this syndrome.

Neuroleptic malignant syndrome occurs with all drugs that affect the central dopaminergic system, including dopamine agonists and levodopa. The classic triad involves the autonomic nervous system (fever in 100% of patients), the extrapyramidal system (rigidity), and cognitive changes. Because this patient is afebrile and cogwheel rigidity was not described, neuroleptic malignant syndrome is not as likely as serotonin syndrome.

Tetanus is caused by the inability to release glycine from Renshaw interneurons and is characterized by painful sustained muscle contractions, usually with extension of the back. Inhibition of acetylcholinesterase causes excessive salivation, lacrimation, urination, diaphoresis, gastrointestinal upset, and emesis (SLUDGE syndrome).

Simon LV, Keenaghan ML. Serotonin syndrome. [Updated 2022 July 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-.

Question

285 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

The Capgras delusion is one of the more common misidentification syndromes in which a patient believes a loved one has been replaced by an imposter, usually with malevolent intent. This delusion can be seen in many psychiatric disorders (including schizophrenia and psychotic depression), as well as in neurodegenerative disorders (including Alzheimer disease and Parkinson disease dementia).

Fregoli syndrome is another misidentification syndrome that is almost the exact opposite of Capgras syndrome. In this syndrome, patients may have a sense of familiarity with strangers but cannot quite recognize them because patients believe them to be in disguise. Patients who believe they are dead are said to have the Cotard delusion. Charles Bonnet syndrome is the occurrence of visual hallucinations in the setting of deteriorating vision. Dorian Gray syndrome is defined as excessive preoccupation with one's own appearance accompanied by difficulties coping with the aging process, including the requirements of maturation.

Pandis C, Agrawal N, Poole N. Capgras delusion: a systemic review of 255 published cases. *Psychopathology*. 2019;52(3):161-173.

301 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

Postictal psychosis can occur in patients with epilepsy, usually in those with intractable seizures between 13 and 22 years after epilepsy onset, consistent with this 40-year-old patient's history of long-standing refractory temporal lobe epilepsy. Psychotic symptoms emerge hours to days after breakthrough seizures. Patients who experience bilateral focal seizures with evolution of tonic-clonic movements are at particularly high risk. Patient stabilization may require benzodiazepines and antipsychotic medications, though definitive treatment involves seizure control.

Postictal agitation is an unlikely diagnosis as it occurs immediately after seizure termination. Profound confusion, restlessness, wandering behavior (poriomania), and in some cases severe aggression are features. EEG may reveal slowing overlying the seizure focus. Ictal psychosis also is unlikely given the static, nonepisodic quality of the

(continues)

Question

patient's symptoms. Ictal psychosis can be a rare manifestation of seizures, though symptoms coincide with seizure activity, which typically lasts 30 seconds to 3 minutes. In addition, a brief EEG in this patient was normal.

A primary psychiatric disorder is less likely in this patient, given the temporal relationship to seizures. Substance-induced psychosis is unlikely given his negative toxicology screening, taken with a history more suggestive of postictal psychosis.

Benjamin S, Basovic L, Romero JM, et al. Case 37-2024: a 41-year-old man with seizures and agitation. *N Engl J Med*. 2024 Nov 28;391(21):2036-2046.

Widdess-Walsh P, Devinsky O. Historical perspectives and definitions of the postictal state. *Epilepsy Behav*. 2010 Oct;19(2):96-99.

319 NO SPECIFIED PATIENT AGE**CORE KNOWLEDGE****Clinical Aspects of Disease**

Panic disorder is manifested by recurrent panic attacks, whereas phobias are strong, emotionally charged aversions to specific activities, places, or things. If this patient was inordinately worried about being involved in a car crash, it would be appropriate to diagnose the specific phobia *amaxophobia*, which is the fear of riding in cars. This patient, however, sometimes experienced episodes while riding in a car but also sometimes while at home.

Social phobia is a fear of appearing ridiculous to others and can be manifested as a fear of completing routine activities including eating, drinking, and speaking in the presence of others. If a patient reports being terrified of how other drivers will appraise his or her driving, social phobia would be a more appropriate diagnosis.

Claustrophobia is the fear of enclosed spaces, but in this patient there is no mention of other similar triggers (eg, elevators) for this type of panic attack. Though this patient may have generalized anxiety disorder, not enough information in the history was supplied to support this diagnosis.

Asmundson GJG, Talyor S, Smits JAJ. Panic disorder and agoraphobia: An overview and commentary on DSM-5 changes. *Depress Anxiety*. 2014 Jun;31(6):480-486.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th Edition. Arlington, VA: American Psychiatric Association; 2013.

Question

335 ADULT NEUROLOGY**Treatment/Management**

Bupropion and mirtazapine are associated with the lowest rates of sexual dysfunction. Citalopram, fluoxetine, sertraline, and duloxetine are associated with high rates of sexual dysfunction, ranging from 58% to 73%.

Malhi GS, Bell E, Bassett D, et al. The 2020 Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. *Aust N Z J Psychiatry*. 2021 Jan;55(1):7-117.

358 ADULT NEUROLOGY**CORE KNOWLEDGE****Treatment/Management**

First-generation (typical) antipsychotic medications (eg, haloperidol, chlorpromazine) are more likely to cause extrapyramidal side effects than second-generation (atypical) antipsychotics (eg, olanzapine, risperidone). Among first-generation antipsychotics, the higher potency medications (eg, haloperidol) are more likely to cause extrapyramidal side effects than lower potency medications (eg, chlorpromazine). Clozapine and quetiapine have the least dopamine blockade.

Feldman M, Marmol S, Margolesky J. Updated perspectives on the management of drug-induced parkinsonism (DIP) :insights from the clinic. *Ther Clin Risk Manag*. 2022 Dec;18:1129-1142.

d'Errico A, Strippoli E, Vasta R, et al. Use of antipsychotics and long-term risk of parkinsonism. *Neurol Sci*. 2022 Apr;43(4):2545-2553. Erratum in: *Neurol Sci*. 2022 Apr;43(4):2909.

384 ADULT NEUROLOGY**Treatment/Management**

Patients taking carbidopa/levodopa should not take monoamine oxidase inhibitors, as these interfere with dopamine metabolism and result in dopamine toxicity, increasing the risk of hypertensive crisis and psychiatric side effects such as potential manic or psychotic symptoms.

Teychenne PF, Calne DB, Lewis PJ, et al. Interactions of levodopa with inhibitors of monoamine oxidase and L-aromatic amino acid decarboxylase. *Clin Pharmacol Ther*. 1975 Sep;18(3):273-277.

Question

1 ADULT NEUROLOGY**Diagnostic Procedures|Clinical Aspects of Disease**

This patient's clinical history and video on polysomnogram (PSG) are consistent with isolated REM sleep behavior disorder (RBD). The diagnostic criteria for RBD are as follows: repeated episodes of sleep-related vocalization or complex motor behaviors; behaviors documented by video-polysomnography occur during REM sleep or, based on a clinical history of dream enactment, presumed to occur during REM sleep; REM sleep without atonia on PSG; disturbances not better explained by another current sleep disorder or mental disorder.

Prolonged REM latency and reduced wake after sleep onset are not part of the diagnostic criteria for RBD. Parasomnias that occur during non-REM sleep (ie, NREM parasomnias) are most likely to occur during NREM stage 3 sleep in the first half of the night.

Schenck CH. Update on rapid-eye-movement sleep behavior disorder (RBD): focus on its strong association with α -synucleinopathies. *Clin Transl Neurosci*. 2023 Jun 9;7(3):19.

Irfan M, Schenck CH, Howell MJ. Non-REM disorders of arousal and related parasomnias: an updated review. *Neurotherapeutics*. 2021 Jan;18(1):124-139.

Video credit: Malkani R. REM sleep behavior disorder and other REM parasomnias. *Continuum Lifelong Learning Neurol*. 2023 Aug;29(4):1092-1116.

37 ADULT NEUROLOGY**Treatment/Management**

REM sleep behavior disorder (RBD) is characterized by complex behavioral manifestations in response to dream content that may cause sleep disruption or injuries to the patient or bed partner. Pharmacologic agents have both positive and negative effects on REM sleep muscle atonia and the motor behaviors associated with RBD. Melatonin and clonazepam have limited evidence but are believed to be efficacious. Melatonin should be considered as initial treatment in patients who have cognitive impairment and are at risk of falling or in those who have obstructive sleep apneas. Melatonin has lower potential for dependency. Anticholinesterase inhibitors and dopaminergic agents are not of clear benefit. Monoamine oxidase inhibitors, tricyclic antidepressants, serotonergic synaptic reuptake inhibitors (SSRIs), and noradrenergic antagonists can induce or aggravate RBD symptoms and should be avoided.

Howell M, Avidan AY, Foldvary-Schaefer N, et al. Management of REM sleep behavior disorder: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2023 Apr 1;19(4):759-768.

Alkhachroum A, Der-Nigoghossian CA, Mathews E, et al. Ketamine to treat super-refractory status epilepticus. *Neurology*. 2020 Oct 2;95(16):e2286-e2294.

Question

64 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neurophysiology

The goal of the multiple sleep latency test (MSLT) is to quantify sleepiness during waking hours and to identify the occurrence of REM sleep near sleep onset. The goal of polysomnography (PSG) is to quantify the amount of time spent in various stages of sleep during the night and to document clinically relevant events such as cardiopulmonary abnormalities or abnormal sleep-related motor activity.

Electrooculography, surface EMG of all four limbs, and EEG recording are all used while performing PSG and the MSLT. It is important to perform a PSG the night before MSLT to assess the quality of sleep the night before. Following this sequence is particularly important when assessing for narcolepsy, as sleepiness due to poor quality fragmented sleep could result in an MSLT that appears to indicate narcolepsy.

Arand DL, Bonnet MH. The multiple sleep latency test. *Handb Clin Neurol*. 2019;160:393-403.

Taylor SA Jr. Clinical evaluation of the sleepy and sleepless patient. *Continuum Lifelong Learning Neurol*. 2023 Aug;29(4):1031-1044.

Question #

96 NO SPECIFIED PATIENT AGE

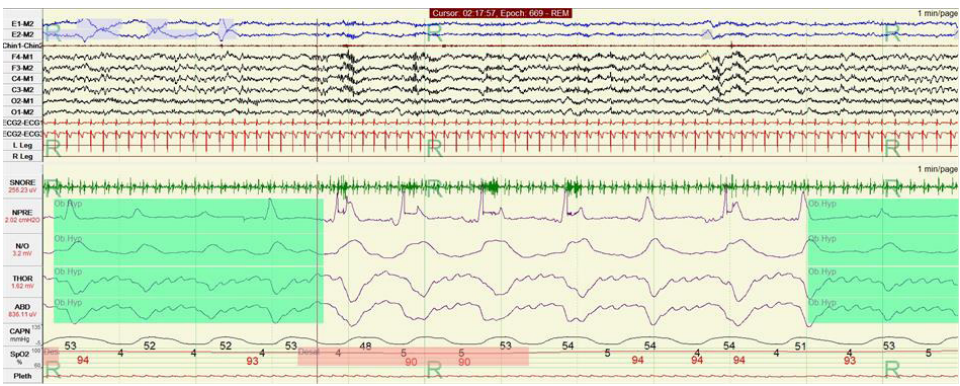
SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease|Diagnostic Procedures

This patient's polysomnogram shows multiple obstructive hypopneas, meeting the criteria for obstructive sleep apnea in adults: five or more predominantly obstructive events per hour of sleep during testing in the setting of daytime sleepiness. An increase in ETCO2 of ≥ 10 mm Hg (compared to awake supine values) to a value exceeding 50 mm Hg for ≥ 10 minutes meets criteria for sleep-related hypoventilation in adults.

Troester M, Quan SF, Berry RB, et al. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. Version 3. Darien, IL: American Academy of Sleep Medicine; 2023.

American Academy of Sleep Medicine. International Classification of Sleep Disorders. 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2023.



112 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Suvorexant, an orexin receptor antagonist that inhibits the wakefulness-promoting orexin neurons of the arousal system, was the first drug used in this class for treatment of insomnia. Additional orexin antagonists include lemborexant and daridorexant.

Zolpidem and zaleplon both bind to the GABA-BZ receptor at a location distinct from either benzodiazepines or barbiturates. The mechanism of action of eszopiclone is unknown but believed to bind to the GABA receptor. Temazepam also binds to the GABA receptor.

Tachibana M, Kanahara N, Oda Y, et al. A retrospective clinical practice study comparing the usefulness of dual-orexin receptor antagonists and a melatonin receptor agonist in patients switching from long-term benzodiazepine receptor agonists. J Clin Sleep Med. 2024 Apr;20(4):603-613.

Question

134 NO SPECIFIED PATIENT AGE**Neuroscience and Mechanism of Disease**

This patient presents with daytime sleepiness and cataplexy, core features of narcolepsy type 1. Of the factors listed, HLA subtype DQB1*0602 is a strong risk factor for narcolepsy type 1, increasing the risk by about 200 and suggesting a possible autoimmune mechanism for the disease.

Biologic sex is not a factor, as males and females are affected by narcolepsy about equally. Narcolepsy rarely runs in families. Such cases, however, are not usually associated with HLA subtype DQB1*0602.

Skull base lesions (eg, craniopharyngiomas) or other lesions that affect the hypothalamus or midbrain may lead to secondary narcolepsy, but in these cases prominent signs of neurologic dysfunction are often seen, given the critical function of these structures. Geographic location has not been identified as a strong risk factor for narcolepsy.

Liblau RS, Latorre D, Kornum BR, et al. The immunopathogenesis of narcolepsy type 1. *Nat Rev Immunol*. 2024 Jan;24(1):33-48.

154 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

REM sleep behavior disorder (RBD) is characterized by complex behavioral manifestations in response to dream content that may cause sleep disruption or injuries to the patient or bed partner. Pharmacologic agents have been reported to have positive and negative impacts on REM sleep muscle atonia and the motor behaviors associated with RBD. Clonazepam is efficacious and well-tolerated by most patients with RBD and should be considered as initial treatment. Monoamine oxidase inhibitors, tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRIs) can induce or aggravate symptoms and should be avoided in patients with RBD.

Lee WJ, Baek SH, Im HJ, et al. REM sleep behavior disorder and its possible prodromes in general population: prevalence, polysomnography findings, and associated factors. *Neurology*. 2023 Dec 4;101(23):e2364-e2375.

Roguski A, Rayment D, Whone AL, et al. A neurologist's guide to REM sleep behavior disorder. *Front Neurol*. 2020 Jul 8;11:610.

Postuma RB, Gagnon JF, Tuineig M, et al. Antidepressants and REM behavioral sleep disorder: isolated side effect or neurodegenerative signal. *Sleep*. 2013 Nov 1;36(11):1579-1585.

Question #

184 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

Night terrors (pavor nocturnus) occur in children between the ages of 3 and 12 years. Episodes are defined as an arousal during slow wave sleep, characteristically occurring during the first half of the night, 30 minutes after the onset of sleep. Children often cry out and are agitated and uncommunicative. Treatment is not necessary, but the episodes often are confused with nocturnal focal seizures with altered consciousness. More than one episode in a night is not typical, however, and should raise concerns about seizures or other parasomnia.

Ashwal S, Pearl PL, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 7th ed. Philadelphia: Elsevier, 2025.

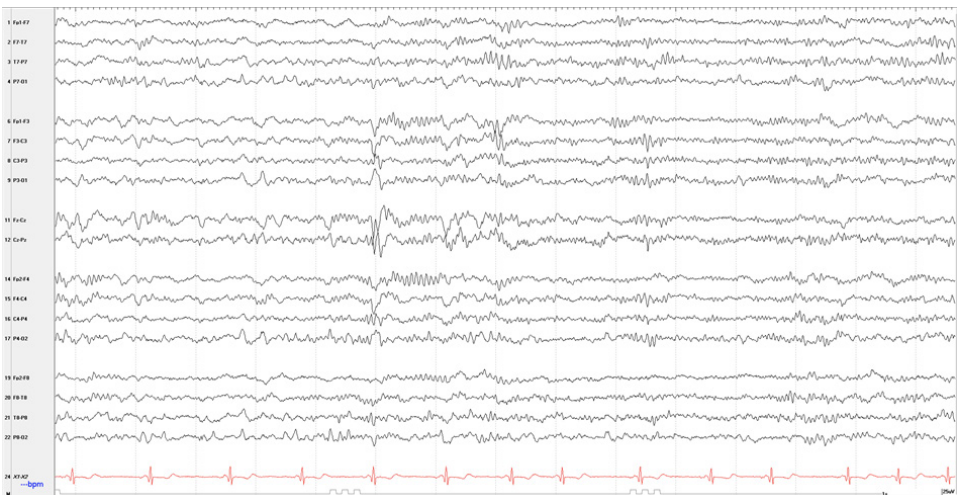
210 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neurophysiology

The EEG tracing shows well-developed sleep spindles, K-complexes, vertex waves, and positive occipital sharp transients of sleep in the absence of high voltage delta, all of which are characteristic findings of stage 2 NREM sleep. These features do not occur during wakefulness. Although vertex waves appear during stage 1 NREM sleep, spindles do not. Stage 3 NREM (slow wave) sleep shows high-voltage delta activity. Background activity during REM sleep resembles that of wakefulness, along with rapid eye movements and sawtooth waves.

Wusthoff CJ, Tatum WO. Normal adult and pediatric EEG. In: Husain AM (ed). Current Practice of Clinical Electroencephalography. 5th ed. Lippincott Williams & Wilkins: Philadelphia, PA; 2024.



Question

240 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Diagnostic Procedures

This patient presents with symptoms typical of restless legs syndrome (RLS): tingling and leg discomfort in the evening and while in bed that is alleviated by ambulation. RLS is associated with iron deficiency and can be managed with iron supplements. Serum ferritin should be measured as part of workup and iron supplements provided if the ferritin level is <75 ng/ml or transferrin saturation is $<20\%$ to 25% .

Folate, copper, pyridoxine, and thiamine deficiency can be associated with peripheral neuropathy, which can be a risk factor for RLS. However, this patient's normal neurologic exam argues against a significant polyneuropathy.

Khan M. Restless legs syndrome and other common sleep-related movement disorders. *Continuum Lifelong Learning Neurol.* 2023 Aug;29(4):1130-1148.

271 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

Current evidence suggests that circadian disruption and neurodegeneration have a bidirectional relationship: the presence of one perpetuates progression of the other. Circadian disruption in the setting of neurodegenerative disorders is attributed to neurodegeneration of central circadian regulatory structures, such as the suprachiasmatic nucleus. This patient's 6-month history of disrupted sleep and notes from the sleep diary shown are most consistent with irregular sleep-wake rhythm disorder.

The diagnostic criteria for this disorder are as follows: The patient or caregiver reports a chronic or recurrent pattern of irregular sleep and wake episodes throughout the 24-hour period, characterized by symptoms of insomnia during the scheduled sleep period (usually at night), excessive sleepiness (napping) during the day, or both. Symptoms are present for at least 3 months. Sleep log and, whenever possible, actigraphy monitoring for at least 7 days (preferably 14 days) demonstrate no major sleep period and multiple irregular sleep bouts with at least three brief sleep periods during a 24-hour period. The sleep

(continues)

Question #

disturbance is not better explained by another current sleep disorder, medical or neurologic disorder, mental disorder, medication use, or substance use disorder.

Videnovic A, Cai A. Irregular sleep-wake rhythm disorder: from the pathophysiologic perspective to the treatment. *Handb Clin Neurol*. 2025;206:71-87.

Shen Y, Lv QK, Xie WY, et al. Circadian disruption and sleep disorders in neurodegeneration. *Transl Neurodegener.* 2023 Feb 13;12(1):8.

American Academy of Sleep Medicine. International Classification of Sleep Disorders. 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2023.

[illegible]

Question #

298 PEDIATRIC NEUROLOGY CORE KNOWLEDGE

Clinical Aspects of Disease

Self-limited epilepsy with autonomic seizures (SeLEAS) (formerly known as Panayiotopoulos syndrome) is a benign (nonlesional) age-related focal epilepsy of childhood. It differs from self-limited epilepsy with centrotemporal spikes (SeLECTs), primarily in episode duration, frequent occurrence of vomiting, and lack of typical centrotemporal spikes on EEG.

Acute confusional migraine may include vomiting, but episodes typically do not begin during sleep and are not associated with epileptiform abnormalities on EEG, as in this patient. Confusion can be seen with familial nocturnal frontal lobe epilepsy, but EEG findings are frontal in location. Low-grade astrocytoma can produce CSF outflow blockage and thus nocturnal headache, but eye deviation and leg abnormalities seen here would be unlikely.

Ashwal S, Pearl PL, et al (eds). Swaiman's Pediatric Neurology. Principles and Practice. 7th ed. Philadelphia: Elsevier, 2025.

Arzimanoglou A, O'Hare A, Johnston M, et al (eds). Aicardi's Diseases of the Nervous System in Childhood. 4th ed. London: Mac Keith Press; 2018.

Wyllie E, Gidal BE, Goodkin HP, et al (eds). Wyllie's Treatment of Epilepsy: Principles and Practice. 7th ed. Philadelphia: Wolters Kluwer; 2021.

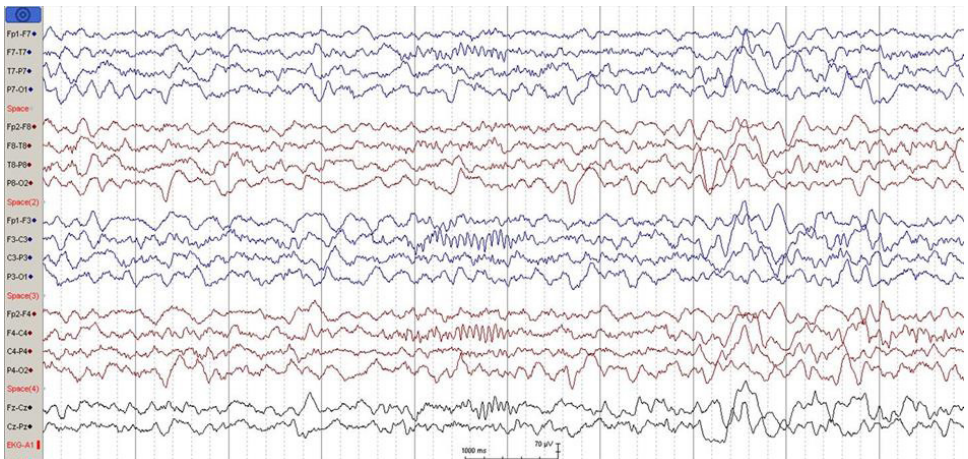
326 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Diagnostic Procedures

The illustration shows sleep spindles which are thought to be generated by the reticular thalamic nucleus.

Trevelyan A, Schevon CA. The cellular basis of EEG. In: Husain AM (ed). Current Practice of Clinical Electroencephalography. 5th ed. Philadelphia: Wolters Kluwer; 2024, pp 3-30.



Question

340 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Clinical Aspects of Disease

REM sleep behavior disorder (RBD) is characterized by lack of atonia during REM sleep and resultant punching, grabbing, talking, or other motions that appear to act out dreams. As periodic limb movements of sleep is a separate entity this is nonspecific. Patients with RBD typically have their eyes closed and do not interact with the environment, unlike sleepwalkers. RBD happens during REM sleep, which occurs later in the night.

Malkani R. REM sleep behavior disorder and other REM parasomnias. *Continuum Lifelong Learning Neurol.* 2023 Aug;29(4):1092-1116.

353 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Diagnostic Procedures

This patient's presentation is concerning for narcolepsy type 1, a diagnosis that requires the following findings: daily periods of irrepressible need to sleep or daytime lapses into drowsiness or sleep; cataplexy and either mean sleep latency of ≤ 8 minutes and two or more sleep-onset REM periods on a multiple sleep latency test or CSF analysis of hypocretin-1 concentration, measured by radioimmunoassay, of < 110 pg/mL (using a Stanford reference sample) or less than one third of mean values obtained in normal subjects with the same standardized assay; and symptoms not better explained by chronic insufficient sleep, a circadian rhythm sleep-wake disorder or other current sleep disorder, mental disorder, medication/substance use or withdrawal.

Gabryelska A, Szmyd B, Maschauer EL, et al. Utility of measuring CSF hypocretin-1 level in patients with suspected narcolepsy. *Sleep Med.* 2020 Jul;71:48-51.

American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2023.

Question

390 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Diagnostic Procedures

The video shows a 7-year-old patient snoring during sleep, followed by a pause in breathing, subsequent snoring/gasping, then resumption of breathing accompanied by arm movements. This pattern is consistent with obstructive sleep apnea, a disorder that can cause daytime fatigue, but in children can also cause hyperactivity and irritability. Sleep apnea can worsen epilepsy, but the arm movements shown are not consistent with seizure activity. In addition, the movements are too brief to be consistent with restless legs syndrome, tonic or generalized tonic-clonic seizures, or sleep terrors, which often occur for an extended period of time overnight.

Solano-Pérez E, Coso C, Castillo-García M, et al. Diagnosis and treatment of sleep apnea in children: a future perspective is needed. *Biomedicine*. 2023 Jun 14;11(6):1708.

Goyal M, Mishra P, Jaseja H. Obstructive sleep apnea and epilepsy: understanding the pathophysiology of the comorbidity. *Int J Physiol Pathophysiol Pharmacol*. 2023 Aug 15;15(4):105-114.

Video credit: Hoban TF. Sleep disorders in children. *Continuum Lifelong Learning Neurol*. 2013 Feb;19(1):185-198.

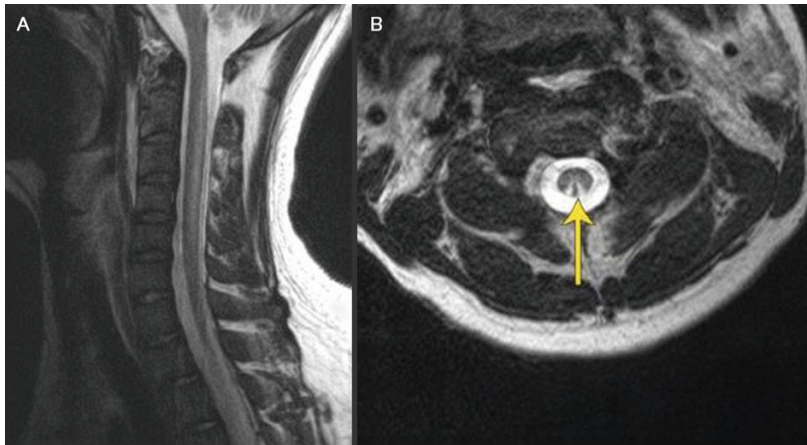
Question

33 NO SPECIFIED PATIENT AGE

Treatment/Management

Nitrous oxide is used for dental procedures as a means of managing pain and anxiety, but it is also misused for recreational purpose in nitrous oxide charger canisters. Nitrous oxide induces oxidation of the cobalt ion of vitamin B12, which results in abnormal myelin synthesis and subacute combined degeneration of the spinal cord. Impaired vibration sense and weakness represent the dysfunction of the dorsal column and the corticospinal tract. Classic MRI findings include T2 hyperintensities in bilateral dorsal columns, an "inverted V" or "rabbit ears" pattern.

Holroyd KB, Berkowitz AL. Metabolic and toxic myelopathies. *Continuum Lifelong Learning Neurol.* 2024 Feb;30(1):199-223.

**40** ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Ethambutol is the drug most frequently associated with toxic optic neuropathy. Toxicity most commonly occurs with doses of at least 25 mg/kg/d and may be more common in patients with renal tuberculosis. Visual loss is insidious and usually symmetrical. Yellow-green dyschromatopsia is the earliest symptom. There is no treatment other than withdrawal of the drug. Isoniazid is associated with seizures in toxic amounts. Pyrazinamide is associated with easy bruising, joint stiffness and swelling, or hepatic issues including jaundice. Liver problems are also common with use of rifampin. Vestibular ototoxicity can be seen with streptomycin, including nausea, vomiting, and vertigo.

Mehta S. Patterns of ethambutol ocular toxicity in extended use therapy. *Cureus.* 2019 Apr;11(4):e4408.

Question

81 ADULT NEUROLOGY

CORE KNOWLEDGE

Diagnostic Procedures

Vitamin B12 (cobalamin) plays an important role in DNA synthesis and neurologic function. Deficiency can lead to a wide spectrum of hematologic, neurologic, and psychiatric manifestations. It is a common cause of macrocytic (megaloblastic) anemia and, in advanced cases, pancytopenia. Neurologic sequelae include paresthesias, peripheral neuropathy, and demyelination of the corticospinal tract and dorsal columns (subacute combined systems disease). Vitamin B12 deficiency can occur after gastric surgery due to loss of intrinsic factor, which is needed for B12 absorption from food.

The diagnosis traditionally has been based on low serum vitamin B12 levels, usually <200 pg/mL (150 pmol/L), along with clinical evidence of disease. Older patients can present with neuropsychiatric disease in the absence of hematologic findings. Vitamin B12 is essential for the conversion of methylmalonic acid (MMA) into succinyl-CoA; without B12, MMA accumulates and thus serum levels will be elevated. Measuring MMA is a more sensitive test of B12 deficiency than serum measurement.

Serum protein electrophoresis is used to evaluate for multiple myeloma and other disorders of serum proteins. Serum thiamine can help detect Wernicke encephalopathy and Korsakoff psychosis. Serum angiotension-converting enzyme is used to diagnose sarcoidosis. Glutamic decarboxylase antibodies are present stiff-person syndrome, cerebellar ataxia, and limbic encephalitis.

Lee SM, Oh J, Chun MR, et al. Methylmalonic acid and homocysteine as indicators of vitamin B12 deficiency in patients with gastric cancer after gastrectomy. *Nutrients*. 2019 Feb 21;11(2):450.

Question

100 NO SPECIFIED PATIENT AGE**Diagnostic Procedures**

This patient's presentation is characteristic of NMDA receptor encephalitis. CSF pleocytosis is a typical finding, whereas MRI findings are less predictable: only 55% of patients will have increased FLAIR or T2 signal in one or more brain regions, without significant correlation with symptoms.

Anti-NMDA receptor encephalitis is diagnosed by CSF anti-NMDA receptor antibodies. Serum testing has lower specificity and sensitivity.

Anti-LGI1 presents in older adults with faciobrachial dystonic seizures and encephalopathy, which may be accompanied by hyponatremia. MRI scans and CSF analysis are generally normal. The diagnosis is made by serum anti-LGI1 antibodies.

Sarkis R, Coffet MJ, Cooper JJ, et al. Anti-N-methyl-D-aspartate receptor encephalitis: a review of psychiatric phenotypes and management considerations: a report of the American Neuropsychiatric Association Committee on Research. *J Neuropsychiatry Clin Neurosci*. 2019 Spring;31(2):137-142.

Dalmau J. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol*. 2008 December;7(12):1091-1098.

116 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

A pregnant woman with intractable vomiting presents with the triad of confusion, nystagmus, and ataxia, suggesting Wernicke encephalopathy due to thiamine deficiency. If not treated acutely with thiamine repletion, she is at high risk for irreversible anterograde memory loss (Korsakoff amnesic syndrome). Aphasia, cortical blindness, hemiparesis, and seizures are not part of the syndrome seen with thiamine deficiency.

Kumar N. Nutrients and neurology. *Continuum Lifelong Learning Neurol*. 2017 Jun;23(3):822-861.

Question

171 NO SPECIFIED PATIENT AGE

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Botulism can be caused by contaminated foods but also by infected wounds. In the United States, parenteral drug use, especially of black tar heroin, is associated with wound botulism. Along with a history of exposure, descending paralysis with autonomic dysfunction are valuable clues to the diagnosis. Symptom onset usually occurs within 1 to 5 days for foodborne and within 10 to 14 days for wound botulism.

Antitoxin helps neutralize toxin still in blood circulation but has a limited effect on reversing paralysis. Anti-GQ1b antibody is used to diagnose Guillain-Barré syndrome, with IVIg a common treatment. HIV can be associated with a variety of neurologic issues but not this patient's combination of symptoms (ie, ptosis, dysconjugate eye movement, suppressed gag reflex, nasal voice, and weakness). Gastric lavage and IV atropine are used to treat overdose of cholinergic drugs or mushrooms. EMG/nerve conduction studies identify peripheral nerve issues, with IV prednisolone used for acute inflammatory conditions.

Awsare S, Chirikian D, Lui F. Wound botulism caused by botulinum neurotoxin type A in a chronic parenteral drug abuser. *Case Rep Neurol*. 2020 Nov;12(3):422-427.

207 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

Serotonin syndrome often presents with autonomic instability, mental status changes, and motor hyperexcitability. It is most commonly associated with combinations of monoamine oxidase inhibitors and selective serotonin reuptake inhibitors. Withdrawal of the offending medications often resolves symptoms, though some patients can progress to rhabdomyolysis, respiratory failure, and seizures.

Uddin MF, Alwies R, Shah SR, et al. Controversies in serotonin syndrome diagnosis and management: a review. *J Clin Diag Res*. 2017 Sep;11(9):OE05-OE07.

Question

228 NO SPECIFIED PATIENT AGE**Neuroscience and Mechanism of Disease**

Organophosphate pesticides phosphorylate the hydroxyl group of the serine residue of acetylcholinesterase, which irreversibly inhibits the function of this enzyme. As a result, acetylcholine accumulates in the synaptic cleft; this continuously binds to the acetylcholine receptor on the muscle cell membrane, increasing the resting muscle cell membrane potential. Voltage-gated sodium channels on the muscle remain in an inactive state at this raised resting muscle cell membrane potential, preventing muscle cell depolarization and contraction.

Jayawardane P, Senanayake N, Dawson A. Electrophysiological correlates of intermediate syndrome following acute organophosphate poisoning. *Clin Toxicol (Phila)*. 2009 Mar;47(3):193-205.

269 NO SPECIFIED PATIENT AGE**Clinical Aspects of Disease**

Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) is a mitochondrial disease characterized by stroke-like episodes, though lesions do not follow vascular boundaries. Lesions are often seen in more posterior structures, and seizures are a frequent complication. CSF analysis may reveal elevated lactate. Urine organic acids may show a generalized aminoaciduria due to renal dysfunction, but this finding typically rules out other inborn errors of metabolism that have specific profiles, such as maple syrup urine disease (which typically presents in infancy).

Viral encephalitis could feature seizures, but CSF results would likely demonstrate a pleocytosis and urine organic acids would be normal. CADASIL results from an autosomal dominant pathogenic variant in *NOTCH3*, with sequential generations of family with migraines and strokes early in life. Multiple sclerosis is characterized by patchy demyelination — in this series of MRI scans, the lesions appear largely cortical with some subcortical involvement.

Tetsuka S, Ogawa T, Hashimoto R. et al. Clinical features, pathogenesis, and management of stroke-like episodes due to MELAS. *Metab Brain Dis*. 2021 Dec;36(8):2181-2193.

Question

300 ADULT NEUROLOGY

Treatment/Management

This patient most likely has zinc toxicity causing copper deficiency, which presents with neuropathy, posterolateral myelopathy (subacute combined degeneration), or both. The other medications listed (sertraline, lisinopril, echinacea, atorvastatin) would not cause neuropathy or myelopathy.

Kumar N. Nutrients and neurology. *Continuum Lifelong Learning Neurol.* 2017 Jun;23(3):822-861.

332 NO SPECIFIED PATIENT AGE

Neurophysiology

Beta frequency coma is usually seen with drug toxicity or anesthesia. Focal vascular insult, posterior fossa lesion, increased intracranial pressure, and NREM stage 4 sleep would not be expected to produce beta activity superimposed on background delta.

Rubin DI (ed). *Clinical Neurophysiology*. 5th ed. New York: Oxford University Press; 2021.

348 ADULT NEUROLOGY

Clinical Aspects of Disease

This patient has a progressive parkinsonian syndrome consistent with hepatocerebral degeneration, a disorder sometimes seen with severe chronic hepatic cirrhosis. Anecdotal case reports have described neurologic improvement in some patients after liver transplant. High signal in the basal ganglia on T1-weighted images is a common finding in patients with cirrhosis but is not specific for hepatolenticular degeneration. Neither of the patient's medications (lactulose and spironolactone) has antidopaminergic or toxic basal ganglia effects and thus do not cause parkinsonian syndromes.

Parkinson disease is possible, but given the patient's age (42 years) and medical history (hepatitis B cirrhosis), it is much less likely than hepatolenticular degeneration. Onset of neurologic Wilson disease is typically the second decade, with tremor, dysarthria, dystonia, cerebellar dysfunction, and psychiatric dysfunction the most common features. Though cerebellar disorders can be seen with gastrointestinal disorders, such as celiac disease, or as a toxic effect of alcohol, this is not the picture of cerebellar impairment.

Baijavant M, Perlmuter JS. Imaging in movement disorders. *Continuum Lifelong Learning Neurol.* 2023 Feb;29(1):194-218.

Question

351 ADULT NEUROLOGY**Clinical Aspects of Disease**

Use of dental fixatives containing zinc or a history of gastric bypass surgery can result in a copper deficiency. Presentation is similar to vitamin B12 deficiency, including neuropathy, myelopathy, or both. Vitamin A deficiency can cause vision loss. Vitamin D deficiency may be associated with myopathy but typically not sensory neuropathy. Iron deficiency can cause restless legs syndrome. Thiamine deficiency can cause a neuropathy but not a myelopathy.

Kumar N. Nutritional neuropathies. *Continuum Lifelong Learning Neurol.* 2023 Oct;29(5):1469-1491.

379 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuropathology

Superficial siderosis is a rare disorder characterized by chronic hemosiderin deposition in areas of the CNS that are in close proximity to the CSF, including the subpial and subependymal regions. The peripheral nervous system is not involved.

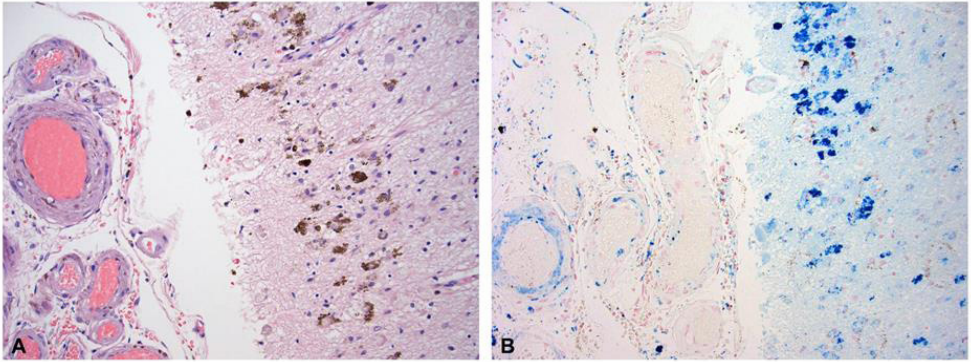
Deposition of hemosiderin principally affects the cerebellum, brainstem, and cranial nerves, but it can also affect the cerebral cortex, basal ganglia adjacent to the ventricles, and spinal cord. Over time, chronic gliosis, neuronal loss, and demyelination develop. The etiology is believed to be chronic subarachnoid hemorrhage, frequently occurring in a slow, intermittent fashion. Subarachnoid hemorrhage has been confirmed by testing in two of three of the roughly 140 cases reported to date. However, the source of hemorrhage could be identified in only 53% of subjects.

(continues)

Question

Clinically, patients usually present several months to years after the initial hemorrhagic event with progressive sensorineural hearing loss, cerebellar ataxia, dementia, and myelopathy. Cranial nerve deficits and hydrocephalus have also been described. Imaging reveals T2 hyperintensity along the superficial aspects of the CNS.

Saha K. Vertigo related to central nervous system disorders. *Continuum Lifelong Learning Neurol.* 2021 Apr;27(2):447-467.



Question

10 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Clinical Treatment

As hypoglycemia can cause focal neurologic deficits, the exclusion of hypoglycemia is a necessary criteria for the use of IV thrombolytics within the 4.5-hour window. While the remainder of the tests listed (INR, PTT, platelets and hemoglobin) are sent, results are not required before administration of IV thrombolytics and should not delay treatment unless the patient history suggests an abnormality.

Patients on anticoagulation with vitamin K antagonists require INR to be <1.7 prior to treatment. Patients with known thrombocytopenia or who are at high risk for thrombocytopenia require platelets of $>100,000$. If the patient is on heparin or low-molecular-weight heparin, then a PTT below the upper limit of normal is required before treatment with thrombolytics.

Warner JJ, Harrington RA, Sacco RL, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke. *Stroke*. 2019 Dec;50(12):3331-3332.

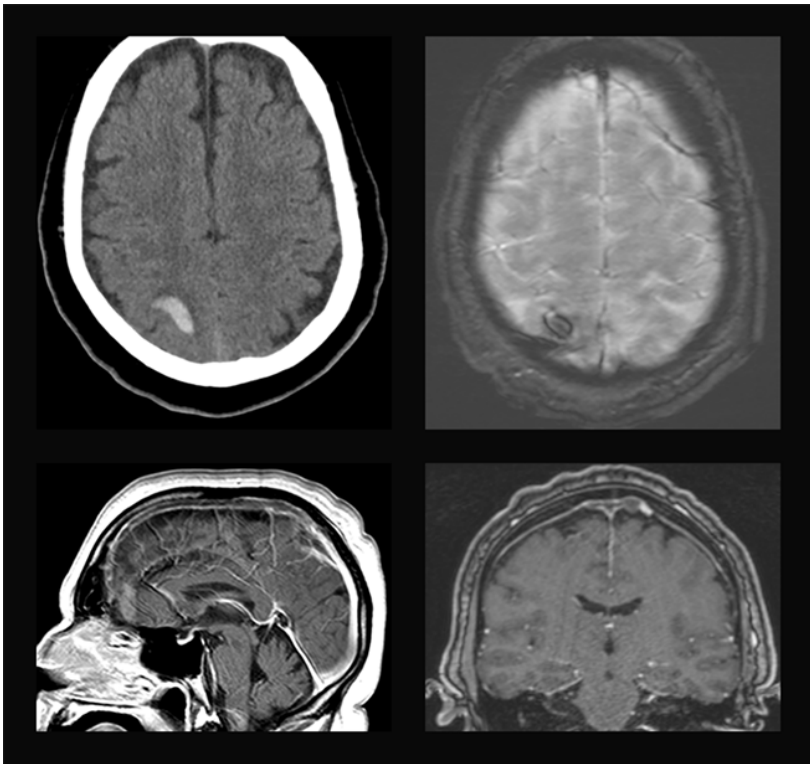
Demaerschalk BM, Kleindorfer DO, Adeoye OM, et al; American Heart Association Stroke Council and Council on Epidemiology and Prevention. Scientific rationale for the inclusion and exclusion criteria for intravenous alteplase in acute ischemic stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2016 Feb;47(2):581-641.

Question

21 NO SPECIFIED PATIENT AGE**Neuroimaging**

The images show a hyperdense superior sagittal sinus and right-sided parietal hemorrhage; lack of enhancement on the postcontrast images is consistent with a dural sinus thrombosis. Intracranial hemorrhage is a sequela of venous thrombosis.

Coutinho JM, Stam J, Canhão P, et al. Cerebral venous thrombosis in the absence of headache. *Stroke*. 2015 Jan;46(1):245-247.



Question

28 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

The combination of the patient's physical exam and neuroimaging findings is consistent with a right anterior choroidal artery infarction. The anterior choroidal artery is a branch of the internal carotid artery and supplies the posterior limb of the internal capsule and the lateral thalamus. The paramedian thalamic artery is a branch of the posterior cerebral artery and supplies the medial thalamus. The ophthalmic artery is a branch of the internal carotid artery and supplies the retina.

Salzman KL, Jhaveri MD, Osborn AG (eds). *Diagnostic Imaging: Brain*. 5th ed. Philadelphia: Elsevier; 2025.



36 ADULT NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

Cerebral amyloid angiopathy (CAA)-related transient focal neurologic episodes (TFNE, also known as "amyloid spells") occur in older adults with cortical superficial siderosis (cSS) and lobar microbleeds on susceptibility-weighted imaging. Episodes are stereotyped, often with positive sensory (tingling) or motor symptoms that spread over minutes, preserved awareness, brief-to-moderate duration (minutes up to about an 1 hour), and no persistent deficit. Vascular/cardiac studies and EEG are frequently noncontributory. Susceptibility-weighted/T2* MRI scans demonstrating lobar microbleeds and cSS support CAA as the etiology.

(continues)

Question

Migraine with aura classically presents with spreading cortical symptoms (visual more than sensory) and is usually followed by headache; new-onset aura at age 87 is atypical, and MRI evidence of lobar microbleeds or cSS argues for CAA.

Focal seizures can mimic TFNE with positive sensory phenomena, but seizures are typically shorter (seconds to a few minutes), may show epileptiform activity (occasionally absent), and are less specifically associated with lobar microbleeds or cSS. The prolonged stereotyped spreading sensory march and the MRI pattern favor CAA.

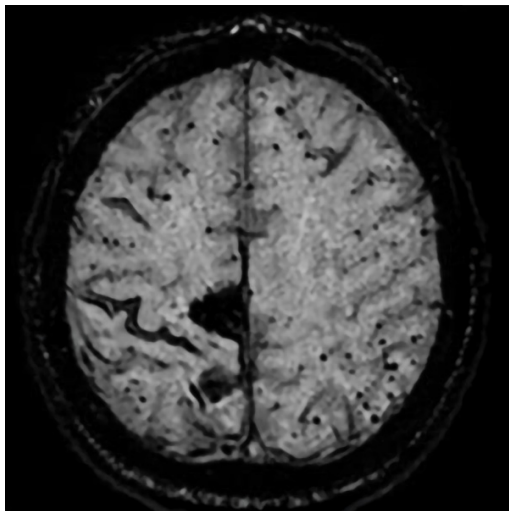
Transient ischemic attack (TIA) typically causes sudden negative deficits (numbness/weakness) in a vascular territory, often abrupt in onset and shorter in duration; vascular imaging may show stenosis and/or an embolic source. The positive spreading sensory symptoms and susceptibility-weighted MRI findings point away from TIA.

Faciobrachial dystonic seizures (caused by LGI1 antibodies) are very brief, often lasting only seconds. Motor or dystonic symptoms are frequent, not prolonged sensory spreading spells. These seizures are linked to LGI1 antibodies and hyponatremia.

Silbert LC. Vascular cognitive impairment. *Continuum Lifelong Learning Neurol.* 2024 Dec;30(6):1699-1725.

Cooperman SS, Shah AK, Rajamani K. Amyloid spells. *Neurol Clin Pract.* 2019 Apr;9(2):e17-e18.

Image credit: Silbert LC. Vascular cognitive impairment. *Continuum Lifelong Learning Neurol.* 2024 Dec;30(6):1699-1725.



Question

46 ADULT NEUROLOGY

CORE KNOWLEDGE

Contemporary Issues

In this case, the patient is unable to provide the necessary history for the neurologist to make a clinical decision regarding thrombolytic therapy, but the electronic health record and the history obtained from EMS supplies the critical components of the history for thrombolytic eligibility. Thrombolytic decision making does not require formal consent from the patient or surrogate decision maker, but instead falls under the doctrine of emergency or implied consent. While the treatment team often requires collateral to determine treatment eligibility, if the treating team can determine essential history to rule out contraindications, thrombolytics can and should be administered even if no surrogate decision maker can be reached for discussion.

Kass JS, Rose RV. Legal liability associated with rtPA administration and surrogate decision makers. *Continuum Lifelong Learning Neurol.* 2020 Apr;26(2):499-505.

50 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroanatomy

This patient has a lateral medullary syndrome caused by occlusion of the posterior inferior cerebellar artery. Ipsilateral signs include loss of pain and temperature on the face, Horner syndrome, and cerebellar signs. Patients also develop contralateral hemibody anesthesia. Nausea and vertigo are related to involvement of the vestibular nuclei. Dysphagia and a diminished gag reflex are associated with nucleus ambiguus.

Brazis PW, Masdeu JC, Biller J (eds). *Localization in Clinical Neurology*. 8th ed. Philadelphia: Wolters Kluwer; 2022.

Question

55 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Treatment/Management

Ticagrelor, an antiplatelet that binds to P2Y₁₂ receptor, acts to prevent adenosine diphosphate-mediated platelet activation and aggregation. The increase in extracellular adenosine leads to contraction of bronchial smooth muscle cells and stimulation of vagal fibers on the bronchial wall, leading to bronchospasm. One of the most common side effects of ticagrelor is shortness of breath. Dyspnea is not a known common side effect of amlodipine, atorvastatin, or aspirin.

A carotid stent could alter baroreceptors; however, this adverse affect has been reported infrequently. Additional symptoms, including flushing and palpitations, would also be expected to accompany dyspnea.

Krakowiak A, Kuleta J, Plech I, et al. Ticagrelor-related severe dyspnoea: mechanisms, characteristic features, differential diagnosis, and treatment. *Clin Med Insights Case Rep*. 2020 Oct 8;13:1179547620956634.

66 ADULT NEUROLOGY

Neuroanatomy

Ischemia of the midbrain tectum can result in visual hallucinations known as peduncular hallucinosis. Unlike other hallucinations, these hallucinations are very realistic, and sometimes it is difficult to convince patients of their "unreal" origin.

Bilateral basilar midbrain ischemia and medullary infarcts may cause quadriparesis; anterior cerebral infarcts may cause paraparesis but neither of these infarcts causes visual hallucinations. Posterior cerebral artery infarcts may cause visual hallucinations (usually not formed) but will not cause paresis. Temporal lobe infarct may cause psychosis but not quadriparesis.

Grotta JC, Albers GW, Broderick JP, et al (eds). *Stroke: Pathophysiology, Diagnosis, and Management*. 7th ed. Philadelphia: Elsevier, 2021.

Question

78 ADULT NEUROLOGY

CORE KNOWLEDGE

Diagnostic Procedures

This patient's head CT scan shows three distinct ischemic strokes of varying ages, a large left posterior carotid artery (PCA) territory subacute to chronic stroke, a chronic small right PCA territory stroke, and an acute to subacute right middle carotid artery territory stroke. This pattern, along with the patient's risk factors, suggests a cardioembolic etiology.

Paroxysmal atrial fibrillation is a common cause of cryptogenic ischemic stroke in elderly patients (about 2% in the population and up to 6% in older adults) but frequently missed on initial ECG or short-term telemetry. Prolonged cardiac monitoring (inpatient telemetry, Holter, or extended patch/event monitor) has the highest diagnostic yield in this setting. Identifying occult atrial fibrillation guides secondary stroke prevention with anticoagulation, which is critical in reducing recurrent stroke risk.

TTE with bubble study can detect low ejection fraction, left ventricle thrombus, endocarditis, or patent foramen ovale (PFO). While useful, TTE in this patient was unremarkable, and repeat imaging is less likely to reveal the etiology compared to prolonged monitoring. In elderly patients, paroxysmal atrial fibrillation remains more common than embolism from PFO.

Lumbar puncture is used for suspected CNS infection, inflammatory, or neoplastic processes. It does not, however, identify common embolic or vascular causes of ischemic stroke in this clinical setting.

Temporal artery biopsy is indicated when giant cell arteritis (GCA) is suspected (eg, headache, jaw claudication, visual symptoms, elevated erythrocyte sedimentation rate/C-reactive protein). The lifetime risk for GCA is 1%, much lower than that for atrial fibrillation. Also, this patient lacks clinical features suggestive of GCA, which makes temporal artery biopsy a low yield study.

(continues)

Question

While hypercoagulability may cause multifocal strokes, antiphospholipid syndrome would be rare in a patient this age (75 years).

Putala J. Ischemic stroke in young adults. *Continuum Lifelong Learning Neurol.* 2020 Apr;26(2):386-414.



88 NO SPECIFIED PATIENT AGE

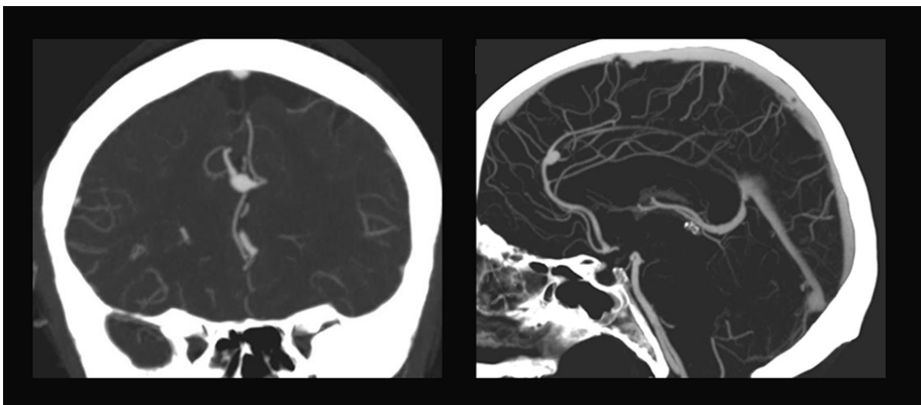
CORE KNOWLEDGE

Neuroimaging

There is a saccular or ovoid enlargement arising along the course of the left anterior cerebral artery just anterior genu of the corpus callosum. This appearance is characteristic of a saccular aneurysm.

Badary A, Alrefaie K, Azab MA, et al. Pericallosal artery aneurysms: an evidence-based analysis of clinical presentations, therapeutic approaches, and outcome. *Neurosurg Rev.* 2025 Apr 3;48(1):348.

Wermer MJH, van der Schaaf IC, Velthuis BK, et al. Yield of short-term follow-up CT/MR angiography for small aneurysms detected at screening. *Stroke.* 2006 Feb;37(2):414-418.



Question

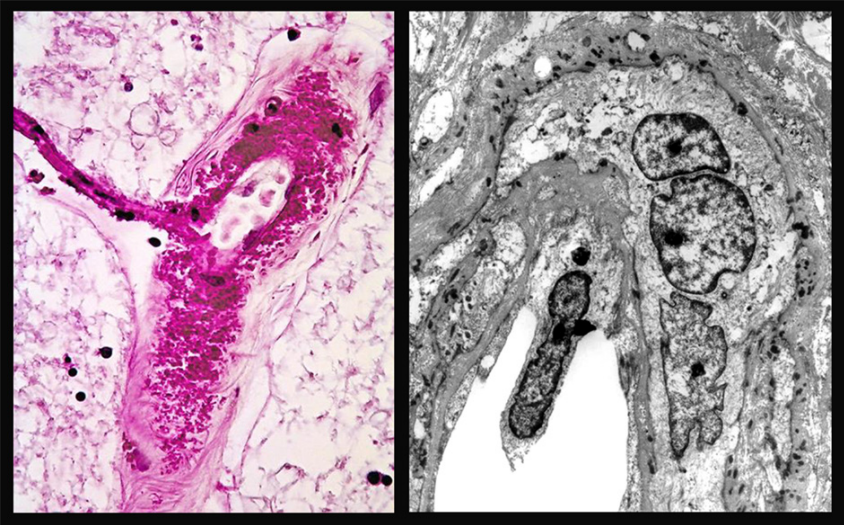
98 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuropathology

The clinical, histologic, and ultrastructural findings presented are diagnostic of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). The electron micrograph shows numerous accumulations of granular osmiophilic material (GOM) in the basal lamina of a small cutaneous arteriole. Similar findings would be present in CNS arteries. This CNS vascular disease is associated with a pathogenic variant of *NOTCH3*.

Smith C, Perry A, Kovacs G, et al (eds). Greenfield's Neuropathology. 10th ed. Boca Raton, FL: CRC Press; 2024.



Question

104 ADULT NEUROLOGY

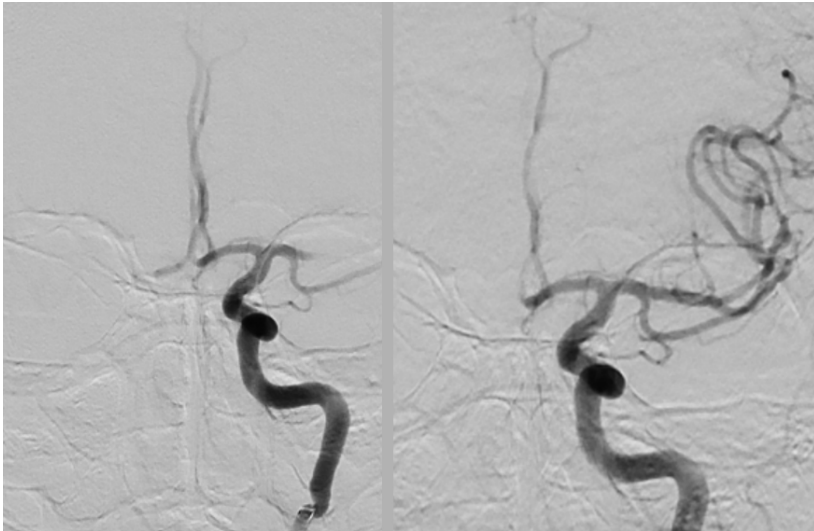
CORE KNOWLEDGE

Treatment/Management

This patient has a large vessel occlusion without residual vessel stenosis after recanalization. Vessel imaging reportedly does not show large artery disease in the carotid artery. The diagnosis is cryptogenic stroke, specifically embolic stroke of undetermined source (ESUS), for which aspirin monotherapy would be most appropriate at this time.

The large vessel occlusion without clear etiology is concerning for cardioembolic stroke, but there is no current evidence of cardioembolism or indication for anticoagulation. Previous ESUS trials have not shown benefit of anticoagulation over aspirin. This patient does not meet criteria for dual antiplatelet therapy in the absence of symptomatic intracranial atherosclerosis or a minor ischemic stroke (NIHSS <3).

Kleindorfer DO, Towfighi A, Chaturvedi S, et al. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: A guideline from the American Heart Association/American Stroke Association. *Stroke*. 2021 Jul;52(7):e364-e467. Erratum in: *Stroke*. 2021 Jul;52(7):e483-e484.



Question

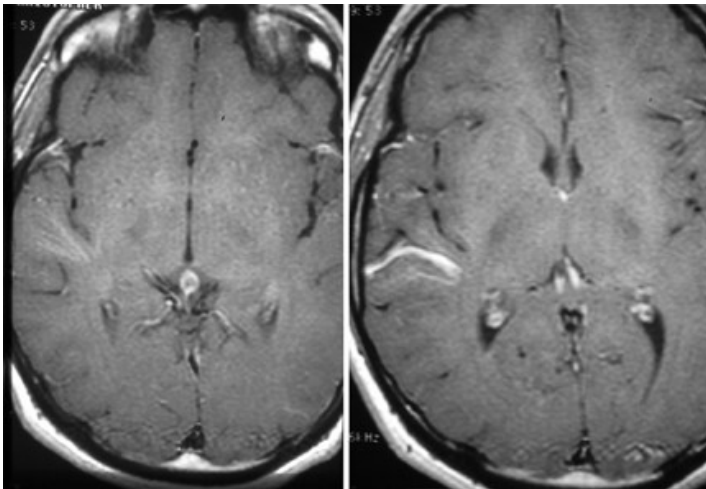
114 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroimaging

A developmental venous anomaly (DVA) or venous angioma is occasionally identified in the workup of patients with neurologic symptoms. The lesion itself is typically asymptomatic, but seizures may occur if there is an associated area of cortical dysplasia or arteriovenous malformation. It is important to understand that the DVA contributes to venous drainage of the brain tissue in which it is situated. Removal of the DVA may cause a venous infarction.

Spetzler RF, Kalani MY, Nakaji P (eds). *Neurovascular Surgery*. 2nd ed. New York: Thieme Medical Publishing; 2015.



128 ADULT NEUROLOGY

Clinical Aspects of Disease

Saccular ("berry") aneurysms of the circle of Willis are present in up to 30% of adult patients with polycystic kidney disease and are responsible for significant morbidity and an important cause of mortality. Saccular aneurysms are also seen with fibromuscular dysplasia, coarctation of the aorta, and moyamoya disease.

Borghol AH, Alkhatib B, Zayat R, et al. Intracranial aneurysms in autosomal dominant polycystic kidney disease: a practical approach to screening and management. *Mayo Clin Proc*. 2025 Jun;100(6):1030-1050.

Kuo IY, Chapman A. Intracranial aneurysms in ADPKD. *Clin J Am Soc Nephrol*. 2019 Jul 30;14(8):1119-1121.

Question

136 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Diagnostic Procedures

This 36-year-old male patient presents with a stroke and skin changes (ie, purple, lacy rash on her arms and legs), findings consistent with livedo racemosa. In a middle-aged woman, this presentation would raise concern for Sneddon syndrome. While there is no specific test for Sneddon syndrome, it is most classically associated with positive antiphospholipid antibodies (APLs), though in some patients positive APLs are not seen.

While assessing erythrocyte sedimentation rate and C-reactive protein is reasonable, the results are nonspecific. Patients can have valvular thickening such as with Liebman-Sacks endocarditis, but this finding would not be diagnostic. While this Sneddon syndrome is a vasculopathy, noninvasive imaging is often normal.

Samanta D, Cobb S, Arya K. Sneddon syndrome: a comprehensive overview. *J Stroke Cerebrovasc Dis*. 2019 Aug;28(8):2098-2108.

Image Credit: Tiwari S, Gunasekaran PK, Bainaboina R, et al. Neuroimaging features of Sneddon syndrome. *Neurology*. 2025 Apr 8;104(7):e213510.



Question

141 ADULT NEUROLOGY

SUBSPECIALTY KNOWLEDGE

Neuroscience/Mechanism of Disease

Fusiform aneurysm (dolichoectasia) most commonly affects the supraclinoid segment of the internal carotid artery and the basilar artery; it is seen in patients with advanced cerebral atherosclerosis. Berry aneurysms are associated with both coarctation of the aorta and arteriovenous malformations (AVMs) (up to 9% of patients with intracranial AVMs have berry aneurysms), but fusiform aneurysms are not. Fungi cause arteritis and aneurysmal change but not the elongated vessel distention of dolichoectasia.

Preston DC, Shapiro BE. Electromyography and Neuromuscular Disorders: Clinical-electrophysiologic Correlations. 4th ed. Philadelphia: Elsevier Saunders; 2020.

151 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Direct oral anticoagulants (DOACs) are now commonly used for secondary stroke prevention in patients with nonvalvular atrial fibrillation due to their improved safety profile, lower rates of intracerebral hemorrhage, and lack of need for INR monitoring. However, patients with valvular atrial fibrillation, including those with mechanical valves and moderate or severe mitral stenosis, still require warfarin. Warfarin should not be used during pregnancy due to teratogenic effects on the fetus.

According to reporting from the ROCKET-AF, ARISTOTLE, and RELY-AF trials, bioprosthetic mitral valves are considered nonvalvular atrial fibrillation and thus would benefit from DOACs.

A BMI of 35 does not require warfarin in lieu of DOACs. In patients whose BMI is 40 and over, however, warfarin may be safer by allowing for direct monitoring. The FDA approved the use of apixaban in patients with end stage renal disease and atrial fibrillation.

Patel MR, Mahaffey KW, Garg J, et al; ROCKET AF Investigators. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. *N Engl J Med.* 2011 Sep 8;365(10):883-891.

Granger CB, Alexander JH, McMurray JJV, et al; ARISTOTLE Committees and Investigators. Apixaban versus warfarin in patients with atrial fibrillation. *N Engl J Med.* 2011 Sep 15;365(11):981-992.

Paikun JS, Haroun MJ, Eikelboom JW. Dabigatran for stroke prevention in atrial fibrillation: The RE-LY trial. *Expert Rev Cardiovasc Ther.* 2011 Mar;9(3):279-286.

Question

160 ADULT NEUROLOGY

CORE KNOWLEDGE

Neuroimaging

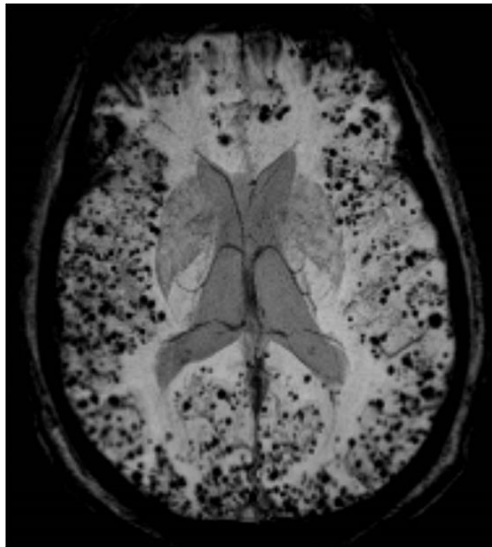
The image shows multiple cortical and subcortical lobar microhemorrhages with complete sparing of deep structures, a pattern is seen in cerebral amyloid angiopathy. Cerebral amyloid angiopathy has been associated with mutations in the *APOE* gene.

Pathogenic variant in *NOTCH3* is associated with CADASIL, *GLA* mutation is associated with Fabry disease, and *RNF213* is a susceptibility gene for moyamoya. ATP-binding cassette transporters are a large family of proteins; *ABCB1* encodes one member of this family enriched on the blood-brain barrier and controls drug and toxin efflux and may influence amyloid-beta plaque deposition in Alzheimer disease.

Camacho J, Moliné T, Bonaterra-Pastra A, et al. Brain ApoA-I, ApoJ and ApoE immunodetection in cerebral amyloid angiopathy. *Front Neurol*. 2019 Mar 13;10:187.

Matarin M, Singleton A, Hardy J, et al. The genetics of ischaemic stroke. *J Intern Med*. 2010;267:139.

Greenberg SM, Briggs ME, Hyman BT, et al. Apolipoprotein E epsilon 4 is associated with the presence and earlier onset of hemorrhage in cerebral amyloid angiopathy. *Stroke*. 1996;27:1333.



Question

166 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

Therapeutic hypothermia to 92.3°F (33.5°C) for 72 hours, followed by rewarming over 6 to 12 hours, is standard of care for term or near-term (≥ 36 weeks) newborns with moderate or severe encephalopathy with presumed hypoxic ischemic encephalopathy (HIE), if started within 6 hours after delivery. Evidence of both HIE (eg, cord blood gas pH ≤ 7 or Apgar score ≤ 5 at 10 minutes) and moderate to severe encephalopathy (including seizures) is required. Contraindications to therapeutic hypothermia include intracranial hemorrhage or evidence of a coagulopathy.

Glass HC. Hypoxic-ischemic encephalopathy and other neonatal encephalopathies. *Continuum Lifelong Learning Neurol.* 2018 Feb;24(1):57-71.

Jacobs SE, Berg M, Hunt R, et al. Cooling for newborns with hypoxic ischaemic encephalopathy. *Cochrane Database Syst Rev.* 2013 Jan 31;2013(1):CD003311.

175 ADULT NEUROLOGY**Clinical Aspects of Disease**

This patient's angiogram shows a tapered carotid occlusion distal to the carotid bifurcation, typical of carotid artery dissection. Fibromuscular dysplasia is a risk factor for dissection. Hyperlipidemia and diabetes mellitus are risk factors for atherosclerotic disease. Autoimmune disease is a risk factor for vasculitis and congenital heart disease for embolic stroke.

Salehi Omran S. Cervical artery dissection. *Continuum Lifelong Learning Neurol.* 2023 Apr;29(2):540-565.



Question

187 NO SPECIFIED PATIENT AGE

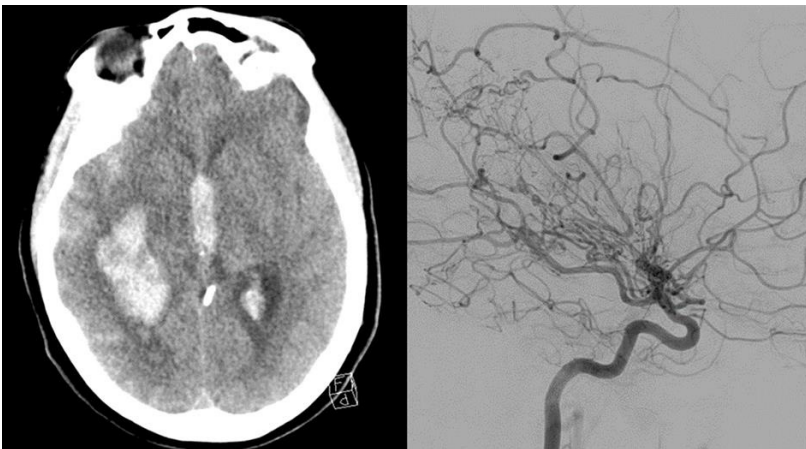
Neuroscience and Mechanism of Disease

This patient's cerebral angiogram shows a "puff of smoke" capillary network consistent with a moyamoya pattern. Characteristic angiographic findings include stenosis of the terminal portion of the internal carotid artery and evidence of an abnormal network of dilated, fragile perforators at the base of the brain.

Moyamoya disease is diagnosed when this abnormal vascular pattern occurs in the absence of other causes, and moyamoya syndrome is diagnosed when other comorbidities that may lead to the steno-occlusive condition are present. Several disorders are associated with moyamoya syndrome, including neurofibromatosis type 1, autoimmune disorders (eg, systemic lupus erythematosus, antiphospholipid syndrome, Sjögren syndrome), meningitis, Down syndrome, and sickle cell disease. A history of cranial radiation has also been linked with this disorder.

Pathogenic variations in *KRIT1* lead to familial cavernous cavernomas. *COL4A1* pathogenic variants lead to dysfunctional collagen IV, a protein critical for the basement membrane of blood vessels, resulting in fragile blood vessels that are prone to rupture, particularly in the perinatal period. Somatic pathogenic variants in *GNAQ* are associated with Sturge-Weber syndrome.

Gonzalez NR, Amin-Hanjani S, Bang OY, et al; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; and Council on Clinical Cardiology. Adult moyamoya disease and syndrome: current perspectives and future directions: a scientific statement from the American Heart Association/American Stroke Association. *Stroke*. 2023 Oct;54(10):e465-479.



Question

193 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

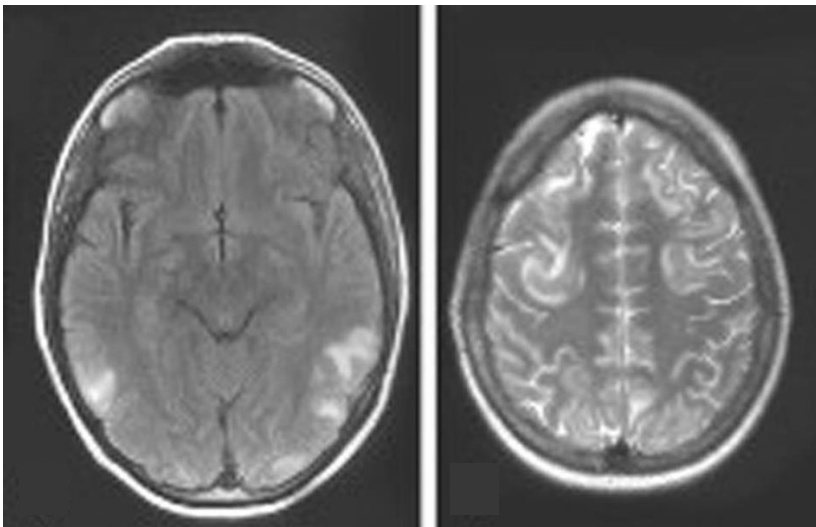
Posterior reversible encephalopathy syndrome (PRES) classically presents with encephalopathy. Seizures develop in up to two thirds of patients. Headaches, vision issues, and focal deficits due to vascular complications (eg, ischemic stroke, hemorrhage, edema) can also be seen. This patient's MRI scans show the bilateral, symmetric, and subcortical white matter vasogenic edema, all classic features of PRES.

PRES has multiple risk factors, including uncontrolled hypertension, immunosuppression, renal failure, sepsis, eclampsia and preeclampsia, and use of one of several cytotoxic and immunosuppressive medications. This patient's immunosuppressed status following kidney transplant and use of tacrolimus are also risk factors.

Triplett JD, Kutlubaev MA, Kermode AG, et al. Posterior reversible encephalopathy syndrome (PRES): diagnosis and management. *Pract Neurol*. 2022 Jun;22(3):183-189.

Singhal AB. Posterior reversible encephalopathy syndrome and reversible cerebral vasoconstriction syndrome as syndromes of cerebrovascular dysregulation. *Continuum Lifelong Learning Neurol*. 2021 Oct 1;27(5):1301-1320.

Feske SK. Posterior reversible encephalopathy syndrome: a review. *Semin Neurol*. 2011 Apr;31(2):202-215.



Question

195 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Contemporary Issues

In almost all circumstances, no images of a patient should ever be shared on any form of social or electronic media. Under rare circumstances and if compliant with institutional media policies, as well as with informed consent by the patient or surrogate, an image for teaching purposes could be shared without any identifying information.

Busl KM, Rubin MA, Tolchin BD, Larriviere D, et al; Ethics, Law, and Humanities Committee, a joint committee of the American Academy of Neurology, American Neurological Association, and Child Neurology Society. Use of social media in health care--opportunities, challenges, and ethical considerations: a position statement of the American Academy of Neurology. *Neurology*. 2021 Sep 21;97(12):585-594.

204 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroanatomy

The nucleus ambiguus contains motor neurons that supply striated muscles of the palate, pharynx, and larynx.

Blumenfeld H. *Neuroanatomy Through Clinical Cases*. 3rd ed. Sunderland: Sinauer Associates; 2021.

Brazis PW, Masdeu JC, Biller J (eds). *Localization in Clinical Neurology*. 8th ed. Philadelphia: Wolters Kluwer; 2022.

215 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

The ABCD2 score is a validated tool that assigns 7-day risk for severe stroke and recurrent transient ischemic attack (TIA) after an initial TIA. Studies validating the ABCD2 score reported a 7-day hazard ratio of 2.64 for major stroke in patients with TIAs >60 minutes. Patient age >60 years, systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg, a history of diabetes mellitus, and clinical findings of speech disturbance also confer an increased risk for major stroke, but to a lesser degree than symptom duration >60 minutes.

Chandratheva A, Geraghty OC, Luengo-Fernandez R, et al. ABCD2 score predicts severity rather than risk of early recurrent events after transient ischemic attack. *Stroke*. 2010 May;41(5):851-856.

Question

222 PEDIATRIC NEUROLOGY

Neuroimaging

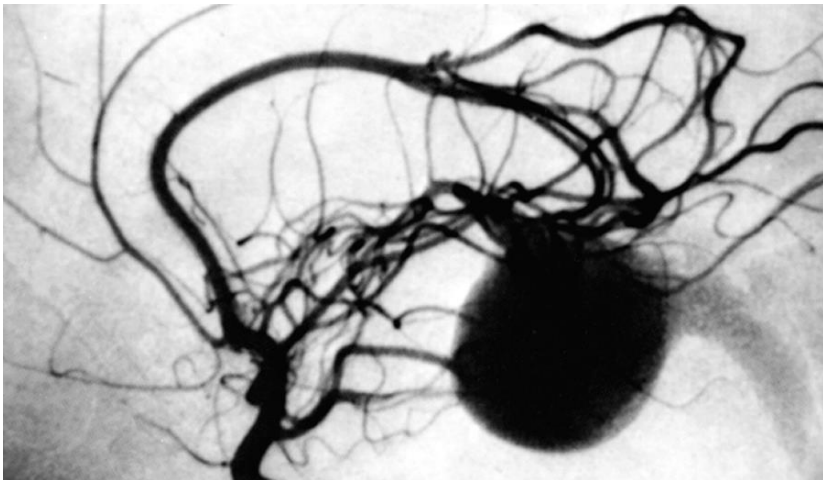
Based on this neonate's history of congestive heart failure, a high-flow arteriovenous malformation, such as a vein of Galen malformation, must be considered. These malformations occur during embryonic development when the median prosencephalic vein fails to regress.

This is not a basilar tip or anterior communicating artery aneurysm given its location; additionally, aneurysms in these locations do not result in high output cardiac failure in a neonate. The history is not consistent with a mycotic aneurysm in the absence of infection, and the location is not typical for a mycotic aneurysm. Hemangioblastomas tend to occur more commonly in the cerebellum and are rare in neonates.

Cordova EG, Levy P, Kheir JN, et al. Vein of Galen malformation. *Neoreviews*. 2020 Oct;21(10):e678-e686.

Society for Maternal-Fetal Medicine; Monteagudo A. Vein of Galen aneurysmal malformation. *Am J Obstet Gynecol*. 2020 Dec;223(6):B27-B29.

Recinos PF, Rahmathulla G, Pearl M, et al. Vein of Galen malformations: epidemiology, clinical presentations, management. *Neurosurg Clin N Am*. 2012 Jan;23(1):165-177.



Question

237 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Treatment/Management**

Pregnancy is not an absolute contraindication to IV alteplase. In the absence of clear contraindications and given the severity of this patient's symptoms (aphasia and hemiparesis) which are likely to be disabling, IV alteplase should be administered as soon as possible.

Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patient with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019 Dec;50(12):e344-e418. Erratum in: *Stroke*. 2019 Dec;50(12):e440-e441.

Gartman E. The use of thrombolytic therapy in pregnancy. *Obstet Med*. 2013 Sep; 6(3):105-111.

250 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

This patient has a spontaneous hemorrhage into the tegmentum of the left pons, most likely secondary to hypertension. In this location, ipsilateral involvement of cranial nerves V, VI, and VII would be expected. Horner syndrome involves the ipsilateral descending sympathetic fibers. The spinothalamic tract is located in this region and would produce contralateral hemibody anesthesia. The corticospinal tract is ventral to the lesion. Moreover, if upper motor neuron function was affected, the right hemibody, not the left as described here, would be involved. The nuclei and fibers of cranial nerves IV and XII are above and below the level of the lesion, respectively.

Brazis PW, Masdeu JC, Biller J (eds). *Localization in Clinical Neurology*. 8th ed. Philadelphia: Wolters Kluwer; 2022.

Southerland AM. Clinical evaluation of the patient with acute stroke. *Continuum Lifelong Learning Neurol*. 2017 Feb;23(1):40-61.



Question

256 ADULT NEUROLOGY

CORE KNOWLEDGE

Treatment/Management

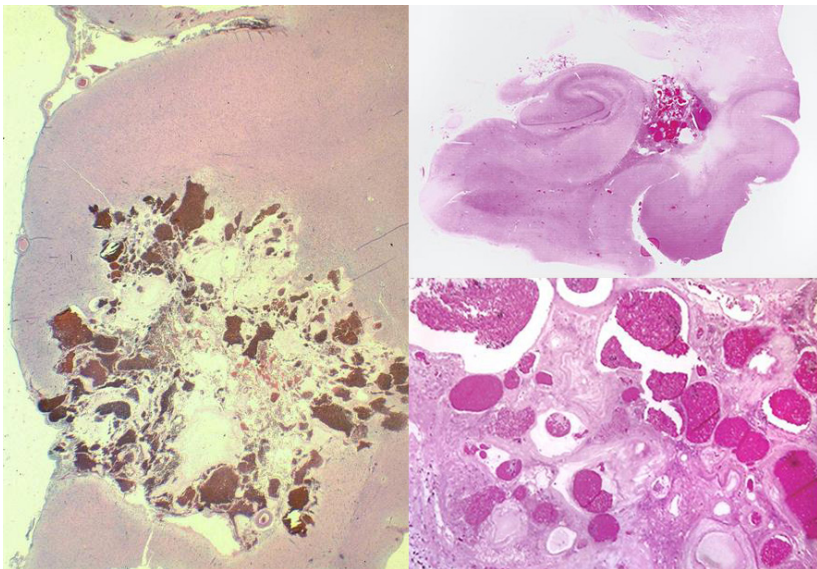
This patient presents with an acute stroke and is evaluated rapidly in an emergency setting. She appears to be a potential candidate for IV thrombolysis (tissue plasminogen activator [tPA] or tenecteplase [TNK]) based on her NIH Stroke Scale score, the time window (2 hours), and absence of contraindications to the drug; however, her blood pressure (190/110 mm Hg) exceeds the guidelines for use of thrombolytics, thus indicating treatment with IV labetalol.

owers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2019 Dec;50(12):e344-e418. Erratum in: Stroke. 2019 Dec;50(12):e440-441.

266 ADULT NEUROLOGY**Neuropathology**

Autosomal dominant cavernous malformation is characterized by intraparenchymal cavernous malformations that can produce seizures, impaired function, or hemorrhage. The photographs illustrate a multichanneled vascular malformation composed of closely juxtaposed hyalinized, nonarterial vessels.

Smith C, Perry A, Kovacs G, et al (eds). Greenfield's Neuropathology. 10th ed. Boca Raton, FL: CRC Press; 2024.



Question

276 ADULT NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

The most common cause of elevated body temperature associated with acute stroke is pneumonia, caused by aspiration, atelectasis, and lack of mobility. Pneumonia accounts for about 60% of poststroke complications, with urinary tract infections between 11% and 15%. Anhydrosis, drug toxicity, and intracerebral hemorrhage are not associated with poststroke complications.

Huang JF. Prevention and management of poststroke complications. *Continuum Lifelong Learning Neurol.* 2017 Feb;23(1):93-110.

291 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Neuroimaging

Herniation syndromes are caused by intracranial mass effect. The MRI scan shown illustrates a transtentorial herniation of the left temporal lobe and uncus.

Subfalcine herniation is not the best choice because the image does not show the level of the falx. Tonsillar herniation occurs at the level of the foramen magnum when cerebellar tonsillar tissue is forced out by mass effect. The foramen magnum is not visible in the image supplied. Extracranial herniation occurs in the setting of a skull defect (either traumatic or therapeutic) that allows brain to pass through the defect. No skull defect is present in the image. Ascending herniation occurs when a mass in the posterior fossa forces cerebellar tissue to move upward and cross the tentorial incisura, also not seen in the current image.

Salzman KL, Jhaveri MD, Osborn AG (eds). *Diagnostic Imaging: Brain.* 5th ed. Philadelphia: Elsevier; 2025.

Kalita J, Misra UK, Vajpeyee A, et al. Brain herniations in patients with intracerebral hemorrhage. *Acta Neurol Scand.* 2009 Apr;119(4):254-260.



Question

308 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Treatment/Management

Cerebral venous sinus thrombosis is treated with anticoagulation, even in the presence of intracranial hemorrhage. Endovascular therapy may be considered in patients with worsening clinical status and failure of recanalization despite anticoagulation. Osmotic therapies and hemicraniectomy can be considered if there is hematoma expansion or cerebral edema causing elevated intracranial pressure.

Lieberman AL. Diagnosis and treatment of cerebral venous thrombosis. *Continuum Lifelong Learning Neurol.* 2023 Apr;29(2):519-539.

316 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

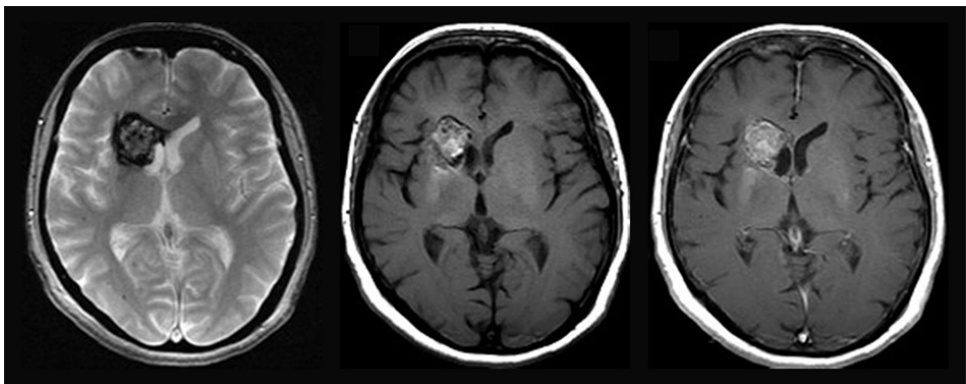
Neuroimaging

The mass lesion shown has heterogenous T2- and T1-weighted signal, characteristic of chronic hemorrhage with hemosiderin. The lesion has a speckled or popcorn-like appearance typical of a cavernous angioma, also known as cavernoma or cavernous malformation.

An aneurysm has a smooth margin and more homogenous central hemorrhagic pattern. A developmental venous anomaly typically has a spider-like appearance (also known as caput medusae). Hemorrhagic metastasis is unlikely because of the lack of enhancement and vasogenic edema.

Greenberg JO (ed). *Neuroimaging: A Companion to Adams and Victor's Principles of Neurology*. 2nd ed. New York: McGraw-Hill, 1999.

Dulamea AO, Lupescu IC. Cerebral cavernous malformations - an overview on genetics, clinical aspects and therapeutic strategies. *J Neurol Sci.* 2024 Jun 15;461:123044.



Question

328 ADULT NEUROLOGY**CORE KNOWLEDGE****Clinical Aspects of Disease**

A person's dominant hemisphere is predominantly responsible for language, regardless of whether communication relies on visual or auditory information. In patients who are deaf and use sign language, the left frontal regions are involved in sign production, whereas areas of the auditory cortex contribute to sign comprehension—even though signers do not depend on hearing to process language. Similar to those who use spoken language, a left hemisphere dominance persists even when a patient signs with the left hand.

Goldberg EB, Hillis AE. Sign language aphasia. *Handb Clin Neurol*. 2022;185:297-315.

Blumenfeld H. *Neuroanatomy Through Clinical Cases*. 3rd ed. Sunderland: Sinauer Associates; 2021.

338 ADULT NEUROLOGY**SUBSPECIALTY KNOWLEDGE****Neuroimaging**

This patient has a spinal dural arteriovenous fistula. A history of a fluctuating lower thoracic myelopathy, worse with exertion and when performing the Valsalva maneuver, is characteristic. The MRI scans show lower spinal cord edema, and the FIESTA (fast imaging employing steady-state acquisition) view, which is particularly useful, shows abnormal vessels typical of these lesions.

Da Ros V, Picchi E, Ferrazzoli V, et al. Spinal vascular lesions: anatomy, imaging techniques and treatment. *Eur J Radiol Open*. 2021 Jul 14;8:100369.

Gelmacher DS, Shah L. Vascular myelopathies. *Continuum Lifelong Learning Neurol*. 2008 Jun;14(3):71-90.

Lev N, Maimon S, Rappaport ZH, et al. Spinal dural arteriovenous fistulae--a diagnostic challenge. *Israel Med Assoc J*. 2001;3(7):492-496.



Question

344 ADULT NEUROLOGY

Neuroscience/Mechanism of Disease

The medial striate artery (also known as the recurrent artery of Heubner) is a branch of the anterior cerebral artery that supplies part of the caudate head. The caudate head is also supplied by branches of the middle cerebral artery.

The pericallosal arteries are branches of the anterior cerebral artery that supply the medial aspects of both hemispheres. The anterior choroidal artery supplies the posterior limb of the internal capsule, the medial globus pallidus, and the lateral geniculate body. The posterior choroidal artery supplies the lateral geniculate body, pulvinar, posterior thalamus, hippocampus, and parahippocampal gyrus. The artery of Percheron is a variant that supplies both thalami.

Brazis PW, Masdeu JC, Biller J (eds). *Localization in Clinical Neurology*. 8th ed. Philadelphia: Wolters Kluwer; 2022.

356 NO SPECIFIED PATIENT AGE

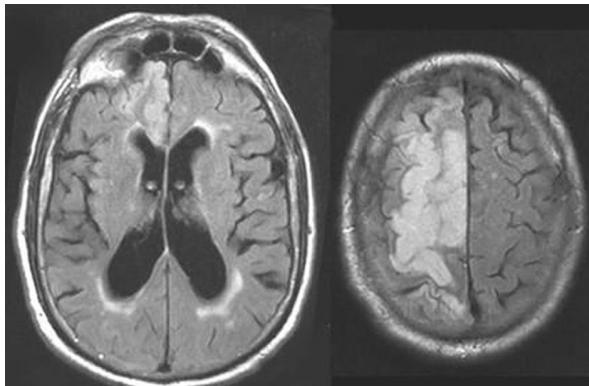
CORE KNOWLEDGE

Neuroimaging

The changes on the FLAIR sequence images shown are consistent with an acute infarct in the distribution of the anterior cerebral artery.

Herpes encephalitis typically involves the anterior and medial temporal lobes and the inferior frontal lobes. The recurrent artery of Heubner is a branch of the anterior cerebral artery that supplies the inferior half of the anterior limb of the internal capsule, the head of the caudate, and the anterior portion of the lentiform nucleus. Internal artery occlusion would affect both the anterior and middle cerebral arteries. Occlusion of the middle cerebral artery affects circulation to the lateral areas of the frontal, parietal, and temporal lobes.

Salzman KL, Jhaveri MD, Osborn AG (eds). *Diagnostic Imaging: Brain*. 5th ed. Philadelphia: Elsevier; 2025.



Question

364 NO SPECIFIED PATIENT AGE**Treatment/Management**

Moyamoya disease is an idiopathic, chronic, progressive vaso-occlusive disorder of the terminal internal carotid arteries and its proximal branches, resulting in an abnormal collateral network ("puff of smoke"). Acute management focuses on neuroprotective measures to maintain and promote cerebral perfusion and includes maintenance of normovolemia, normotension, and normoglycemia. Antiplatelet therapy can be initiated if the patient has no contraindications.

Definitive treatment is surgical revascularization aimed at bypassing the occlusive vessel segments, but it is not typically performed in the hyperacute period. IV thrombolysis, endovascular thrombectomy, and IV corticosteroids are not indicated in acute management of moyamoya disease.

Sun LR, Vossough A, Kossorotoff M, et al. Moyamoya across the lifespan: current neurologic care and future directions. *Neurology*. 2025 Apr 8;104(7):e213484.

375 PEDIATRIC NEUROLOGY

CORE KNOWLEDGE

Clinical Aspects of Disease

This 9-month-old male patient presents with an asymmetric crawl in which he leads with the left arm to commando crawl. Early handedness in a young infant like this raises suspicion for prenatal or perinatal brain injury. The parachute reflex is a primitive reflex that typically presents after age 6 months; this patient has an asymmetric parachute reflex. Asymmetry, defined as lack of arm extension on one side or delayed arm extension on one side, provides clues regarding potential brain injury impacting the motor pathways.

Perinatal brachial plexus injury is typically detected in the neonatal period with decreased movement of the injured arm. Unilateral brain malformations can result in asymmetric motor development but would be more likely to impact other areas of development, such as feeding or communication, and may result in early onset of seizures.

Ilves P, Laugesaar R, Loorits D, et al. Presumed perinatal stroke: risk factors, clinical and radiological findings. *J Child Neurol*. 2016 Apr;31(5):621-628.

Question

387 NO SPECIFIED PATIENT AGE**Neuropathology**

Mycotic aneurysms are most commonly found in the distal branches of the middle cerebral artery.

Smith C, Perry A, Kovacs G, et al (eds). Greenfield's Neuropathology. 10th ed. Boca Raton, FL: CRC Press; 2024.

397 NO SPECIFIED PATIENT AGE

CORE KNOWLEDGE

Clinical Aspects of Disease

The anterior spinal artery supplies the descending corticospinal tracts and ascending spinothalamic tracts. The dorsal columns are supplied by the posterior spinal arteries; thus, fine touch and joint position sense are classically preserved in anterior spinal artery occlusion. However, clinically, spinal cord infarctions often cross these classic vascular territories.

Haines DE, Mihailoff GA (eds). Fundamental Neuroscience for Basic and Clinical Applications. 5th ed. Philadelphia: Elsevier; 2018.