Clinical Reasoning:

An unusual cause of indeterminate spells

Anteneh M. Feyissa, MD,
MSc*
Daniel L. Kenney-Jung,
MD*
Cheolsu Shin, MD
John C. Cheville, MD
Elson L. So, MD

Correspondence to
Dr. Feyissa:
Feyissa.Anteneh@mayo.edu

SECTION 1

A 38-year-old, right-handed woman presented to the epilepsy clinic for evaluation of recurrent spells. These spells are characterized by an aura of a “rushing” cephalic sensation and a sense of “spaciness” or “dizziness” followed by loss of awareness with subsequent amnesia for the event. During these events, the patient is observed by family to sit down and slump forward or fall, followed by hyperventilation and occasionally staring, for up to 3 minutes. There is no head turn, eye deviation, or abnormal body movements. Postictally, she reports generalized weakness without focalities and confusion. The spells occurred sporadically for 8 years, but recently increased in frequency to 5 to 20 times per day. Triggers included lack of sleep, stress, and various food products. The patient reported some improvement with levetiracetam therapy at 1,500 mg twice daily.

The patient was hospitalized for head injury from a motor vehicle accident at 16 years of age. She was amnesic for the event but was told that there were “contusions” in her brain. She endorses significant psychosocial stressors including a recent divorce and loss of her business. She reports a 10 pack-year history of smoking but denies excessive use of alcohol or illicit drugs. Neurologic examination at presentation was unremarkable. Basic laboratory tests including electrolytes, random blood glucose, and drug screening were normal. Likewise, ECG was normal. Outside EEGs reported left temporal slowing. Seizure protocol brain MRI showed multiple linear T2 hyperintensity, most prominent subcortically in the left frontal lobe, presumably posttraumatic (figure, A).

Question for consideration:

1. What differential diagnosis should be considered?

[GO TO SECTION 2](#)

*These authors contributed equally to this work.

From the Departments of Neurology (A.M.F., C.S., E.L.S.), Child and Adolescent Neurology (D.L.K.-J.), and Laboratory Medicine and Pathology (J.C.C.), Mayo Clinic, Rochester, MN.

Go to Neurology.org for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Figure Syncope as a presenting feature of carotid body tumor and masquerading as psychogenic nonepileptic events

Coronal MRI showing T2 signal hyperintensity in the left anterior frontal lobe, presumably posttraumatic (A). EEG-ECG tracings a few seconds before, during, and immediately after a typical spell (B); single-lead ECG monitor showing bradycardia a few seconds before onset of symptoms (tracing with white background), a 12-second-long asystole (arrow) accompanied by the development of diffuse nonspecific theta and delta range slowing (tracing with yellow background), and return of normal sinus rhythm a few seconds after the event (tracing with green background). Coronal multiplanar reconstructed neck CT with contrast depicting an avidly enhancing mass at the left carotid bifurcation, which splays the left internal and external carotid arteries with mild mass effect on both vessels (arrow, C). Low-power hematoxylin & eosin-stained section showing entrapped carotid artery (arrow) by the tumor (D). High-power hematoxylin & eosin-stained section showing neoplastic cells with basophilic granular cytoplasm and round hyperchromatic nuclei with dispersed chromatin, a well-developed "Zellballen" growth pattern (E). A photomicrograph showing strong reactivity of tumor cells with chromogranin staining by immunohistochemical technique (F).

SECTION 2

The patient's spells have some elements consistent with focal dyscognitive seizures, including the presence of an aura, loss of awareness, and the possible response to levetiracetam. Nonspecific symptoms such as a "rushing sensation" or dizziness have also been described as preictal symptoms in both generalized and focal epilepsies.¹ An aura of fear or panic may be associated with focal dyscognitive seizures of mesial temporal onset.² The patient's reported falls could be attributable to atonic seizures (unlikely in a normal adult) or syncope from ictal asystole. Ictal syncope, which can result in falls causing serious injury, is uncommon but treatable in some patients with focal epilepsy. Pacemaker placement in these patients seems to prevent fall-related injuries.³ Lastly, the presence of risk factors for epilepsy (head injury) and the focal T2 signal changes on MRI support the diagnosis of epilepsy.

Psychosocial stressors, age, semiology, frequency of the spells, and the presence of unusual food triggers in this patient raised the suspicion that these spells may be psychogenic rather than epileptic.⁴ Psychogenic nonepileptic events (PNEEs) are paroxysmal, time-limited alterations of bodily/mental function, manifested by movements, behavior, or symptoms that are of psychological etiology.^{1,4} PNEEs constitute by

far the most common condition misdiagnosed as epilepsy. The majority of patients with PNEEs are young women between 15 and 40 years of age.⁵ Spells associated with a gradual loss of tone and sliding down have been reported in individuals with psychogenic pseudosyncope.⁵ Video-EEG monitoring is considered the "gold standard" in distinguishing between epileptic and nonepileptic attacks.⁶

Our patient's history of falls with loss of consciousness, improvement with positional changes, and characteristic prodromal symptoms may suggest syncope or presyncope. Pathophysiologic classification of syncope consists of the following: (1) neurally mediated syncope with a vasovagal response due to emotional stress, carotid sinus stimulation, or during other circumstances involving a potential increase in vagal tone, such as micturition; (2) dysautonomia, e.g., orthostatic hypotension; (3) cardiac arrhythmias; (4) structural cardiac or cardiopulmonary diseases; and (5) cerebrovascular causes.⁷

Other nonepileptic physiologic causes of indeterminate spells including hypoglycemia, panic attacks, or vertebrobasilar TIAs may also be entertained.

Question for consideration:

1. What additional diagnostic tests would you consider at this time?

GO TO SECTION 3

SECTION 3

The patient was admitted to the EMU for spell classification. Two typical spells with symptoms of a “rushing” sensation, dizziness, “racing thoughts,” and numbness were recorded on day 1 of monitoring. She was unable to recall a memory phrase given during the event. The EEG showed diffuse 3- to 4-Hz slowing, while the single-lead ECG monitor showed prolonged

pauses in QRS complexes of 7 to 15 seconds (figure, B). Awake and asleep interictal EEG was otherwise normal. Her blood glucose was >90 mg/dL in both instances. The patient was transferred to a cardiology unit.

Questions for consideration:

1. What is the most likely diagnosis?
2. Would you order any further tests?

[GO TO SECTION 4](#)

SECTION 4

A tilt table test is often used to diagnose dysautonomia or syncope. It tests for causes of syncope by attempting to reproduce syncope by having the patient lie flat on a special table or bed that creates changes in posture from lying to standing. Continuous ECG and noninvasive blood pressure monitoring are used throughout the test.⁷ Our patient underwent tilt table testing, demonstrating mixed cardioinhibitory and vasodepressor presyncope induced by upright tilt. A spontaneous 4.3-second pause in the supine position was noted. Holter monitoring revealed a greater than 12-second cardiac pause with syncope. Transthoracic echocardiography and overnight oximetry were unremarkable. Symptomatic bradycardia was diagnosed, and she was dismissed on 2.5 mg midodrine every 4 hours.

One day after her dismissal, she presented to the emergency room with recurrence of spells and was admitted to the cardiology service. On day 1, she

had 3 cardiac pauses in sleep (the longest 14.4 seconds) and a symptomatic 12.5-second pause while awake. While being evaluated for pacemaker placement, she mentioned to the attending cardiologist that she had a “swollen lymph node” and asked whether that had anything to do with her spells. On examination, a 3-cm tender nodule was palpated at the angle of the left jaw. Palpation of the mass produced lightheadedness without heart rate changes. Contrast CT scanning of the chest and neck revealed a 2.6-cm enhancing mass at the left carotid bifurcation, consistent with a carotid body tumor (CBT) (figure, C). Scattered enhancing pulmonary nodules were also detected. The neck mass did not demonstrate 123-meta-iodobenzylguanidine (MIBG) uptake. Urine metanephrines and dopamine were normal.

Question for consideration:

1. What action would you take at this point?

GO TO SECTION 5

SECTION 5

Resection of the left carotid mass was performed. The tumor was very fibrotic and invaded the carotid artery wall. Pathology showed a paraganglioma with metastasis to a regional lymph node (figure, D–F). The tumor was associated with dense fibrosis, lymphatic space invasion, and invasion around vessels and nerves. The postoperative course was uneventful, and she was dismissed 4 days later. Levetiracetam was discontinued. Subsequently, she received adjuvant radiation therapy to the left neck. The spells resolved with no recurrence at 2-month follow-up.

Questions for consideration:

1. What is the final diagnosis?
2. Could anything have helped speed this patient's diagnostic journey?

DISCUSSION Paragangliomas are uncommon tumors of chromaffin cells, developing from sympathetic or parasympathetic ganglia.⁸ Although it is estimated that less than 10% of paragangliomas are malignant, in some studies, malignancy rates are as high as 50%.⁸ Common sites of occurrence include the abdomen, chest, mediastinum, and various head and neck locations including the vagus nerve and carotid body. Carotid body paragangliomas (also known as carotid body tumors or CBTs) are rare neoplasms representing less than 0.5% of all head and neck tumors.⁹ They can be hormonally active, with secretion of catecholamines sometimes resulting in hypertension and arrhythmia.⁹ Most CBTs, however, are nonsecreting, asymptomatic, slow-growing tumors. When symptomatic, they present with a slowly enlarging, painless neck mass, which is often anterior to the sternocleidomastoid muscle at the level of the hyoid. Other presentations include neck discomfort, dysphagia, or dyspnea due to the size of the mass, or hoarseness, dysphagia, or tongue weakness due to lower cranial nerve involvement (VII–XII). Syncope as a presenting feature of CBT is extremely rare.⁹

CBTs can be a diagnostic challenge for the neurologist. The diagnostic workup of CBT may involve one or more of the following: duplex ultrasound scanning, contrast CT of chest and neck, MIBG, MRI, magnetic resonance angiography, carotid angiography, and serum and urinary catecholamine level assessment. When CBT is suspected, screening for catecholamines or their metabolites is important, for guiding management, ensuring hemodynamic stability, and detecting recurrence after resection.⁸ Surgical removal remains the only curative therapy for the majority of cases.⁹ Adjuvant radiotherapy is recommended in cases of incomplete resection and in

malignant paraganglioma.⁸ Overall prognosis is quite good with complete surgical resection. However, malignant paragangliomas have less than a 50% 10-year survival rate.⁸

Our patient's tumor showed no evidence of hormonal activity, with normal urine metanephrines and catecholamines. The symptomatic bradycardia is thought to have been due to traction on the carotid body by the mass, stimulating the carotid baroreceptor reflex and resulting in increased vagal stimulation of the heart.⁹ In addition to highlighting CBT as an uncommon cause of syncope masquerading as epileptic seizures, this case demonstrates the importance of the physical examination. While listening for carotid bruits is a part of most neurologists' repertoire, careful attention to the appearance of the neck itself might have hastened the diagnosis.

AUTHOR CONTRIBUTIONS

Study concept and design: Drs. Feyissa, Kenney-Jung, Shin, and So. Acquisition of data: All authors. Drafting of the manuscript and literature search: Drs. Feyissa and Kenney-Jung. Manuscript editing for appropriate grammar and syntax: Dr. Shin. Critical revision of the manuscript for important intellectual content: Drs. Feyissa, Shin, Cheville, and So.

STUDY FUNDING

No targeted funding reported.

DISCLOSURE

The authors report no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

REFERENCES

1. Benbadis S. The differential diagnosis of epilepsy: a critical review. *Epilepsy Behav* 2009;15:15–21.
2. Goldstein LH, Mellers JD. Ictal symptoms of anxiety, avoidance behaviour, and dissociation in patients with dissociative seizures. *J Neurol Neurosurg Psychiatry* 2006;77: 616–621.
3. Moseley BD, Ghearing GR, Munger TM, Britton JW. The treatment of ictal asystole with cardiac pacing. *Epilepsia* 2011;52:e16–e19.
4. Devinsky O, Gazzola D, LaFrance WC Jr. Differentiating between nonepileptic and epileptic seizures. *Nat Rev Neurol* 2011;7:210–220.
5. Blad H, Lamberts RJ, Gert van Dijk J, Thijs RD. Tilt-induced vasovagal syncope and psychogenic pseudosyncope: overlapping clinical entities. *Neurology* 2015;8:2006–2010.
6. Labiner DM, Bagic AI, Herman ST, et al. Essential services, personnel, and facilities in specialized epilepsy centers: revised 2010 guidelines. *Epilepsia* 2010;51:2322–2333.
7. Task Force for the Diagnosis and Management of Syncope, European Society of Cardiology (ESC), European Heart Rhythm Association (EHRA), et al. Guidelines for the diagnosis and management of syncope (version 2009). *Eur Heart J* 2009;30:2631–2671.
8. Wieneke JA, Smith A. Paraganglioma: carotid body tumor. *Head Neck Pathol* 2009;3:303–306.
9. Janda PH, Veerappan V, McKenzie ME, Dhudshia NV. Carotid body tumor as a reversible cause of syncope. *J Am Osteopath Assoc* 2011;111:638–644.

Neurology®

Clinical Reasoning: An unusual cause of indeterminate spells

Anteneh M. Feyissa, Daniel L. Kenney-Jung, Cheolsu Shin, et al.

Neurology 2016;87:e275-e280

DOI 10.1212/WNL.0000000000003403

This information is current as of December 5, 2016

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/87/23/e275.full
References	This article cites 9 articles, 1 of which you can access for free at: http://n.neurology.org/content/87/23/e275.full#ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Clinical neurology examination http://n.neurology.org/cgi/collection/clinical_neurology_examination Epilepsy monitoring http://n.neurology.org/cgi/collection/epilepsy_monitoring_ Nonepileptic seizures http://n.neurology.org/cgi/collection/nonepileptic_seizures Other cerebrovascular disease/ Stroke http://n.neurology.org/cgi/collection/other_cerebrovascular_disease__stroke Syncope http://n.neurology.org/cgi/collection/syncope
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright © 2016 American Academy of Neurology. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.