Clinical Reasoning: A Young Man With Daily Episodes of Altered Awareness

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Abstract

Stretch syncope is a distinct entity characterized by transient alteration in awareness (TAA) induced by neck hyperextension during stretching. Few cases of stretch syncope have been reported in the literature. Nevertheless, this is a highly relevant diagnosis as it can be easily mistaken for epilepsy for a number of reasons. These include stereotypical motor activity associated with the events, development of ictal tachycardia, and the presence of rhythmic/semirhythmic slowing on EEG in the context of transient cerebral hypoperfusion.
We present the case of a young man who was referred to our comprehensive epilepsy center for frequent episodes of TAA. After careful evaluation, the episodes were initially considered to be epileptic. Given that he had negligible clinical response to antiseizure medications, he underwent an experimental protocol at a cardiovascular research laboratory that ultimately confirmed the diagnosis of stretch syncope. The present article describes an approach to the evaluation of TAA and illustrates a typical case of stretch syncope. The importance of considering stretch syncope in the differential diagnosis of TAA is exemplified. Finally, our analyses help elucidate the pathophysiology of this rare entity.
Section 1

A 21-year-old right-handed man with a history of depression, attention-deficit/hyperactivity disorder, and obsessive-compulsive disorder presented for evaluation of spells of altered awareness. The episodes began when he was 15 years old. While studying for an examination, he stood up from his chair, stretched his arms up, and then lost awareness for an unclear period of time. His father found him lying on the floor. Shortly after, he started having spells on a daily basis.

He reports a 1 to 2-second prodrome where he “can feel them coming.” This is followed by sensations described as blacking out, feeling in a roller coaster, vision flashing in and out, feeling a pulse in the brain, brain fuzziness, and/or body numbness. He then “leaves his mind for about 30 seconds, but quickly returns to his normal self.” Postural tone is typically preserved. However, some events are accompanied by nonstereotypical, brief body shaking and, rarely, by falls.

He has not experienced serious injuries, oral trauma, or urinary/bowel incontinence. He has not noticed obvious triggers. He denies orthostatic intolerance to postural changes alone. He has no history of migraine or migraine aura. He has no sleep disorders, endocrine conditions, or epilepsy risk factors. There is no family history of neurologic disorders or recurrent syncope. Over the last few years, he has been prescribed trials of fluoxetine, atomoxetine, lisdexamfetamine, vortioxetine, and buspirone for psychiatric indications, but none of these medications affected his spells. He continues to have numerous episodes every day, which impair his academic performance in college. General physical and neurologic examinations are normal, including orthostatic vital signs.

Question for Consideration:
1. What is the differential diagnosis?
Section 2

Transient alteration in awareness (TAA) typically occurs as a manifestation of temporary cortical dysfunction. In the absence of head trauma or acute effects from drugs or toxins, different epileptic and nonepileptic phenomena can result in TAA with spontaneous recovery. Clinical history is essential in establishing a differential diagnosis.

In this patient, syncope/presyncope causing transient cerebral hypoperfusion is a consideration given the visual and sensory disturbances at onset and the brief duration of TAA. Syncope is commonly accompanied by abnormal motor activity.\textsuperscript{1,2}

Episodes could also be epileptic. For instance, vague cephalic sensations, autonomic manifestations, and/or somatosensory/viscerosensory symptoms followed by impaired awareness can occur with ictal involvement of frontal, insulo-opercular, or cingulate cortices. Somatosensory auras occur frequently in parietal lobe epilepsy. Visual symptoms are common in occipital lobe epilepsy.\textsuperscript{3,4}

The patient has no migraines or migraine aura. He does not have sleep disorders. Vertebrobasilar insufficiency is typically associated with brainstem deficits, which are not present. Although he reports symptoms consistent with derealization, feeling like passing out, and paresthesias, he does not meet the criteria for panic attacks per the \textit{Diagnostic and Statistical Manual of Mental Disorders, 5th Edition}. Functional neurologic disorder is a possibility, particularly in the context of his mental health comorbidities. Rare etiologies of syncope/presyncope including Eagle syndrome, carotid body tumors, or pheochromocytoma should be considered, but are improbable. Finally, overvigilance or an overinterpretation of benign, nonspecific symptoms is possible but unlikely as some events result in falls.\textsuperscript{1}

The patient saw numerous specialists. He underwent the following studies, which were all normal: transthoracic echocardiogram, tilt-table testing, 1.5 Tesla brain MRI, and MR angiogram of the head and neck. Over 30 days of cardiac event monitoring, there were “7 episodes of self-limited premature atrial contractions; otherwise, normal sinus rhythm and sinus tachycardia.” A 72-hour ambulatory EEG, performed at another facility, was reported as normal. Given his psychiatric comorbidities and normal workup, functional neurologic disorder was presumed. However, his psychiatrist was skeptical and referred him to our comprehensive epilepsy center for evaluation.

\textbf{Question for Consideration:}

1. What would be your next step in his evaluation?
Section 3

The patient had undergone appropriate initial evaluation for cardiovascular and autonomic causes of syncope/presyncope. Given his normal test results, syncope/presyncope was not favored. An outside ambulatory EEG showed no electrographic seizures. However, focal seizures from deep foci can be inapparent or subtle on scalp EEG.

We admitted the patient to the epilepsy monitoring unit (EMU) for continuous video-EEG monitoring. Dozens of typical events were captured, clinically characterized by extension of the back and shoulders, neck hyperextension, and concomitant lateral and upward head rotation, followed by TAA. Ictal EEG showed bitemporal polymorphic mixed theta/delta activity. Interictal EEG was normal. Although no definite electrographic seizures were noted, his fairly stereotypical semiology and consistent EEG pattern made us suspect the possibility of poorly lateralized and poorly localized epileptic seizures originating from a deep focus (such as insulo-opercular/cingulate).

PET and 7 Tesla MRI of the brain were normal. As epileptiform discharges were never captured on scalp EEG, magnetoencephalogram was ordered. Magnetoencephalogram was performed to investigate the presence of ictal discharges by evaluating their magnetic fields. Magnetoencephalography can be particularly helpful for seizure-onset zones originating from deep foci that are not well evaluated on scalp EEG. However, 2 magnetoencephalograms showed no definite abnormalities. Ictal single-photon emission CT was performed at another institution. Injection was done “within 10 seconds of the onset of presumed epileptic dysrhythmia”. The study showed “multiple cortical foci of increased radiotracer activity in the temporoparietal regions bilaterally”. An intracranial evaluation was considered, but there was not a strong hypothesis to guide electrode implantation.

He received trials of 7 different antiseizure medications (ASMs) with no significant change in spell frequency. He was also evaluated at 2 other comprehensive epilepsy centers, with similar results and conclusions as at our institution.

Questions for Consideration:
1. Are there features that argue in favor or against an epilepsy diagnosis?
2. What additional evaluation would you consider?

GO TO SECTION 4
Section 4

The presence of very frequent events showing negligible response to ASMs suggests that these could be nonepileptic. We admitted the patient to the EMU again, 1 year after his initial admission, and captured approximately 100 episodes with a constellation of the same symptoms described in Section 1. Spells occurred exclusively during wakefulness. Despite their high frequency, they never occurred out of sleep. On video-EEG, the background was normal just before the onset of the events. Then, the patient exhibited the same motor behaviors described in Section 3. This coincided with a transient reduction in the amplitude of the QRS complex in the ECG channel and was followed by the emergence of very brief, diffuse, polymorphic, mixed theta-delta activity on EEG. The patient then experienced typical TAA. One event was followed by a few clonic movements of the right upper extremity. He consistently pushed the event button a few seconds after the end of each episode (Video 1). In retrospect, ECG changes had been present during the patient’s first EMU admission. Interictal EEG was again normal.

At this point, we suspected a diagnosis of stretch syncope. The patient was referred to a cardiovascular research laboratory, and an experimental protocol was designed to test potential deficits in arterial pressure and cerebrovascular regulation. The primary focus was the beat-by-beat cardiovascular response to Valsalva maneuver because the events resembled strain maneuvers with a characteristic reduced QRS amplitude. The full study protocol is described as a supplement (eMethods, links.lww.com/WNL/B769). Valsalva maneuvers produced the characteristic 4 phases with adequate arterial pressure and cerebrovascular regulation (Figure). The patient did not have typical events while resting supine or during controlled breathing in either the supine or seated positions. However, during periods of quiet rest in the seated position, he demonstrated frequent motor behaviors consistent with his typical events (see Section 3). This was accompanied by a breath-hold and strain maneuver (Figure). Immediately after these motor behaviors, the patient reported symptoms consistent with his usual episodes. Monitoring during these events indicated that he performed a Valsalva-like maneuver.

Figure Cardiovascular and Autonomic Measurements

Valsalva maneuver performed by the patient, followed by a stretch event where he reported his typical symptoms. Both cases involve a deep breath (A), a decrease in ECG amplitude (B), shortening of R-R interval (C), a decrease in blood pressure (D), and a decrease in cerebral blood flow (E). However, the stretch event is of shorter duration than the Valsalva and yet causes a larger drop in both blood pressure and cerebral blood flow.
with a simultaneous stretch, inducing his typical symptoms. With the stretch event, both arterial pressure and cerebral blood flow dropped more precipitously than with Valsalva maneuver (Figure). The diagnosis of stretch syncope was confirmed. Sudomotor evaluation and skin biopsy performed later were consistent with an idiopathic small-fiber cholinergic neuropathy (eMethods).”

**Discussion**

Stretch syncope (SS) is a rare, distinct entity characterized by TAA induced by neck hyperextension during stretching.7 The few cases that have been published occurred in males > females between the ages of 7 and 26 years.5-10 Individuals with SS typically do not have a history of syncope other than that induced by stretching and neck hyperextension.9 Some have an apparent compulsion to self-induce their events.8

Our patient did not experience an urge to perform the movements. He did not see a reasoning behind them, they did not occur as a result of intrusive or distressing thoughts, and he did not report a sense of relief or completeness after performing the movements. There was no history of vocal tics. The duration of his motor behaviors was longer than that usually seen with motor tics. Given these considerations, the patient’s presentation was atypical for a tic disorder. Moreover, the patient underwent multiple trials of psychoactive medications (as described in Section 1), some of which can be used for the treatment of obsessive-compulsive disorder and/or tic disorders. None of these medications affected his spells.

Despite its rarity, SS is a highly relevant diagnosis as it can be easily mistaken for epilepsy for a number of reasons. These include stereotypical motor activity associated with the events; development of ictal tachycardia; and presence of rhythmic/semirhythmic slowing on EEG in the context of transient cerebral hypoperfusion, as can be seen in syncope.11 Moreover, classical presyncopal symptoms are not always present in SS.6,8

Although the pathophysiology of SS has not been fully elucidated, it is clear that Valsalva maneuver alone is insufficient to precipitate SS5-10 (including our patient’s case). Earlier reports proposed that SS may be a form of vertebrobasilar insufficiency, possibly related to mechanical compression of the vertebral arteries during neck rotation.5,6,9 We agree with more recent publications that SS is likely a form of vaso-depressor syncope.8,10 As noted by other authors, “given the delay between the stretching and the hypotension and the appearance of the slow wave EEG abnormalities, a reflex mechanism is most likely”.8 We hypothesize that in SS, superimposed stimuli (neck hyperextension during stretching) may restrict cerebral blood flow and induce a countervailing stretch input to the carotid baroreceptors, compromising adequate pressure regulation. The latter would be that, despite falling arterial pressure, the carotid baroreceptors experience increased stretch and hence do not provide an adequate sympathoexcitatory response.12 In this patient, small-fiber cholinergic neuropathy could contribute to his inability to maintain flow via vasodilation in the face of decreasing pressure.13 Reduction in QRS amplitude during stretching in SS (also noted by other authors6,8) may be due to increased distance between the chest wall and the heart during Valsalva/stretching.

Timely diagnosis of SS can avoid excessive diagnostic testing and unnecessary use of ASMs. Moreover, undoing a diagnosis of epilepsy that has previously been ratified by different specialists can be challenging and requires a strong physician-patient relationship. Avoidance of neck hyperextension while stretching effectively eliminates SS.5-7,9 Our patient was referred for cognitive behavioral and yoga breathing therapies to facilitate management of his motor manifestations. The frequency of his episodes has decreased.

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**Disclosure**

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References

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