Differentiating Parasomnias from Nocturnal Seizures

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Case Presentation

Patient with nocturnal events; referral diagnosis is “atypical night terrors.”

History of Present Illness

A 32-year-old woman presented to a sleep disorders center with a history of spells arising from sleep. The spells occurred on a nightly basis and were described as screaming with bilateral thrashing and flailing movements of the arms and legs. They frequently caused injury both to herself and her husband, who sleeps with her. Eyes can be open or closed. These events were also associated with loud screaming. There was no confusion or neurological deficit immediately afterward, and she was later able to remember some of the events. The spells usually lasted from 15 seconds to 1 minute, occurring 2-4 times a night, beginning soon after falling asleep. The patient was unable to recall any specific precipitators. She has tried multiple medications including carbamazepine, primidone, valproic acid, zonisamide, and clonazepam. Following placement of a vagal nerve stimulator, she became convinced that none of the treatments helped, and she stopped all medications on her own, with no change in the frequency of her spells.

Sleep History

The patient had a regular bedtime and wakeup time; she denied snoring. She did, however, complain of excessive daytime sleepiness, with an Epworth Sleepiness Scale score of 11, but denied symptoms of cataplexy, hypnagogic or hypnopompic hallucinations, or sleep paralysis. She had a few episodes of somnambulism as an adult, including one episode in which she defecated in the living room. There was no childhood history of sleepwalking, sleep terrors, or other parasomnia.

Past Medical History

The patient had a history of seizures as a child. However, those events were semiologically very different from her current spells. They began with burning paresthesias in the left face, a sensation of falling, and brief left face and arm movements with loss of awareness. The seizures eventually ceased with anti-epileptic drug therapy. The currently reported noctur-

nal spells with 4-extremity movements began some time after a sexual assault and a prolonged abusive relationship (which ended several years before she was married). She also has a history of depression with suicidal ideation but has never sought therapy.

Family History

There was no family history of seizures or of parasomnias.

Physical Examination

Patient presented in no acute distress, and had a blunted and at times negative affect. Tonsils are not enlarged, nares were patent. BMI was 28.1. Friedman palate position was 2 (allows visualization of the uvula and soft palate but not the tonsils). Respiratory, cardiac, and neurological examinations were all normal.

Workup

1. Nocturnal video-polysomnography (vPSG), with seizure montage:

The patient had a 3-minute sleep onset latency. REM onset latency was moderately prolonged. REM sleep had normal muscular atonia, without excessive twitching or behaviors. Mild snoring was observed, but her respiratory disturbance index was 0.6 events per hour, with a minimum oxygen saturation level of 94%. The patient had 6 spells arising from NREM sleep (usually N2 sleep) that appeared stereotypical and were characterized by violent right leg kicking, right arm extension, generalized thrashing, and prolonged screaming lasting less than a minute, followed by rapid orientation and appropriate interaction with the sleep technologist in which some awareness of the episode was described, along with apologetic comments about “doing it again.” The final spell occurred with the termination of sleep. There was no electrical seizure activity, although movement artifact often obscured the EEG during these spells.

2. Brain MRI and routine EEG: read as normal

3. Epilepsy monitoring unit (EMU):

A total of 43 events were recorded (average of 8 events per night). Each event lasted for about a minute and a half on average. Exemplar EEG tracings are shown in **Figures 1** and **2**. Pictures from the events are shown in **Figure 3**.

QUESTION 1: What do you see on the EEG on Figure 1?

QUESTION 2: Was the patient awake or asleep at the beginning of the event in Figure 2?

QUESTION 3: What is the diagnosis?

Figure 1—EEG recording during one of the typical events

Figure 2—EEG recording at the beginning of another typical event

At the clinical onset there is the appearance of multiple EEG artifacts, including muscle activity, movement artifacts, and a single electrode "pop" at Fp2 that creates a very large, extremely brief potential at the middle of the figure.

Figure 3—Sequence pictures of the patient during an event.

There was a slow, large amplitude circular movement at the right shoulder and hip. Tonic leg extension on the left is obscured by the blanket.

ANSWER 1: No EEG changes are seen during event except for muscle artifact and movement artifact (note that the artifact signal is also seen on EKG signal). A similar event previously recorded at an outside institution was interpreted as being nonepileptic, probably psychogenic.

ANSWER 2: Patient was in stage N2 sleep when the event started, as evidenced by the presence of sleep spindles. If you look carefully at Figure 4, you should see transitional sharp wave preceding the event.¹ This is followed by a subtle faster rhythm seen in the midline frontocentral channels, most prominently on the right. This activity was only apparent on a small portion of her events, due to muscle artifact.

ANSWER 3: Nocturnal frontal lobe epilepsy (NFLE)

PEARLS

We present a challenging case of a 32-year-old woman with nocturnal spells who presents with some of the classic features for frontal seizures, but with enough confounding factors to allow a very broad differential diagnosis. There are several clues from the history that suggest the epileptic nature of the events: the brief duration, the stereotypical presentation, and the history of childhood seizures. Moreover, frontal lobe seizures are known to occur predominantly during sleep.² These seizures may be associated with bizarre hypermotor activity without a clear loss of consciousness and may be unwitnessed by a groggy bed partner.

The differential diagnosis of paroxysmal events during sleep also includes:

1. Parasomnias
2. NREM arousal disorders (confusional arousals, sleep walking, sleep terrors)
 - Parasomnias associated with REM sleep (REM sleep behavior disorder [RBD])
 - Sleep related movement disorders
3. Psychogenic nonepileptic seizures
4. Sleep related dissociative disorders

NREM arousal disorders are common in childhood, can persist into adulthood, and at times can even begin in adulthood.³ The duration and complexity of those events can vary from brief and simple confusional arousals to more prolonged and complex somnambulism. Sleep terrors are usually distinguished by their strong associated autonomic features, including tachycardia and diaphoresis, and lack of recall the next day. Loud and prolonged screaming can occur, along with violent thrashing and bolting from bed in a terrified state. However, it is very rare, if not unprecedented, for sleep terrors to emerge multiple times nightly during virtually every night for a period of months or years.

Differentiating between nocturnal seizures and NREM parasomnias can be challenging, especially in regards to nocturnal frontal lobe epilepsy (NLFE) because of the typically unusual, bizarre presentation of NLFE seizures, along with its common association with a normal EEG. Features supporting an epilep-

Figure 4—Black arrows demonstrate high amplitude sharp waves with a phase reversals at C4/P4 followed by subtle rhythmic activity (white arrow) in the right frontocentral region that evolves in frequency and amplitude, before becoming obscured by muscle artifact on subsequent pages

Sharp waves are defined as sharply contoured electrical activity of < 200 ms duration and asymmetric rates of rise and fall. In comparison, the large amplitude activity immediately preceding the second sharp wave is slow, rounded, and has relatively symmetric positive (up) and negative (down) phases, and therefore represents normal interictal sleep activity.

tic etiology of paroxysmal events are: (1) stereotyped nature of the spells; (2) high frequency and tendency to cluster⁴; (3) timing of the events (NREM parasomnias usually emerge from slow wave sleep, which typically occurs within 2 h of sleep onset,⁵ whereas frontal lobe seizures may occur during any sleep stage, but are common shortly after falling asleep); (4) semiology of events (although frontal lobe seizures may have variable manifestations, the occurrence of prominent unilateral tonic stiffening favors an epileptic origin rather than a parasomnia); (5) duration of events (parasomnias are usually relatively prolonged events, whereas epileptic seizures, especially frontal lobe seizures, tend to be very brief, lasting < 2 min on average)⁴; and (6) presenting age (NREM parasomnias are often limited to childhood, but can occur in adulthood, whereas NFLE often persists into adulthood). In retrospect, the childhood seizures may well have been from the same focus, although it is unclear why the semiology changed with age. Finally, the reported episodes of “somnambulism” during adulthood in this patient, including one episode with defecation, suggests “episodic nocturnal wandering” of epileptic origin more than *bona fide* somnambulism as a parasomnia.⁶

RBD can be ruled out because there was preservation of the normal REM sleep atonia on polysomnography⁶; also RBD typically affects middle-aged or older males, although females of any age can develop medication-induced RBD. Drug-induced RBD is typically caused by SSRI and most other antidepressants (apart from bupropion or trazadone), which does not apply to this patient who never received an antidepressant. In addition, RBD would likely occur toward the end of the sleep cycle, which has not been seen in our patient.

There are several sleep related movement disorders according to the International Classification of Sleep Disorders (ICSD-2),⁷ including restless legs syndrome, sleep related leg cramps, periodic limb movement disorder, sleep related bruxism, and sleep related rhythmic movement disorders. However, the specific historical features for these conditions were absent, along with the lack of complexity and clustering pattern that was evident in our patient.

Although many seizures are easily distinguished from non-epileptic events on the basis of the history, this can be difficult in the case of NFLE. In our patient, the lack of a clear EEG correlate, the dramatic/complex movements, and her psychiatric/social history contributed to an earlier diagnosis of psychogenic events. However, it is important to note that EEG can frequently be normal in NFLE for multiple reasons, including deep generators, few electrodes, and poor field coverage with the international 10-20 system. In addition, the EEG can be frequently obscured by muscle artifact. Moreover, even when epileptiform activity is recorded, it may difficult to correctly lateralize the onset, especially from a parasagittal focus in which the near-midline ictal focus can create an electrical dipole directed toward the contralateral electrodes. There are several semiological features that can be seen in both NFLE and psychogenic nonepileptic seizures: eye closure, hypermotor activity, and partial recall during the events.

On the other hand, while the fact that the events arose out of sleep also support the diagnosis of seizures, it is quite common for patients with psychogenic nonepileptic seizures to describe the events as coming out of sleep; however, these usually arise from “pseudo-sleep,” whereby the patient awakens shortly before the event. Sleep related dissociative disorders typically affect females subjected to physical and/or sexual abuse, which applies to this patient. However, episodes occur during EEG wakefulness after sustained arousals from sleep, and the behaviors are not stereotypical.³

With more prolonged monitoring of this patient at our institution, we were able to confirm the stereotypical nature of the events on video, record several seizures in which the episodes progressed to left eye deviation and rhythmic left face twitching, and then a single episode with onset of fast activity in the right posterior quadrant that then evolved prior to clinical onset.

In diagnostically difficult cases, more prolonged monitoring can be very helpful for two reasons. First, by recording multiple events, the reviewing physician may begin to appreciate subtle but consistent findings in either the seizure semiology or EEG changes. Second, recording multiple events increases the odds of either capturing an event without motion artifact or an event in which electrographic activity builds to the point of being recordable on the scalp.

Diagnostic alternative approaches: when the anatomic imaging is normal, the addition of functional imaging can be very helpful. Ictal single-photon emission computed tomography (SPECT) can be useful to detect subtle areas of increased blood flow, especially when using subtraction ictal SPECT co-registered to MRI (SISCOM) analysis.⁸ Newer technologies, including magnetoencephalography, function resting state, and diffusion tensor imaging, are being explored as alternative approaches to define a seizure focus when clinical suspicion of epilepsy is high.⁹

Figure 5A—SISCOM analysis of her preoperative ictal SPECT

Figure 5B—Postoperative MRI FLAIR sequence images, white arrows refer to the area of resection

Outcome

While her MRI was initially read as normal, there was indeed a slight asymmetry in the cortical gyri in the right paramedian posterior area. While this was not definitely abnormal, ictal SPECT with SISCOM analysis showed very clear increased perfusion during a seizure (**Figure 5A**). She subsequently underwent intracranial recording, which confirmed ictal onset in this region. Following resection of this small area (**Figure 5B**) she became seizure free and had a much better mood and energy level during the day. Her family commented on the disappearance of her longstanding blunted affect. She initially had some left foot weakness that resolved to the point that she was able to take up running. She has returned to work and recently celebrated the birth of her first child.

CITATION

Boursoulian LJ; Schenck CH; Mahowald MW; Lagrange AH. Differentiating parasomnias from nocturnal seizures. *J Clin Sleep Med* 2012;8(1):108-112.

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SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication June, 2011

Submitted in final revised form September, 2011

Accepted for publication October, 2011

DISCLOSURE STATEMENT

This was not an industry supported study. The author has indicated no financial conflicts of interest.