LESSONS LEARNED AT THE INTERFACE OF MEDICINE AND PSYCHIATRY

The Psychiatric Consultation Service at Massachusetts General Hospital (MGH) sees medical and surgical inpatients with comorbid psychiatric symptoms and conditions. Such consultations require the integration of medical and psychiatric knowledge. During their thrice-weekly rounds, Drs. Roffman and Stern discuss the diagnosis and management of conditions confronted. These discussions have given rise to rounds reports that will prove useful for clinicians practicing at the interface of medicine and psychiatry.

This is the last in a series of 3 rounds reports that focus on patients with neuropsychiatric symptoms, which can be especially challenging to diagnose and manage effectively. We hope to provide practical insights for primary care providers who encounter these common symptoms.

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A Complex Presentation of Complex Partial Seizures

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Have you encountered patients with affective, behavioral, and cognitive symptoms that were difficult to place in one diagnostic category? Have you suspected a diagnosis of complex partial seizures but found it difficult to establish this diagnosis with laboratory tests? Moreover, have you ever experienced difficulty distinguishing seizures from nonepileptic seizures ("pseudoseizures")? If you have, then the following case vignette of a man admitted to the general hospital with a complex array of neuropsychiatric symptoms should provide the forum for answers to these and other questions related to psychiatric manifestations of seizures.

Case Presentation

Mr. A, a 34-year-old man with a history of an atypical psychosis and a personality disorder, was admitted to the epilepsy monitoring unit for evaluation of a possible seizure disorder. While being monitored simultaneously with video and an electroencephalograph (EEG), Mr. A had a sudden episode of shaking that consisted of his arms flailing widely and crossing the midline. He was unresponsive to questions but shouting, "Help me!" Following this episode, he appeared fully alert and reported clear memories of the event. Later that night, he complained of abdominal pain. Soon thereafter, he became less and less responsive and continually repeated the phrase "Are those for me?" EEG recordings indicated no evidence of epileptiform activity during either episode. A magnetic resonance imaging (MRI) study showed heterotopic gray matter in the frontal and temporal regions. The next day, after Mr. A's symptoms had resolved, a functional neuroimaging scan revealed an area of decreased brain activity in the left temporal lobe. Mr. A was subsequently started on treatment with valproic acid, which effectively prevented further episodes.

What Are Complex Partial Seizures, and How Do They Present?

Complex partial seizures (CPS) are the most common form of epilepsy in adults.[1] CPS involve abnormal regional discharges of electrical activity in the brain. Unlike generalized seizures (such as tonic-clonic or absence seizures), which involve both cerebral hemispheres, CPS are not associated with a loss of consciousness. However, sensorium is altered in CPS, which distinguishes them from simple partial seizures, in which mental status is not affected. Patients with CPS may manifest a wide variety of symptoms, including stereotyped movements or behaviors, paroxysmal anxiety or somatic symptoms, bizarre or incongruous affect, and changes in cognition. Many of these features characterize the second of Mr. A's episodes.

Because of these affective, behavioral, and cognitive symptoms, patients with CPS are frequently misdiagnosed with psychiatric illnesses.

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Often, these symptoms present with unusual qualities that are atypical for primary psychiatric syndromes. These can include gustatory and olfactory hallucinations; micropsia or macropsia; and intense delusions involving bodily harm, déjà vu, or "out-of-body" experiences. CPS have also been associated with certain personality features including moral rigidity, hyperreligiousity, hypergraphia, and viscosity (or "stickiness," e.g., difficulty ending conversations).[2]

How Can One Establish the Diagnosis of Complex Partial Seizures?

EEGs, which detect abnormal patterns of cortical electrical activity, can be helpful in characterizing and localizing many types of seizures. However, because electrical discharges due to CPS may involve only subcortical brain regions, EEG findings may appear nonspecific or unremarkable even during active seizures. Thus, without further diagnostic workup, patients with CPS may be incorrectly assumed to carry a primary psychiatric diagnosis.

Neuroimaging techniques can sometimes be useful in detecting brain abnormalities associated with CPS. Brain structure should be assessed with MRI, which detects subtle anatomical abnormalities with greater sensitivity than computed tomography scans. These abnormalities may include neurodevelopmental defects (such as heterotopic gray matter in the case of Mr. A), traumatic brain injuries, strokes, and mass lesions, any of which may serve as a seizure focus. Functional neuroimaging scans, such as single photon emission computed tomography (SPECT) and positron emission tomography (PET), may be used to identify aberrant brain activity patterns associated with CPS.[3,4] Patients with active seizures demonstrate increased metabolic activity in corresponding brain areas; moreover, patients who are interictal or postictal may show a "cold footprint" in activity in affected brain regions. Although the sensitivity and specificity of these findings in CPS remain uncertain, functional neuroimaging can serve as a useful diagnostic tool in cases with a high index of suspicion.

How Should Psychiatric Sequelae of Complex Partial Seizures Be Managed?

Treatment with antiepileptic medications may, by itself, diminish or eliminate affective and behavioral disturbances caused by CPS. This effect may reflect adequate control of the underlying electrical disturbance, mood-stabilizing properties of anticonvulsant medications, or both. In some cases, though, psychiatric symptoms may persist and require additional treatment with antidepressants, antipsychotics, or anxiolytics. Two factors merit special consideration in these patients. First, many antiepileptic drugs inhibit or induce hepatic P450 isoenzymes. These effects can substantially alter blood levels of psychotropic medications, necessitating dose adjustments. Second, many psychotropic medications—especially antipsychotics—can lower the seizure threshold, requiring higher doses of anticonvulsant medications. Close collaboration between psychiatrists, neurologists, and primary care physicians who care for patients with CPS can minimize these drug-related effects.

Table 1. Features Consistent With Nonepileptic Seizures[a]

Events occur with suggestion or provocation
Symptoms begin or end gradually
Patients are responsive or speak in the setting of bilateral convulsions
Movements are asymmetric or alternate
Movements cross the midline
Patients exhibit head bobbling, pelvic thrusting, kicking, or thrashing
Symptoms persist for > 3 minutes

[a]Based on Huffman et al.[8]

What Are Nonepileptic Seizures?

Patients with nonepileptic seizures (NES) display abnormal movements as a consequence of psychological factors, rather than electrical dysrhythmia in the brain. NES are frequently a manifestation of a conversion disorder, in which motor symptoms reflect an unconscious effort to externalize intrapsychic conflict. For cases in which patients consciously feign symptoms, NES can represent a form of factitious disorder or malingering. NES occur more frequently in women than men[5] and are seen in up to 20% of patients admitted to epilepsy monitoring units.[6] In most cases, NES present with features similar to generalized tonic-clonic seizures (e.g., bilateral involvement).

How May Clinicians Differentiate Epileptic and Nonepileptic Seizures?

To complicate matters, as seen with Mr. A, epilepsy and NES are highly comorbid, with true seizures occurring in as many as 25% of patients with NES.[7] The ability to differentiate NES from true seizures becomes especially important in these cases. The first step in assessing patients with convulsions, regardless of the degree of suspicion for NES, is a complete medical and neurologic evaluation. In the absence of a clear medical or neurologic etiology, several features of the history, convulsive event, and postconvulsion presentation increase the likelihood of NES. A history of other unexplained neurologic symptoms, especially during periods of stress, is often suggestive. Moreover, the persistence of seizures despite therapeutic drug levels can represent a red flag; however, in some cases, true seizures are also refractory to medical treatment and may ultimately require neurosurgical intervention. Several patterns of convulsions more consistent with NES than with true seizures are listed in Table 1.[8] In many cases, these patterns are clearly linked to provoca-

tion or are inconsistent with functional neuroanatomical processes (e.g., speaking during a tonic-clonic seizure). Although lack of epileptiform findings on EEG during a convulsion may suggest NES, as we have seen, true subcortical seizures may also present this way. Finally, several postconvulsive events can signal NES, including rapid return to full awareness or lucid recall of the convulsions.

Laboratory and neuropsychological testing can also be useful to differentiate NES from a true seizure disorder. Patients with true tonic-clonic seizures can exhibit transient elevations in serum prolactin and creatine phosphokinase; prolactin levels should be drawn within an hour of the event to be clinically useful. Neuropsychological test results consistent with conversion disorder can also be helpful, but should not be considered diagnostic in the absence of clinical and laboratory data.

What Treatment Approach Can Best Help Patients With Nonepileptic Seizures?

Management of NES incorporates several of the themes that have underscored this series on neuropsychiatric symptoms. We will therefore conclude by revisiting each of these themes and focusing on how they apply to the treatment of NES.

1. Early identification and psychiatric intervention lead to better clinical outcomes. In the case of NES, delay in diagnosis and presence of comorbid psychiatric illness have both been associated with refractory symptoms.[9] Rapid referral to a psychiatrist can address both of these issues. Prompt psychiatric referral in the setting of unusual or difficult-to-manage psychiatric symptoms (such as those seen in CPS) can also facilitate diagnosis and appropriate treatment.
2. Direct confrontation of the patient or minimization of symptoms (e.g., "It's just in your mind") is not likely to be helpful. Rather, acknowledging that the function of the central nervous system is impaired provides validation of the patient's experience. This news should be delivered in a positive light, stressing that the electrical function of the brain appears normal, there are no structural abnormalities, and antiepileptic medications (with their many side effects) need not be started.
3. On the other hand, emphasizing that stress, anxiety, and depression may worsen the underlying condition provides an outlet for establishing psychiatric treatment. Furthermore, suggesting that the symptoms will diminish over time can itself contribute to patients' improvement.
4. Integrated follow-up with medical and psychiatric providers assures continuity of care. Moreover, medical (and neurologic, if indicated) follow-up after remission of NES helps to extinguish the relationship between medical settings and active symptoms. Thus, emphasis on physical and mental well-being creates an effective, shame-free environment for treatment of NES; helps prevent recurrence of symptoms; and addresses contributory psychosocial concerns.

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