

Chapter 11

Depression and Epilepsy

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Case Presentation

A 32-year-old, right-handed gentleman with a long history of depression presents with a several-year history of brief paroxysmal recurrent spells of an unpleasant gastric sensation (as if his “stomach is turning around”) and feeling of déjà vu. According to his wife, he will occasionally repeat phrases during the event such as “Oh, my stomach,” and be unaware of the events after they occur. They suspect these events are happening about once or twice per week. He has never experienced a convulsion. The patient’s only potential risk factor for seizures was a traumatic, closed-head injury and brief concussion that he sustained 12 years ago while serving in the military. He was ultimately dismissed from active military duty due to persistent depression, which was severe. He is currently maintained on paroxetine 40 mg daily with some improvement in mood, but admits to occasional passive suicidal ideation without an active plan. MRI of the brain and basic labs are within normal limits. He is admitted to the epilepsy monitoring unit (EMU) to clarify the differential diagnosis of the recurrent spells. Interictally, right temporal sharp waves were present. The following segment of EEG represents a clinical event that progressed to include bicycling motions of legs, mumbling, and inability to communicate (Fig. 11.1). The entire event lasted 1 min and 40 s. After the event the patient was amnesic for the episode that was identified by his family.

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Fig. 11.1 EEG demonstrates an electrographic seizure that is maximal in the right anterior temporal region with a right hemispheric predominant bilateral field

Clinical Questions

1. Does this EEG support a particular clinical diagnosis?
2. What is the relationship between depression, epilepsy, and the risk of suicidality?
3. How does the patient's diagnosis of major depression impact your treatment plan (i.e., choice of AED)?
4. How would a diagnosis of epilepsy impact your recommendations for treatment for his depression?
5. What is the appropriate counseling for patients regarding epilepsy and comorbid depression?

Diagnostic Discussion

1. This EEG demonstrates rhythmic slowing of background activity over the right hemisphere, maximal in the right temporal region, which evolves in frequency and morphology to include sharp components. There is bi-frontal spread of the rhythmic slow waves. Although this is a single EEG "snapshot," it was able to confirm a seizure emanating from the right temporal head region that spreads to

involve both sides of the brain. In combination with the history and clinical picture, this is diagnostic of localization-related epilepsy, likely of right temporal lobe origin.

2. The lifetime prevalence of depression in people with epilepsy is approximately 30 %, which is significantly higher than for the general population. On average, the rate of death by suicide is ten times higher in people with epilepsy than in controls, and this increased risk is largely explained by the presence of comorbid depression. Recent studies have indicated a strong bidirectional association between epilepsy and depression with the presence of depression/suicidality frequently occurring both before seizures develop as well as after epilepsy has been diagnosed. Therefore, major depression puts one at higher than average risk for being diagnosed with epilepsy, and having epilepsy puts one at higher risk of being diagnosed with major depression. It is not only the case where the diagnosis and treatment of epilepsy *confer* a risk of depression (i.e., reactive depression). Rather, the relationship may reflect a common underlying pathophysiological mechanism that is common for both epilepsy and depression.
3. The presence of comorbid depression or other psychiatric comorbidity may lead you to consider an AED with mood stabilization properties, such as valproic acid, lamotrigine, or carbamazepine. Other ASDs such as phenobarbital, topiramate, and levetiracetam may be associated with mood and behavior lability. Therefore, these medications should be used with caution as a first-line treatment for epilepsy in depressed patients. In 2008, the US Food and Drug Administration (FDA) released a safety alert regarding an increased risk of suicidal behavior for patients treated with ASDs. Additional scrutiny has suggested that all ASDs carry an equivalent risk for depression, and the current consensus is that the risk associated with untreated epilepsy is far greater than the risk of AED-associated suicidal behavior.
4. Antidepressants, in general, are not contraindicated in patients with epilepsy, and treatment of comorbid depression in people with epilepsy is critical. Other than bupropion (which should be avoided as it increases the risk of seizures), commonly used antidepressants do not appear to lower the seizure threshold. Fluoxetine and paroxetine are strong inhibitors of hepatic enzymes and, therefore, may increase the levels of ASDs with co-administration, potentially leading to AED toxicity. This is easily avoided by monitoring serum drug levels and making adjustments as needed.
5. It is important to educate patients about the importance of treating *both* their epilepsy and their depression. Because many patients search the Internet for information about their diagnoses and medications, they are likely to have concerns about potential interactions and drug side effects. They should be reassured that the risk of stopping treatment—for either depression or epilepsy—far outweighs theoretical risks that may be associated with the use of their medications. Patients and their families should be counseled to watch for signs of depression and report any changes in mood or the presence of suicidal ideations. These signs should be taken seriously given the nature and chronicity of epilepsy.

If atypical deterioration of mood does occur as a result of the use of a particular AED, then practitioners should strongly consider changing that AED to an alternative agent.

Clinical Pearls

1. Depression, suicidality, and other psychiatric comorbidities are more common in people with epilepsy than in the general population.
2. Epilepsy and depression can—and should—be treated concomitantly. Physicians should consider an AED that has positive mood effects, such as lamotrigine, as a first-line agent for patients with depression. Avoid bupropion, but other antidepressants such as the selective serotonin reuptake inhibitors are not contraindicated in people with epilepsy.
3. Ask about mood and suicidal ideation at every clinic visit when treating people with epilepsy. Be ready to change your treatment plan if there are red flags that implicate AED-induced mood changes.

Bibliography

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