Lacosamide-Induced Tactile Hallucinations in a Patient With Complex Partial Seizures

To the Editor: Anti-epileptic drugs (AED) are known to have psychiatric side effects such as depression, behavioral problems, suicidality, and less commonly, psychosis.[1,2] There have been reports of patients developing psychosis on AEDs including levetiracetam, zonisamide, and topiramate.[1–3] There are very few reported cases of suspected psychotic reaction to the newer AED lacosamide (LCM).[4] In clinical trials in patients with partial onset seizures, LCM caused confusional state, and altered and depressed mood as treatment emergent adverse events. Psychosis and hallucination were identified as adverse effects during its post-approval use.[5] We present a case of a young man who developed severe psychosis with tactile hallucinations following addition of LCM to his AED regimen.

Case Report

"Mr. P" is a 34-year-old man with a past medical history of seizure disorder, hypertension, type 2 diabetes mellitus, and deep venous thrombosis who presented to the emergency room with new acute onset of psychosis. The previous night, he had burst into his parent's bedroom screaming that there were bugs crawling out of his penis. He said he did not see the bugs but felt them on his hands and threw them on the floor. He also claimed to have heard the neighbors talking and making negative comments about him because he urinated while sitting on the toilet rather than standing. He was also preoccupied with persecutory delusion of being poisoned by his brother. According to the family, he was very agitated, exhibited bizarre behaviors, was very angry at the brother, and also punched his father. By the time he reached the emergency room, he did not have detailed recollection of the events and appeared confused.

The patient had been taking carbamazepine 400 mg q.i.d. and topamax 200 mg b.i.d. for complex partial seizures. Ten days prior to presenting to the ED, he had been started on LCM (vimpat) 50 mg twice daily for intractable seizures, and 7 days after that, the dose had been increased to 100 mg b.i.d.. He did not have any prior history of psychiatric diagnoses or treatment.

On examination, he appeared drowsy, had disheveled appearance, spontaneous but slow speech, disorganized thought process, paranoid ideations, and self-reported auditory hallucinations. His affect was appropriately reactive. He denied any suicidal or homicidal ideation, intent, or plans. He was oriented appropriately to time, place, and person. He had no cranial nerves or sensorimotor deficits. At the time, his gait was not assessed because of drowsiness. Physical examination was otherwise within normal limits.

Besides mild leukocytosis, other labs including electrolytes, hepatic function panel, amylase, and lipase were within normal limits. Urinalysis was normal. His urine toxicology was positive for Cannabis. Cardiac enzymes were negative, and ECG was normal. CT scan of head did not show any acute intracranial abnormality.

Differential diagnoses considered were psychosis secondary to LCM use, ictal psychosis, interictal psychosis, substance-induced psychosis, and first onset of primary psychotic disorder. LCM was discontinued and was started on oral risperdal 1 mg twice daily. The patient was transferred to the inpatient medical unit, where he continued to receive risperdal. Seizures were managed with valproic acid and carbamazepine. Video EEG monitoring on the unit did not show any further seizure activity. Psychosis improved gradually and resolved completely 7 days after initial onset. Depakote was added to his antiepileptic regimen. He remained seizure-free for the rest of his hospital stay. He was discharged with neurology and psychiatry outpatient follow-up. Risperidone was gradually tapered off and eventually discontinued. He remained psychosis-free at the 3-month follow-up.

Discussion

AEDs are known to cause mood disorders and other psychiatric disturbances. Some aggressive behavior has been reported with the use of Levetiracetam.[6] LCM is one of the newer AEDs approved in 2008 by the Food and Drug Administration (FDA) as adjuvant treatment in partial–onset seizures in adults. It has two proposed mechanisms of action—by selectively enhancing slow inactivation of sodium channels leading to reduction of pathophysiological hyperactivity, and by binding to the collapsin response mediator protein-2 (CRMP-2) and modulating its function, thereby leading to attenuation of the effects of neurotrophic factors on axon growth. Most commonly observed adverse effects are dizziness, nausea, diplopia, abnormal co-ordination, ataxia, vomiting and nystagmus.[7] According to Halford and Lapointe, about 0.03% of patients have been reported to develop psychosis following LCM use.[4]

Our patient did not have a pre-existing history of psychosis. He had been taking a combination of AEDs for several years without any adverse psychiatric reactions. He developed a severe psychotic reaction characterized by tactile hallucinations, auditory hallucinations, and paranoid delusions about 10 days after starting LCM. His psychotic symptoms resolved within 7 days of discontinuing the suspected offending agent. This temporal relationship suggests a causal role for LCM in development of psychotic symptoms in our patient.

Patients with epilepsy are known to be at a higher risk of developing psychotic symptoms.[8] In partial complex seizures, hallucinations can be a feature of the seizure disorder. Our patient had a long history of intractable seizures but he had never had any psychotic symptoms as part of his seizures. Cannabis use has also been linked with psychotic symptoms but tactile hallucinations and severe delusions are not typically seen with cannabis.[9] Our patient had been using cannabis for almost 10 years without experiencing any psychotic symptoms. A confounding factor in attempting to establish a causal relationship of psychosis with LCM could be that risperidone was started at the same time that LCM was discontinued. Therefore, the possibility that this was a new onset of a primary psychotic disorder that responded to treatment with antipsychotic treatment cannot be completely ruled out. On follow-up at 3 months, the patient was no longer taking risperidone, and he had not experienced any further psychotic symptoms. A rechallenge with LCM leading to re-emergence of psychotic symptoms would have further supported a causal relationship between LCM and psychosis. However, for reasons of clinical safety, a rechallenge was not considered. Instead, his seizure disorder was controlled with topiramate and valproic acid.

It has been suggested that a combination of AED regimen or abrupt change in the regimen rather than a particular drug is responsible for developing psychosis.[3] It is conceivable that the introduction of LCM to his pre-existing AED regimen was responsible for development of psychosis in our patient.

Conclusions

Epilepsy is a complex disorder with psychosis as a possible presentation for complex partial seizures. Furthermore, the treatment with AEDs itself is known to cause significant psychiatric adverse reactions. Depression and suicidality are known potential adverse effects and providers are recommended to monitor carefully for these symptoms. Psychosis is a less common adverse effect of AED treatment. To our knowledge, our patient represents the first reported case of tactile hallucinations likely caused by LCM. Clinicians should monitor patients carefully for new onset or worsening of pre-existing psychiatric symptoms including psychosis while starting a new AED or making significant changes to the AED regimen.

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