Case Report

Acute Psychosis Precipitated by Lacosamide

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Antiepileptic-induced psychosis is a relatively uncommon but well-described adverse effect in patients with epilepsy. Its prevalence has been estimated to occur in 1.0% to 8.4% of individuals in clinical trials.[1] Lacosamide is a newer agent approved by the US Food and Drug Administration in 2008 for the treatment of focal (partial-onset) seizures.[2] Psychotic phenomena have been described in prior case reports after initiation of lacosamide; however, the clinical presentation of these patients has been mixed given comorbid confounding variables.[3–6] In this case report, we present a patient with chronic epilepsy who was started on lacosamide and acutely developed paranoid delusions and hallucinations with no other conflicting symptoms.

Case Report

Mr A was a 52-year-old man with a diagnosis of epilepsy and no prior psychiatric history who presented to the emergency department due to the acute onset of delusions and hallucinations. He was accompanied by his wife, who was able to provide collateral information. During the interview, Mr A perseverated on how his neighbors were plotting to frame him for a murder he did not commit. He shared that the police had come to his home numerous times already to investigate. His wife reported that the patient had been talking to himself incessantly and yelling and conversing with unseen individuals. She stated that his symptoms had developed acutely over the past 3 to 4 days. Notably, his neurologist had just altered his antiepileptic medication. Mr A had been taking valproic acid 500 mg in the morning and 1,000 mg at bedtime for many years given his history of epilepsy. However, due to weight gain and metabolic syndrome, he was gradually tapered off the valproic acid and then switched to lacosamide 50 mg twice/d 4 days ago.

On examination, he was found to have intermittent tangential thoughts and prominent paranoid delusions and was actively responding to auditory hallucinations. He was otherwise cognitively intact with no impairment of his attention, arousal, memory, language, or executive functions. His laboratory workup for substances, infections, or other organic etiologies was unremarkable. Computed tomography and magnetic resonance imaging of the brain revealed no abnormalities. A routine electroencephalogram with provocative stimuli was negative for seizure activity. He was subsequently admitted to the inpatient psychiatric unit for a preliminary diagnosis of late-onset schizophrenia. After repeat evaluation, it was proposed that lacosamide was the likely culprit responsible for his symptoms. No antipsychotics were initiated, and, instead, the patient's lacosamide was discontinued. His psychotic features decreased in severity by the second day and completely resolved after 6 days. At outpatient follow-up 2 weeks later, his symptoms remained in remission.

Discussion

Prior case reports[3–6] describe a mixed presentation for incidents of lacosamide-induced psychosis. The patients had either comorbid substance abuse or altered sensorium and arousal, thus suggesting a delirious state instead of a pure psychosis. Additionally, antipsychotics had been administered in those patients, thus masking true effects from the discontinuation of lacosamide.[3–6] In our patient, his neuropsychological testing was otherwise normal, and he experienced a rapid recovery after discontinuation of lacosamide, with no other interventions.

The putative mechanism of lacosamide's psychotomimetic properties has not been well-established or even routinely discussed. Our proposed theory centers on potential genetic factors and lacosamide's unique mechanism of action. Large genomic studies have suggested that multiple types of voltage-gated sodium channels are involved in the pathogenesis of psychosis.[7] Furthermore, excessive activity of collapsing response mediator protein 2 (CRMP2), which is a master regulator of axon guidance and dendritic branching in neural networks, has also been implicated in the pathophysiology of psychotic symptoms.[8] Lacosamide enhances the slow inactivation of voltage-gated sodium channels and also modulates CRMP2,[2] and this may have negatively precipitated such symptoms in our patient, especially if he possessed any inherent mutations that would have been potentiated by lacosamide. Future basic and translational studies are needed to further investigate the psychosis-inducing properties of lacosamide and other antiepileptics.

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