Development of Posttraumatic Stress Disorder During Treatment of Depression With Lamotrigine

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Lamotrigine is a US Food and Drug Administration–approved drug for the maintenance treatment of adult bipolar disorder and treatment of seizures in patients aged ≥2 years. It is also a recommended option for management of bipolar I or II depression.[1] Lamotrigine augmentation has also been found to be effective for treatment-resistant unipolar depression[2] as well as posttraumatic stress disorder (PTSD).[3] There is accumulating evidence that some patients with seizures[4] or bipolar disorder[5] develop obsessive-compulsive disorder (OCD) following treatment with lamotrigine. These symptoms generally disappear after the discontinuation of lamotrigine.[4,5] This case describes a woman with a history of OCD and major depressive disorder who developed PTSD following treatment with lamotrigine.

Case Report

A 29-year-old woman was initially referred to our tertiary care clinic more than 10 years ago. She had a long-standing history of psychiatric illness and had received various diagnoses including global developmental delay, Tourette's disorder, major depressive disorder, and OCD. She was sexually abused as a child by a close family member. A diagnosis of PTSD was suspected but not confirmed during follow-up visits with various professionals over 15 years. A couple of years ago, she had a recurrence of depression with mixed features following a stillbirth despite treatment with venlafaxine and olanzapine. The discontinuation of venlafaxine resulted in resolution of mixed features but caused worsening of depression. Since she had previously had trials of various antidepressants with limited effectiveness, it was decided to try lamotrigine. Due to concerns about weight gain from olanzapine, a cross-taper with loxapine was also commenced. As the lamotrigine dose was gradually escalated to 75 mg twice/d, the depression remitted. Given the marked overall improvement in her condition, she was maintained on the same combination to which she had responded: loxapine 10 mg/d, olanzapine 15 mg/d, and lamotrigine 150 mg/d.

Approximately 7 months after the addition of lamotrigine, she developed symptoms of PTSD including recurrent intrusive memories and dreams of sexual abuse as well as flashbacks of the traumatic event from her childhood. She also experienced recurrence of symptoms of depression. Using *DSM-5* criteria, she was diagnosed with PTSD with delayed expression. She did not meet the criteria for current major depressive episode or OCD. Lamotrigine was tapered off due to reports of its association with obsessions and compulsions. The PTSD symptoms resolved within 3 weeks of discontinuation of lamotrigine. She had expressed a strong desire to consult a psychotherapist to help her deal with the childhood trauma, but she has not had psychotherapy at the time of this writing. She is currently being treated with loxapine 10 mg/d and olanzapine 15 mg/d.

Discussion

This is the first reported case, to my knowledge, of development of PTSD following treatment with lamotrigine. The temporal association of PTSD symptoms with lamotrigine, the resolution of these symptoms after the discontinuation of the medication, and the absence of other factors such as substance use or a medical condition suggest that lamotrigine likely played a causal role in the induction of PTSD. This case has important diagnostic, therapeutic, and heuristic implications. Diagnostically, it implies that lamotrigine may induce symptoms of PTSD that are reversible following its discontinuation. In terms of treatment, addition of another drug to manage PTSD may have increased the side effect burden without necessarily improving the PTSD. Psychotherapy may have been less effective or not effective at all if the patient had continued taking lamotrigine. Further research is needed to clarify the role of lamotrigine in the onset of PTSD. If it turns out that lamotrigine does indeed precipitate symptoms of PTSD, this association may provide insight into the biological underpinnings of PTSD.[6]

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