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RESEARCH ARTICLE

Lamotrigine-induced manicepisodeina patient with comorbid bipolar disorder and obsessive-compulsive disorder: case report

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Abstract

The coexistence of obsessive-compulsive disorderand bipolar disorder is a prevalent issue in psychiatry.Population studies have found lifetime prevalence rates of comorbid obsessive-compulsive disorderin bipolar disorder patients ranging between 11.1% and 21%. The primary treatmentforobsessive-compulsive disorder, serotonin reuptake inhibitors, can induce manic episodes in bipolar disorder patients. This article presents a case of a 54-year-old woman with bipolar disorder and obsessive-compulsive disorder comorbidity, who experienced a manic shift after the introduction of lamotrigine, a drug commonly used for bipolar disorder and known for its mood-stabilizing properties. Although lamotrigine has been recommended, especially for patients predisposed to depressive bouts, its potential to induce manic or hypomanic states remains controversial. The presented patient's reaction to lamotrigine suggests a possible link between the drug and the onset of manic episodes, especially in those with a history of bipolar disorder and obsessive-compulsive disorder. Furthermore, while lamotrigine offers benefits for bipolar depression, healthcare professionals need to exercise caution due to its potential to initiate manic or hypomanic states, especially in patients with complex clinical backgrounds. Comprehensive research and careful post-marketing observations are crucial to better understand the risk-benefit profile of lamotrigine.

Introduction:

The co-occurrence of obsessive-compulsive disorder (OCD) and bipolar disorder (BD) represents a complex yet not uncommon comorbidity in the field of psychiatry (Sharma and Reddy, 2019).Population-based studies conducted in Italy and the USA have reported lifetime prevalence rates of comorbid OCD in BD patients ranging between 11.1% and 21%. This is further substantiated by a systematic review and meta-analysis, which found a pooled prevalence of OCD in 17% of BD patients, and conversely, a similar pooled prevalence of BD in approximately 18% of OCD patients(Amerio et al., 2015). Such a frequent association underscores the significant nosological and therapeutic implications intrinsic to this comorbidity(Amerio et al., 2015). Although serotonin reuptake inhibitors (SRIs) are the

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first-line treatment for OCD, they can induce manic or mixed mood states in BD patients (Amerio et al., 2015; Amerio et al., 2014; Kazhungil and Mohandas, 2016).Additionally, while the overarching prevalence of BD-OCD comorbidity is well-researched, the optimal treatment approach remains ambiguous (Sharma and Reddy, 2019). This report illuminates these intricacies through the case of a 54-year-old woman with BD-OCD comorbidity who underwent a manic shift after the gradual introduction of lamotrigine, aimed at managing exacerbated obsessive thoughts during a prominent depressive episode. To our knowledge, this article is the first to report in the literature a manic episode induced by lamotrigine in a patient with a comorbidity of bipolar disorder and OCD.Written informed consent was obtained from the patient for publication of this Case report.

Case Report:

A 54-year-old woman, had been under treatment for comorbid bipolar disorder (BD) and obsessive-compulsive disorder (OCD) since the age of 24. Her clinical journey was punctuated by multiple hospital admissions, primarily due to manic shifts, notably when treated with SSRI antidepressants. Her bipolar presentation was mainly depressive, with partial responsiveness to quetiapine 400 mg. During a recent outpatient consultation, she lamented the intensification of her obsessive thoughts of a religious nature over the past months. The clinical assessment revealed a patient exhibiting psychomotor slowing, accompanied by mood sadness, anhedonia, and despair. She described pervasive religious-themed obsessions, manifesting as intrusive thoughts of blaspheming against her deity, compounded by overwhelming anxiety, feelings of guilt, self-deprecation, sleep disturbances, diminished appetite, decreased libido, and limited insight into her ailment.

Considering her previous manic episodes, particularly those precipitated by antidepressants, the clinical decision leaned towards the introduction of lamotrigine, treatment that she has not previously undergone. This choice was influenced by certain studies that proposed its efficacy in bipolar depression and OCD, especially in conjunction with atypical antipsychotics. A cautious titration plan was set in motion, increasing by 25 mg weekly. However, as her daily dose reached 50 mg, she began to experience escalating insomnia and hyperactivity. This trajectory took a steeper turn when the dose was augmented to 75 mg daily. She presented with pronounced psychomotor agitation, irritability, and distractibility. She was distractible and exhibited signs of psychomotor instability, accompanied by a pronounced speech pattern, which included logorrhea and flight of ideas. She verbalized grandiose beliefs, such as identifying herself as the "Queen of Morocco". Notably, even within the context of this manic presentation, her ability to recognize the discrepancy between her beliefs and reality was preserved. she was diagnosed with a manic episode with psychotic symptoms (YMRS = 35). Lamotrigine was suspended and a therapeutic switch to valproate and olanzapine was initiated, which culminated in her complete symptomatic remission within 15 days.

Discussion:

The lamotrigine is a contemporary anticonvulsant, boasting both antiepileptic and mood-stabilizing properties(Zaccara et al., 2017; Naguy and Al-Enezi, 2019; Yatham et al., 2018). As per its official guidelines, it's recommended for individuals aged 18 and over for the prophylaxis of depressive episodes in patients with type I bipolar disorder who are predominantly predisposed to depressive bouts. Lamotrigine has demonstrated notable efficiency in curbing the recurrence of affective episodes in bipolar disorder, primarily depressive ones. Since its debut, lamotrigine has maintained a commendable safety record and is perceived as having an acceptable tolerability index (Yatham et al., 2018). Although there are reports of its effectiveness in the management of bipolar disorder and comorbid obsessive-compulsive disorder (OCD) (Sharma and Doobay, 2019), further research is essential to validate these claims. Furthermore, lamotrigine has been endorsed by the American Psychiatric Association practice guidelines, especially in patients with a history of rapid cycling or those who have experienced antidepressant-induced mania (Marangell et al., 2004). Our 54-year-old patient, with a history of BD and OCD, developed a manic episode following the initiation of lamotrigine, sparking debate around its potential implications.

The potential of lamotrigine to induce manic or hypomanic states is a topic of ongoing debate (Pereira-Pinto et al., 2021). Using the adverse drug reaction causality criteria by Naranjo et al (Naranjo et al., 1981), our initial analysis for this patient yielded a score of 5, indicating a “probable” effect. This was informed by previous reports of the adverse effect (+1), the onset of the adverse effect after drug initiation (+2), and the symptom improvement after discontinuing the treatment (+1). However, after a meticulous review of existing literature and the patient's clinical presentation, the point for previous reports of the adverse reaction was removed. Despite the presence of prior reports, they remain inconclusive, necessitating a more conservative analysis. Consequently, the recalculated score on this scale would be 4 points, translating to a “possible” effect. Moreover, the resolution of symptoms upon

lamotrigine cessation in our case, mirrored by other reported cases, may bolster the theory of lamotrigine-induced symptomatology. However, it's critical to note the concurrent introduction of olanzapine and sodium valproate following lamotrigine's withdrawal. Even without the point for "symptomatic improvement after treatment cessation", a score of 3 points would still classify it as a "possible" effect.

The intersection of our patient's OCD and the onset of the manic episode provides an intricate backdrop. Studies highlight that the coexistence of OCD and bipolar disorders can increase vulnerability to mood destabilization, suggesting an intricate interplay of pathophysiological mechanisms (Sharma and Reddy, 2019; Carta et al., 2020; Amerio et al., 2015; Andrea et al., 2018).The speculation arises – could the underlying OCD have primed our patient for this manic transition upon lamotrigine administration?

Many studies have indicated that the inclination of lamotrigine to trigger manic episodes might be attributed to its absence of antimanic properties, coupled with its antidepressant qualities, potentially linked to reduced glutamate release. Secondary evaluations from lamotrigine randomized clinical trials have omitted individuals more susceptible to manic shifts, which could mean the risk of lamotrigine-induced mania has been downplayed. The onset of lamotrigine-induced mania appears more probable in patients with BD-I, a dominant manic polarity, a primary manic episode, or those with past instances of an antidepressant-caused manic shift (Anmella et al., 2022).

Conclusion:

In summation, while lamotrigine presents undeniable benefits in managing bipolar depression, especially in treatment-resistant depressive patients, clinicians must tread with caution. The drug's potential to induce manic or hypomanic states, particularly in individuals with intricate clinical profiles like our patient, warrants vigilance. A broader spectrum of research and vigilant post-marketing surveillance will be pivotal in sculpting a more transparent risk-benefit profile for lamotrigine.

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Conflict of Interest:

The authors declare that there is no conflict of interest.

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