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LETTER TO THE EDITOR

Efficacy of electroconvulsive therapy (ECT) in a treatment-resistant bipolar mixed state with metabolic comorbidity

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Dear Editor,

Mixed-feature episodes in bipolar disorder are clinically challenging conditions characterized by the simultaneous presence of manic and depressive symptoms. These episodes are associated with treatment resistance, an increased risk of suicide, psychotic features, and higher rates of comorbidity, all of which negatively affect prognosis (1, 2). Atypical antipsychotics, mood stabilizers, and electroconvulsive therapy (ECT) are key treatment options in such cases. The literature primarily includes case series and naturalistic follow-up studies on the use of ECT in patients with mixed features who do not respond to effective doses or adequate durations of pharmacological treatment.

In this report, we present the case of a 39-year-old male patient with obesity and a treatment-resistant mixed manic episode, who showed significant clinical improvement following ECT. The patient was admitted with symptoms of irritability, increased energy, insomnia, anhedonia, impulsive spending, and feelings of guilt, and was diagnosed with a mixed manic episode. He had been under psychiatric follow-up for bipolar I disorder since the age of 21 and had experienced four hospitalizations within the past year. It was reported that his first episode began with mania without psychotic symptoms. At that time, treatment with lithium and olanzapine 20 mg/day was initiated. Following the first manic episode, he experienced a depressive episode accompanied by suicidal ideation, for which he was hospitalized. He was discharged on lithium, olanzapine 20 mg/day, and quetiapine 400 mg/day. Two years later, a manic episode recurred, and he was hospitalized. Due to complaints of hand tremors, lithium was discontinued and replaced with valproic acid. It was noted that during follow-up, at least one manic episode occurred each year. Aripiprazole 20 mg/day was introduced due to weight gain concerns, but quetiapine was increased to 600 mg/day and zuclopenthixol 200 mg every 15 days was added due to an increase in episode frequency. The patient had no prior history of ECT. Over the past year, he experienced recurring episodes of mixed mania, and no clinical improvement was observed despite a treatment regimen of valproic acid 2500 mg/day, quetiapine 900 mg/day, lamotrigine 100 mg/day, aripiprazole 30 mg/day, and diazepam 10 mg/day, all with gradual dose increases over the last three months. Moreover, prominent side effects, such as tremor and hypersalivation, negatively impacted his quality of life. Consequently, medications were gradually tapered, and ECT was initiated, maintaining only quetiapine at 300 mg. After eight ECT sessions, significant clinical improvement was observed, with the Young Mania Rating Scale (YMRS) score

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decreasing from 19 to 2. The patient was discharged on quetiapine and valproic acid alone. Additionally, it was noted that the patient's body mass index decreased from 32.8 kg/m^2 to 25.8 kg/m^2 over the course of ECT treatment. While this finding is notable, it is more plausibly attributed to behavioral changes associated with clinical remission—such as improved psychomotor function and appetite regulation—as well as the discontinuation or dose reduction of psychotropic agents known to contribute to weight gain, rather than a direct effect of ECT itself.

Compared to classic mania, mixed episodes often present with distinctive clinical features such as dysphoric mood, guilt, and suicidal ideation (3, 4). These symptoms may be mistaken for agitated depression or borderline personality disorder, highlighting the importance of accurate diagnosis for appropriate treatment planning (5). Nevertheless, randomized controlled trials targeting this subgroup remain limited, particularly following the classification changes introduced in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).

Treating mixed episodes is especially challenging due to the need to manage both manic and depressive symptoms concurrently. Monotherapy with either antipsychotics or antidepressants may exacerbate symptoms of the opposite polarity. Therefore, avoiding polypharmacy while implementing effective interventions is essential. Agents such as aripiprazole, olanzapine, quetiapine, and valproate have demonstrated efficacy in this context (6). ECT has also been shown to be effective across all phases of bipolar disorder, with response rates ranging from 56% to 93% in treatment-resistant and severe mixed episodes (7). Additionally, an association between bipolar disorder with mixed features and obesity has been reported, with obesity potentially linked to greater illness severity. These factors include childhood trauma, emotional dysregulation, sleep disorders, overeating, and side effects of medications commonly used to treat mixed features. Additionally, biological mechanisms such as systemic inflammation and insulin resistance may contribute to the pathophysiology of both conditions (8). Given the side effects associated with evidence-based treatments for mixed features, such as olanzapine, valproic acid, and quetiapine, ECT is a suitable treatment alternative for patients with obesity and could be preferred in select cases. Although the literature indicates that ECT is effective and safe in mixed episodes, randomized controlled trials are needed to establish its superiority.

In conclusion, this case highlights electroconvulsive therapy as a safe and effective treatment option for managing treatment-resistant mixed episodes of bipolar disorder, particularly in patients with comorbid obesity. It underscores the potential of ECT not only to achieve symptom remission but also to improve quality of life when pharmacological strategies are insufficient. Clinicians should recognize ECT as a viable and timely intervention in complex cases, reinforcing its role as an essential tool in the treatment of bipolar disorder with mixed features.

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