

Delirious Mania in Bipolar Disorder

To the Editor: Delirious mania is a significant, potentially dangerous, and possibly overlooked psychiatric syndrome generally characterized by a rapid onset of mania and delirium with no identifiable organic cause. Misdiagnosis or inappropriate treatment may result in the progression of delirious mania to its malignant form.

Case report. Mr A is a 56-year-old man with a history of bipolar I disorder (*DSM-IV*) previously maintained on carbamazepine monotherapy. He was admitted to a psychiatric hospital in January 2015 with hypomanic symptoms, including irritability, racing thoughts, and decreased need for sleep, after discontinuation of his medication 2 weeks prior. Standard admission laboratory tests were performed, a blood carbamazepine level was drawn, and carbamazepine was restarted at a dosage of 400 mg 2 times daily.

Mr A's symptoms persisted despite a supratherapeutic carbamazepine level of 60.91 $\mu\text{mol/L}$. On day 4, lurasidone 40 mg with dinner was added as an adjunct mood stabilizer. Hyponatremia with a serum sodium level of 127 mmol/L was found, which resolved with fluid restriction. On day 8, his mental status acutely worsened and erratic behavior (eg, bathing fully clothed, blocking the toilets with paper) and aggression emerged but with intact orientation. Additionally, he walked naked around the unit. Lurasidone and carbamazepine were discontinued, and a combination of aripiprazole 10 mg every morning and clonazepam 0.5 mg 2 times daily was started.

Over several days, Mr A exhibited a state of variable restlessness and hyperactivity with purposeless movements. Standard encephalopathy, autoimmune, and some screening oncologic laboratory test results were negative, including complete blood count, comprehensive metabolic panel, vitamin B₁₂, folate, rapid plasma reagin, urinalysis, full thyroid panel, magnesium, phosphorus, antinuclear antibodies, thyroid peroxidase antibodies, antithyroglobulin antibody, carcinoembryonic antigen, human immunodeficiency virus, and prostate specific antigen. He was found to have a slightly elevated C-reactive protein level (56.19 nmol/L; normal range, 0.0–46.67 nmol/L). Head computed tomography and brain magnetic resonance imaging scans were unremarkable. On day 18, Mr A further decompensated with intermittent incontinence and inconsistent disorientation to date followed by place. Valproic acid 1,000 mg/d was started, which resulted in a serum level of 547.47 $\mu\text{mol/L}$, and increased to 1,250 mg/d with no clinical response. Similarly, he failed a monotherapy trial of olanzapine 7.5 mg/d. Quetiapine monotherapy was initiated at 100 mg/night, which was titrated to 500 mg over the following days. However, his insomnia and agitation persisted, and he would make bizarre comments such as claiming to be under water.

After considering delirious mania and his lack of response to standard therapies, lorazepam was initiated at 1 mg 3 times daily. Lorazepam was titrated to 6 mg/d and continued for 5 days. During this time, Mr A became calmer with improvement in orientation and memory, and his erratic behaviors ceased. He became stable enough for discharge to outpatient care on quetiapine and lorazepam.

Because delirious mania lacks formal diagnostic criteria, most descriptions of this syndrome are derived from case series.^{1,2} In addition to the concurrent exhibition of mania and delirium, 1 case series¹ reports symptoms considered distinctive of this condition, which are incontinence, disrobing, and water pouring; the majority of these patients also had a previous diagnosis of bipolar disorder. Mr A matches these descriptions. Another case series² describes the course of the illness as one wherein delirium may present after the onset of mania, which is consistent with the current case.

Delirious mania may be of a nonmalignant or malignant form, which is marked by significant catatonia, hyperthermia, muscular rigidity, or autonomic instability. Delirious mania has the same potential complications as malignant catatonia, ranging from organ failure to coma and death.³ Jacobowski et al³ detail potential treatment options for the 2 forms of delirious mania. Although antipsychotics and mood stabilizers have the potential to be beneficial in the treatment of nonmalignant delirious mania, patients should be monitored carefully for symptoms of the malignant form. In malignant delirious mania, the authors³ recommend using higher doses of lorazepam or electroconvulsive therapy, both of which have shown efficacy. Antipsychotics should be discontinued. Although Mr A exhibited no signs of the more severe presentation of delirious mania, he did demonstrate nonresponse to multiple psychotropic medications, including 3 different antipsychotics and 2 mood stabilizers, which may have been indicative of this diagnosis.

Accurate identification of delirious mania is important to prevent potentially life-threatening consequences of this syndrome. The prevalence of delirious mania is uncertain, although 1 review⁴ notes "confusion" in 19% of a sample of patients with mania. Increased awareness of this syndrome will foster prompt diagnosis and treatment and thus improve patient outcomes.

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