Ziprasidone-Associated Mania in a Case of Obsessive-Compulsive Disorder

To the Editor: *July 9, 2007*

INTRODUCTION

A PubMed search revealed 14 cases of ziprasidone associated mania, which carried primary diagnoses of mood disorders, generalized anxiety disorders (GAD), panic disorder, and psychotic disorders. To our knowledge, we report the first case of mania associated with ziprasidone augmentation of a selective serotonin reuptake inhibitor in a 60-year-old man (at time of ziprasidone-induced mania) with obssessive-compulsive disorder (OCD).

CASE REPORT

Mr. B is a 64-year-old male, treated for over 30 years for GAD with obsessive features, later more accurately defined as OCD per *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*[1] criteria. His obsessions of contamination and time-consuming cleaning rituals had been resistant to trials of several medications, including all available selective serotonin reuptake inhibitors, clomipramine up to 75 mg/day and venlafaxine up to 150 mg/day, as well as cognitive-behavioral therapy. A trial of fluvoxamine up to 150 mg/day was discontinued due to limiting side-effects. He never met full criteria for major depression and no manic/hypomanic symptoms had ever been reported. History for substance abuse and suicide was negative. Family history was positive for OCD in his father and anxiety in his daughter. Medical history is significant for coronary artery disease, hypertension, coronary artery disease, diabetes mellitus, autoimmune hemolytic anemia, and eczema.

In May 2002, after partial response to citalopram 80 mg and low-dose clonazepam 1.5 mg/day in three divided doses, ziprasidone was initiated as an augmenting agent at a dose of 20 mg/day and increased to 20 mg BID. Within 7 days of starting ziprasidone family members noted a decreased need for sleep, impulsivity, grandiosity, and increased energy. He was brought to the emergency room after 17 days with florid manic symptoms. Physical and neurological exams were unremarkable. Routine laboratory work, including a drug screen, was non-contributory. His non-psychiatric medications included fexofenadine, hydroxyzine, and sodium nitroprusside. He was hospitalized and ziprasidone was stopped with reduction in the dose of citalopram to 20 mg. Manic symptoms promptly resolved within 3 days.

In the past 4 years, the patient has had no recurrence of manic symptoms but has had one major depressive episode after the end of a romantic relationship.

DISCUSSION

Here we cite a case of a patient with OCD, without any previous history of mood disorder, who developed mania with low doses of ziprasidone used as an augmenting agent. Of previous cases of ziprasidone-induced mania reported in the literature, only one had comorbid diagnoses panic disorder and GAD in addition to major depression.[2]

Ziprasidone has been promoted as a safe and efficacious first-line option for treatment of manic and mixed episodes of bipolar disorder[3] as well as an augmenting agent in major depression and anxiety disorders.[4] This effect has been

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attributed to its unique receptor profile. Like other atypical antipsychotics, it is an antagonist at the serotonin $(5\text{-HT})_2$ and dopamine $(D)_2$ receptors, but differs in its higher ratio of 5-HT_2 to D_2 activity. While it has been theorized that this ratio may be responsible for its significant effect on mood (and risk of mania), it also has 5-HT and noradrenaline reuptake inhibition similar to tricyclic antidepressants, a receptor profile expected to confer efficacy in its role as an augmenting agent in anxiety disorders.[4] Both mechanisms could be implicated in the increased risk of induction of mania. Patel and Keck[2] have proposed that occurrence of mania might be a dose-related phenomenon. In our case, the temporal correlation between the onset of manic symptoms and their rapid resolution upon stopping the drug, age of onset, and absence of an underlying mood disorder all strongly implicate ziprasidone.

We agree with Duggal and colleagues[5] who emphasize the need for clinicians to be aware of the possibility of mania occuring during treatment with ziprasidone when used as augmenting agent in anxiety disorders, even at relatively low doses.

Sincerely,
Randall Wickham, MD
Anjali Varma, MD

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Dr. Wickham is associate professor and Dr. Varma is PGY3 resident, both in the Department Of Psychiatry at Carilion University of Virginia Roanoke—Salem Program, at the Salem VA Medical Center.

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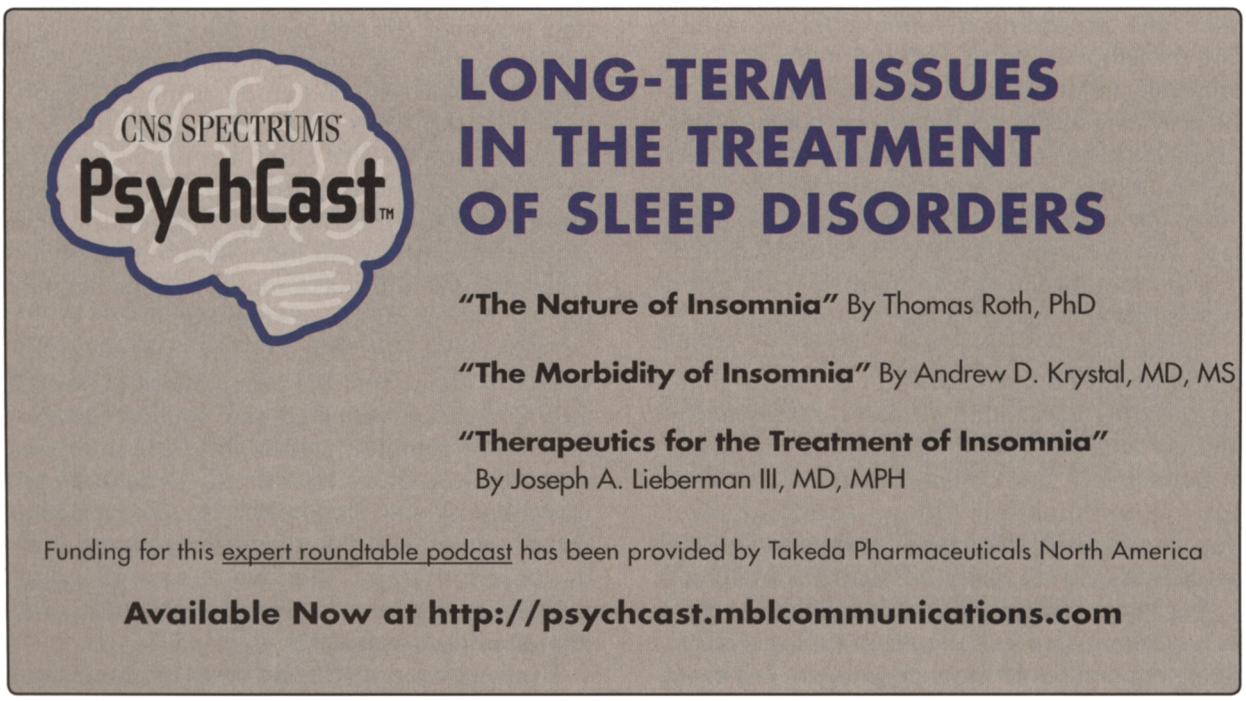

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