Tardive Dystonia Associated With Ziprasidone

TO THE EDITOR: Although the new atypical neuroleptics have held the promise of fewer extrapyramidal signs, there have been several reports of tardive movement disorders associated with their use. Ziprasidone-associated tardive dyskinesia has been rarely described (1). However, to our knowledge, there have been no reports of tardive dystonia caused by ziprasidone.

Ms. A, a 56-year-old woman, was seen with a chief complaint of involuntary jaw movements. She had a 35-year history of migraines for which she had received a number of treatments (triptans, beta-blockers and calcium channel blockers, antiepileptics, antidepressants, and clonazepam) with limited success. Her first trial with an atypical neuroleptic was 2.5 years before her presentation, when she was administered ziprasidone (80 mg/day). Ms. A experienced a moderate decrease in the frequency and severity of her migraine attacks. Eleven months later, she started noticing mild involuntary movements of her tongue, and ziprasidone was gradually discontinued. Within 2 weeks, involuntary movements involving jaw opening were superimposed on the involuntary movements of her tongue. Gradually, her symptoms intensified, causing eating difficulties accompanied by weight loss (5–6 kg). She also experienced occasional tongue and oral mucosa injuries. Her past medical history was remarkable only for a hysterectomy performed for an ovarian cyst.

A neurological examination revealed frequent, sustained jaw opening, with occasional tongue protrusions and rare dystonic furrowing of her eyebrows. No other abnormalities were noted; brain magnetic resonance imaging was normal. Ms. A had already received botulinum toxin type A injections without success and declined repeat injections.

Tardive dystonia is a late-onset complication of treatment with dopamine-blocking agents consisting of persistent dystonic movements of focal onset involving mainly the craniocervical region. It usually appears while receiving a stable dose, but it may manifest while tapering the dose or even 1–3 weeks after discontinuation (as in our case) (2). In many patients, tardive dystonia is combined with the classic tardive oral-buccal-lingual dyskinesias (3). Tardive dystonia is very resistant to treatment and can occur in patients with psychiatric as well as other conditions (in our case, migraine headaches) (2). Although very rare, tardive dystonia has been reported with the use of other atypical neuroleptics, including clozapine, risperidone, and olanzapine (4).

We found no reports of tardive dystonia occurring with ziprasidone on PubMed. Although our patient's clinical diagnosis was unequivocally tardive dystonia, with its time course consistent with ziprasidone monotherapy as the precipitant, the remote possibility of dystonia due to other causes (i.e., idiopathic, psychogenic) may be considered. Clinicians should keep in mind that there is no "absolutely safe" atypical neuroleptic since there is always a potential for the appearance of extrapyramidal signs.

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Memantine for Treatment-Resistant OCD

TO THE EDITOR: Current options for treatment-resistant obsessive-compulsive disorder (OCD) include switching to an alternative selective serotonin reuptake inhibitor or augmentation with dopamine antagonists or other agents (1). Evidence from genetic, behavioral, and neuroimaging studies have indicated glutamatergic alteration in OCD (2). In pediatric OCD patients, the glutamate caudate concentration was abnormally increased, but it decreased after paroxetine treatment (3). Thus, attenuating glutamatergic hyperactivity might be beneficial in OCD. We report a therapeutic effect of add-on memantine, an *N*-methyl-D-aspartic acid glutamatergic receptor antagonist, in treatment-resistant OCD.

Ms. A, a 34-year-old woman, was seen with incapacitating ego-dystonic obsessions, including fear of harm to her daughter and of losing her mind. She developed compulsive checking behavior to decrease the associated anxiety. Obsessive-compulsive symptoms, initially detected at age 16, remitted spontaneously 2 years later. Subsequent postpartum exacerbation of DSM-IV OCD symptoms associated with major depression occurred at age 30. She also met DSM-IV criteria for schizotypal personality disorder.

Subsequent adequate trials with paroxetine and sertraline were ineffective. Add-on risperidone caused marked akathisia and was discontinued. At her presentation, oral clomipramine was initiated and titrated to 300 mg/day; however, 10 weeks later, there was no significant clinical improvement (Yale-Brown Obsessive Compulsive Scale [4] score=35). Addition of a selective dopamine D_2 antagonist, sulpiride (up to 400 mg/day for 4 weeks), was also ineffective (Yale-Brown Obsessive Compulsive Scale score=34). At this point, adding memantine to Ms. A's regimen of clomipramine (300 mg/day) and sulpiride (400 mg/day) was suggested, and she signed informed consent after explanation of this off-label therapy. Memantine was started at 5 mg/day and titrated to 20 mg/day within 2 weeks. Ms. A reported initial relief on day 7 of combined treatment, and a significant decrease in symptom severity was noted 3 weeks later (Yale-Brown Obsessive Compulsive Scale score=22). There was a substantial reduction in the time occupied by OCD and distress, followed by increased control over obsessions. No clinically significant side effects were noted. Improvement was maintained after 3 months.

Add-on memantine was well tolerated and resulted in clinically significant reduction of OCD symptom severity. Prior treatment resistance and the proximity between symptomatic improvement and the initiation of memantine point to its