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A Nearly Overlooked Mild Case of Ziprasidone-Induced Lingual Dystonia

Alexander C. Tsai, M.D., Ph.D.

Langley Porter Psychiatric Institute, University of California, San Francisco

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To the Editors:

The rate of acute extrapyramidal symptoms (EPS), including dystonic reaction subtypes, attributable to ziprasidone is thought to be relatively low (1), possibly due to its high 5-HT_{2A} / dopamine D₂ receptor affinity ratio as compared to risperidone and haloperidol (2). In the first randomized efficacy trial conducted in the setting of acute bipolar mania, among 140 patients randomized to receive ziprasidone, 16 developed hypertonia (11.4%), compared to 2 of 70 (2.9%) in the placebo arm (3). Some of the risk factors thought to be associated with acute dystonia include young age, male sex, prior history of acute dystonia, cocaine use, and administration of high-potency antipsychotic medications (4).

I report here a case of a female patient admitted to an inpatient psychiatric ward with acute mania with psychotic features, who developed a mild isolated lingual dystonia shortly after initiating pharmacotherapy with ziprasidone.

Case Report

A 38 year-old Caucasian woman with a history of bipolar type I disorder self-presented to the emergency department with both manic and psychotic symptoms. She described, variously, paranoid fears related to feelings of derealization, a sexual harassment lawsuit against her employer, “the devil” trying to kill her, and neighbors who were spying on her; these were confirmed as delusional beliefs by her outpatient therapist, who confirmed prior episodes of mania and a baseline mental status devoid of psychotic symptoms and stated that the patient had never voiced such beliefs or described these situations during periods of euthymia. The patient had not slept for at least two days and was unsure if she had been taking her medications appropriately during this time. On mental status examination, she voiced psychotic thought content and grandiose ideas, jumped from topic to topic, demonstrated marked distractibility and elevated mood, and giggled inappropriately throughout during the admission interview. Screening labs for admission included a

complete blood count, basic metabolic panel, urine pregnancy test, and urine toxicology screen, all of which were either negative or within normal limits.

Her outpatient medication regimen consisted of lamotrigine 200mg daily and escitalopram 20mg daily, both of which she had been taking consistently (with the exception of, possibly, the prior two days) for at least six months. The only recent medication change had been a decrease in the dose of escitalopram from 30mg daily the week prior to presentation. The patient had no history of drug allergies or prior episodes of acute dystonia. She had never taken antipsychotic medications previously and was extremely reluctant to take a medication that would potentially cause her to gain weight. In light of the acuity of her mania and psychosis, oral ziprasidone was chosen and initiated at a dose of 60mg twice daily.

She tolerated the first two doses with no complaint other than mild drowsiness. Approximately one hour after the third dose, she began to complain of a strange sensation in her tongue but was at a loss for words to further describe her symptoms; she denied any pain, subjective dyspnea, muscle weakness, or urinary or bowel incontinence. The resident assigned to her care performed a focused physical examination and was unable to appreciate any frank movement disorder including muscle stiffness in the extremities or trunk, blepharospasm, eye deviation, torticollis, trismus, or opisthotonic posturing. An Abnormal Involuntary Movement Scale (AIMS) was scored at zero. She was neurologically intact with the exception of cranial nerve I, which was not tested at the time. He asked the patient to monitor her symptoms and notify staff if they continued to worsen.

Four hours later, the patient informed nursing staff that the abnormal sensation in her tongue was intensifying. When the resident returned to the bedside, her tongue was visibly protruding and she demonstrated marked dysphonia. Vital signs included a temperature of 97.9 degrees Fahrenheit, pulse of 82 beats per minute, respiratory rate of 16 breaths per minute, blood pressure of 110/64 mm Hg, and a pulse oximetry reading of 99% on room air. She was not drooling, did not voice any complaint of pain or subjective dyspnea, and could cough appropriately. Her mental status was at baseline. Palpation of her musculature in the submandibular region revealed spasm, but her physical examination was otherwise normal. She was given benztropine 1mg intramuscularly, which produced full resolution of symptoms by the time she was reassessed 25 minutes later. Oral benztropine treatment was continued for the next three days at 1mg twice daily, while the ziprasidone was discontinued and replaced with olanzapine at 2.5mg daily. For the remainder of the hospitalization, the signs and symptoms of dystonia did not resurface.

Discussion

Acute dystonic reactions are known to commonly occur with administration of conventional antipsychotic medications (5). They are less well characterized with respect to treatment with atypical antipsychotic medications, specifically ziprasidone. A PubMed literature search revealed only three previously reported cases of acute dystonic reactions attributable to treatment with ziprasidone for acute bipolar mania (6;7). In all of these previously published case reports, the severity of the dystonic reaction described was much more severe than the case described above. Although the escitalopram could have been a potential

contributor to the dystonia (8;9), the patient had been on a longstanding dose of this medication, with the exception of a brief treatment interruption during the manic episode.

This case report illustrates how an acute dystonic reaction can be easily overlooked in the setting of mild symptoms and soft signs. Indeed, the patient's dystonic reaction was initially dismissed by the resident when first brought to his attention, given the lack of physical examination findings, pain, or respiratory distress. It may be that painful or life-threatening dystonic reactions are more clinically obvious and therefore less likely to be overlooked, but this has not been systematically studied. As indications for the use of atypical antipsychotic medications continue to broaden (10;11) and conventional antipsychotic medications fall out of favor, the frequency with which acute dystonic reactions are encountered in clinical practice can be expected to decline further. Trainees should be taught to maintain a high index of suspicion for acute dystonic reactions, including mild cases that are not painful or life-threatening.

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