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Diabetes Insipidus Induced by Oral Olanzapine at Therapeutic Dose

Sir,

Diabetes insipidus (DI) is characterized by the passage of excess amounts of dilute urine. In central DI, antidiuretic hormone (ADH) is deficient; in nephrogenic DI, there is decreased response of the kidneys to ADH.[1] Hypovolemia, dehydration, and electrolyte imbalance can occur as complications of DI. In addition to various congenital and acquired causes, several drugs have been implicated in the etiology of DI. Lithium, foscarnet, and clozapine are the most common drugs implicated in drug-induced DI.[2] With olanzapine, drug-induced DI is relatively rare and is reported in the literature as case reports. Olanzapine-induced DI has been reported to occur primarily in the context of overdose.[3,4] Here, we describe the clinical manifestations and outcome of a patient who developed olanzapine-induced DI at a therapeutic dose.

A 35-year-old male was admitted to the psychiatry ward with diagnoses of alcohol dependence syndrome, alcohol-induced psychotic disorder, recurrent depressive disorder, nicotine dependence syndrome, acute on chronic pancreatitis, seizure disorder, and bilateral varicose veins. He was treated with lorazepam, thiamine, and multivitamins parenterally (changed to oral formulations after five days) and levetiracetam and pancreatin-dimethicone combination orally. As auditory and visual hallucinations persisted after the resolution of alcohol withdrawal symptoms, he was started on oral olanzapine at 2.5 mg per day. The dose was titrated to 10 mg per day over one week. With the initiation of olanzapine, the frequency and intensity of hallucinations significantly reduced over the next few days. Ten days after initiating olanzapine, he reported increased urine output and nocturia. He also reported increased thirst and excessive consumption of water. An input-output chart was maintained, which showed that his urine output was 4000–5000 ml/day. Further investigations revealed that his urine osmolality was 100 mosmol/kg (reference range—200–1200 mosmol/kg) and serum osmolality was 289 mosmol/kg (reference range—275–300 mosmol/kg). The presence of polyuria, decreased urine osmolality, and normal plasma osmolality favored the diagnosis of DI in this patient. Blood investigations did not show any electrolyte imbalance (serum sodium level was 140 mEq/L), and the blood sugar levels were in the normal range. In the absence of recent trauma, surgery, neurological symptoms/signs (headache, vomiting, or visual field defects), and other urinary symptoms, a diagnosis of drug-induced DI was considered. Among the medications the patient was taking, olanzapine was considered the most likely causative agent based on the temporal relationship and the existence of previous reports. A score of 7 was obtained on the Naranjo adverse drug reaction probability scale,[5] indicating that olanzapine was a "probable" cause of DI in this patient. Olanzapine was stopped, and over the next five days, the urine output became normal (average of 2800 ml per day), and other symptoms, namely nocturia and excessive thirst, also subsided. The patient was not started on any other antipsychotic as he did not have a relapse of psychotic symptoms after discontinuation of olanzapine.

Various causes for DI were considered and ruled out based on the clinical picture. Both central and nephrogenic DI can be congenital in origin. The onset of symptoms in the fourth decade was a strong pointer against a congenital cause in this patient. Acquired forms of central DI can occur due to trauma, surgery,

hypoxic brain injury, metastasis, and autoimmune diseases. In the absence of suggestive history, examination findings, and blood investigations, the above conditions were considered unlikely in this patient. Acquired causes of nephrogenic DI include renal disease, sickle cell disease, obstructive uropathy, pregnancy, and electrolyte disturbances. Normal renal parameters, complete blood count, and electrolyte levels and absence of other urinary symptoms ruled out the above conditions in this patient. The presence of previous conclusive reports, the temporal relationship of DI symptoms with the initiation of olanzapine, resolution of symptoms with olanzapine discontinuation, and absence of other causes indicated that olanzapine was the most likely cause for DI. Re-challenge with olanzapine was not attempted. Water deprivation test, desmopressin test, serum ADH levels, and serum copeptin assays could have helped differentiate between central and peripheral mechanisms of DI in this patient, had the symptoms persisted.

Previous cases of olanzapine-induced DI were following a drug overdose.[3,4] In both the previous reports, olanzapine-induced DI was found to be of the central type, as evidenced by rapid resolution of polyuria and rise in urine osmolality after administration of desmopressin. In one report, olanzapine-induced DI was described, in the context of pneumonia and sepsis, in a 64-year-old male who was on a regular dose of olanzapine 10 mg/d.[6] In contrast to olanzapine-induced DI, lithium-induced DI is far more common in patients on long-term lithium treatment and is almost always nephrogenic in origin.[7]

Thus, in rare instances, olanzapine can cause DI at a therapeutic dose. In patients reporting polyuria, careful evaluation to confirm the presence of DI and identify the possible cause is warranted. In suspected olanzapine-induced DI, a trial of drug discontinuation may be considered.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his clinical information to be reported in the journal. The patient understands that his names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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