Case Report

Olanzapine-induced tender pitting pre-tibial edema

Kaliaperumal Mathan, Venkatesan Muthukrishnan, Vikas Menon

Department of Psychiatry, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

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ABSTRACT

Antipsychotic-induced edema is uncommonly encountered in clinical practice. We report a case of tender pitting pre-tibial edema with olanzapine in a woman with no medical comorbidities. The peculiar distribution of edema resulted in diagnostic confusion necessitating specific investigations. Eventually, the edema resolved following complete stoppage of the drug, but caused distress to the patient and the caregiver.

Key words: Adverse reaction, antipsychotic, edema, olanzapine

INTRODUCTION

Olanzapine is a popular second-generation antipsychotic widely used in the treatment of major psychiatric illness. The most commonly reported adverse effects with this agent are weight gain and somnolence.[1] Edema with olanzapine, though less common, can engender unique diagnostic and management issues. Here, we report a case of non-dependent tender pitting pre-tibial edema induced by olanzapine in a medically healthy subject.

CASE REPORT

A middle-aged (45 years) married housewife presented to the outpatient psychiatry department with symptoms suggestive of paranoid schizophrenia including auditory hallucinations and delusions of persecution. We admitted her for management issues including poor long-term drug compliance. The patient had no known medical co-morbidities. Oral olanzapine was initiated at 10 mg for a week following which it was deemed necessary to increase the dose to 12.5 mg. After a week of hiking the dose, she developed bilateral nondependent pitting edema restricted to the pre-tibial region with minimal involvement of foot. The edema was more pronounced on the left side and was described as tender. No diurnal variation of the edema was observed. No local skin changes or itching was reported. There was no history of local trauma or edema in the past.

A physician's opinion was obtained and multiple investigations were conducted to assess the cause of the edema, including a complete blood count, renal, cardiac, and liver function tests, thyroid function test, compression ultrasound of both lower limbs, and ultrasound abdomen. All the test results were found to be within normal limits. We reassured the patient and her caregiver regarding the non-threatening nature of the adverse effect, as they expressed concerns over continuing the medications. Conservative measures like limb elevation and usage of compression stockings relieved her pain substantially. Hence, we decided to wait and watch. In view of her repeated long-term compliance issues, it was decided to initiate depot antipsychotic injections (bimonthly fluphenazine) while simultaneously overlapping the oral olanzapine for 8–10 weeks. The edema continued to persist

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Address for correspondence:
Vikas Menon, Department of Psychiatry, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry - 605 006, India.
E-mail: drvmenon@gmail.com

in a low-grade fashion during this overlap period. Eventually, olanzapine was tapered following which the edema resolved completely. The adverse effect was scored on the Naranjo adverse drug reaction (ADR) probability scale[2] and a score of 8 was obtained indicating strong association of edema with olanzapine use.

DISCUSSION

The above case is reported not only for the unusual adverse reaction to olanzapine but also because it occurred at an unusual site and caused diagnostic confusion. Possibilities of hypothyroidism and deep vein thrombosis were considered due to the pre-tibial restriction of edema and its unequal nature, but both were ruled out through specific testing. Since all possible medical etiologies were ruled out, the edema can be attributed to drug therapy. Further, though the patient also received fluphenazine, the edema was present prior to its initiation and resolved promptly with taper and stoppage of olanzapine even though fluphenazine was continued. Hence, the offending agent in this case was concluded to be olanzapine. Only a few cases of olanzapine-induced edema have been reported in literature. No gender predilections for this adverse reaction have been noted by investigators.[3] Almost all the reports described the development of dependent pedal edema,[4-7] though one case of facial edema due to olanzapine has also been reported recently.[8] In the present case, the edema was tender and non-dependent in distribution. It required a careful patient and caregiver education on our part to alleviate distress due to the adverse drug reaction. The reasons for edema due to olanzapine are mostly speculative and include blocking of alpha 1 receptors leading to vasodilatation and decreased venous return. Other proposed theories are drug-induced blocking of M_1, H_1 and 5-HT_2 receptors, which results in modulation of inositol-1,4,5-triphosphate (IP_3) and diacylglycerol (DAG) levels leading to down-regulation of ATP-dependent calcium pump and increase in cyclic adenosine monophosphate levels (cAMP), both of which increase smooth muscle relaxation causing vasodilatation and edema.[3] Adverse effects like these can have negative implications on compliance to medication, especially in chronic illnesses like schizophrenia. Patient education and a judicious wait and watch policy may obviate the need to undertake a potentially risky cross-taper of medications in similar cases. More research is needed to identify the possible risk factors for such adverse reactions, given that most patients tolerate oral olanzapine reasonably well. We hope this case sensitizes clinicians to look for, educate, and manage edema while initiating oral antipsychotics.

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