

# Olanzapine-induced peripheral oedema: A case report of an unusual antipsychotic adverse effect

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**ABSTRACT**

**Background:** Atypical antipsychotics have been associated with pedal oedema. It is not yet certain the exact cause of this side effect which can often be troublesome. Few cases have been reported with olanzapine, almost all from developed countries.

**Case Report:** Here is reported the case of a 34-year old hair stylist with a first episode of mood disorder (mania) who developed pedal oedema when commenced on olanzapine. The oedema resolved only when the drug was completely withdrawn.

**Conclusion:** Clinicians are reminded that there is a possibility of peripheral oedema following olanzapine medication. As such, routine enquiries on this side effect as well as education of patients about it are recommended. The early recognition of peripheral oedema and a prompt intervention by the discontinuation of olanzapine can be of great value.

**Key words:** Olanzapine, Psychosis, Pedal oedema, Side effect

**Introduction**

Olanzapine is an atypical antipsychotic of the thienobenzodiazepine class that mediates its antipsychotic activity through serotonin type 2 (5-HT<sub>2A</sub>) and dopamine type 2 (D<sub>2</sub>) antagonism as well as via other multiple neurotransmitter receptors: D<sub>1</sub>, D<sub>4</sub>, α<sub>1</sub>, 5-HT<sub>1A</sub>, muscarinic M<sub>1</sub> – M<sub>5</sub>, and H<sub>1</sub> receptors [1].

Patients often complain of adverse effects of psychiatric medications and when not addressed, compliance to medication could be compromised. Bilateral leg oedema has been infrequently described with olanzapine [2, 3], mostly by researchers from developed countries. In a Nigerian institution was this case managed and for the purpose of knowledge sharing, the author has found it necessary to report it with the accompanying explicit images.

**Case report**

Mrs AA is a 34-year old hair dresser and a foreigner who has been living in Nigeria since the age of 25 years. She developed mental illness in February 2017, five months after her third childbirth. Her key features were restlessness, the elation of mood, inflated self-esteem, racing thoughts, second person auditory hallucination, and decreased need for sleep – each lasting for about two to three weeks. A diagnosis of mania with psychotic symptoms (ICD-10, Code F30.2) was made and she was admitted and commenced on parenteral haloperidol and diazepam for 2 days before her drug was changed to oral olanzapine, 10mg nocte because of worsening tremor and rigidity. She developed obvious swelling both legs by the third day of the olanzapine medication (Figure 1).

The swelling was moderately pitting, non-tender, and up to the knees. The Naranjo score was 9. She was not a known hypertensive nor did she have any other co-morbid physical illness and she had no previous history of drug allergy, oedema or local trauma. There was no associated raised temperature or any evidence of rash, skin thickening, ulceration or pigmentation and she did not take any other medicine outside the ones prescribed for her in the ward. There was also no diurnal variation of the oedema.

She was referred to a cardiologist and a nephrologist who did thorough independent evaluations and investigations without anything to lay hand on as the cause of the oedema. Both physicians reported back that the blood pressure was normal and that all the haematological and biochemical parameters - full blood count (FBC), serum electrolyte, urea, and creatinine (SEUCr), immunoglobulin

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E antibody (IgE), fasting blood sugar (FBS), thyroid function test, liver function test, serum proteins, and so on - were within normal range. Radiological and electrocardiographic results were also normal. The dosage of the olanzapine was reduced to 5mg every night but the oedema persisted. Diuretic (frusemide) had no effect. The olanzapine was then stopped and the patient placed on aripiprazole, 10mg every night. The oedema gradually started resolving and by the 20th day, it had completely resolved (Figure 2).

Patient was on the aripiprazole for many months before she claimed that she was no longer sleeping adequately and for why she switched back to olanzapine by her own self prescription. Two days later, swellings re-occurred, this time on both the legs and the hands. She resumed her aripiprazole and the oedema resolved after 4 days. She has since remained stable on aripiprazole and side effect-free for over 10 months.



**Figure 1: Day 3 of olanzapine medication**



**Figure 2: Day 20 of olanzapine withdrawal**

## Discussion

The mechanism(s) by which antipsychotics lead to oedema is not very clear [4] but various suggestions have been made [2]. Olanzapine-related oedema can present unique diagnostic and management challenges as noticed in this case.

There was a temporal relationship between the commencement and withdrawal of olanzapine and the development and resolution of oedema, respectively, as previously reported [5, 6].

A re-challenge led to the re-emergence of oedema, a finding corresponding to some earlier reports [7, 8] suggesting that prior reactions may pose a risk for re-occurrence.

Though immune reactions have been implicated in the mechanism of drug-induced oedema [9], no immunological abnormality was remarked in this patient just as have been reported, not only with olanzapine [6, 10] but also with other atypical antipsychotics such as quetiapine [11] and risperidone [12].

The Naranjo score - an Algorithm or Adverse Drug Reaction Probability Scale used to assess whether there is a causal relationship between an identified untoward clinical event and a drug using a simple questionnaire to assign probability scores [13] - was 9, suggesting a definite probability of the oedema is due to olanzapine medication.

A diuretic could not resolve the swelling as long as the patient was on olanzapine - an earlier experience [8]. Unlike in the case reported by Umar and Abdullahi [7] where the reduction of the dosage of olanzapine from 20mg to 10mg led to the resolution of the oedema, the reduction from 10mg to 5mg did not lead to the resolution of the oedema in this case.

Though many reported cases have it that oedema cleared within few days to two weeks of olanzapine withdrawal, the oedema, in this case, lasted close to three weeks just as in the German patient reported by Vohra [5].

Results of the investigations carried out were negative as in most cases of olanzapine-related peripheral oedema [5, 8, 10] but the negative results notwithstanding, the oedema resolved each time the drug was withdrawn suggesting that olanzapine was the offending agent.

The strength of the report was the temporal relationship between the commencement of olanzapine and onset of oedema as well as the resolution of oedema following olanzapine withdrawal. Extensive examination and investigations did not incriminate any aetiological factor and the Naranjo score lent more credence to the susceptibility to developing oedema was due to the olanzapine medication.

## Conclusion

Olanzapine medication is associated with peripheral oedema which may not often be brought to the notice of the clinician but can impact negatively on the patient by leading to poor medication adherence, unnecessary costly investigations, or relapses, among others. Clinicians should adopt measures that will timely address this adverse effect on the interest of the patients, their families, and the health workers themselves.

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## References

1. Sadock BJ, Sadock VA. Kaplan & Sadock's synopsis of Psychiatry: behavioural sciences/clinical psychiatry, 10th Ed. Lippincott Williams & Wilkins, Philadelphia, USA 2007; 1094.
2. Thippaiah SM, Singh VK. Pedal oedema associated with atypical antipsychotics. *Prog Neurol Psychiatry* 2010; 30-32.
3. Yalug I, Ozten E, Evren Tufan A, Alemdar M, Cerit C. Bilateral pedal oedema associated with olanzapine use in manic episode of bipolar disorder: report of two cases. *Prog Neuropsychopharmacol Biol Psychiatry* 2007; 31:1541–1542.
4. Koleva HK, Erickson MA, Vanderlip ER, Tansey J, Mac J, Fiedorowicz JG. Oedema associated with quetiapine. *Ann Clin Psychiatry* 2009; 21(2): 77–80.
5. Vohra A. Olanzapine-induced peripheral oedema in a pregnant patient with bipolar affective disorder. *Ger J Psychiatry* 2013; 16(2): 84-86.
6. Toz İH , Taşdemir DM, Özer Ü, Toz B, Özgen G. Bilateral pedal oedema associated with olanzapine treatment: A case report. *J Neurobehav Sc* 2015; 2(1): 42-44.
7. Umar MU, Abdullahi AT. Self-limiting atypical antipsychotics-induced oedema: Clinical cases and systematic review. *Indian J Psychol Med* 2016; 38(3): 182– 188.
8. Deshauer D, Erwin L, Karagianis J. Case Report: Oedema related to olanzapine therapy. *Can Fam Physician* 2006; 52 (May): 620 – 621.
9. Ku HL, Su TP, Chou YH. Ziprasidone-associated pedal oedema in the treatment of schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry* 2006; 30:963– 964.
10. Mathan K, Muthukrishnan V, Menon V. Olanzapine-induced tender pitting pre-tibial oedema. *J Pharmacol Pharmacother* 2015; 6(2): 114-115.
11. Chen CY, Yeh YW, Kuo SC, Shiah IS, Liu PY, Chen CL. Pedal oedema associated with addition of low-dose quetiapine to valproate treatment in bipolar disorder. *Prog Neuropsychopharmacol Biol Psychiatry* 2009; 33:1551–2.
12. Obayi NOK, Igwe MN, Ndukuba AC, Achor JU, Adagam G, Ojiako IS, et al. Risperidone-related pedal oedema: Report of two cases from Nigeria. *Nig J Psychiatry* 2016; 14(2): 48 – 53.
13. Naranjo CA, Busto U, Sellers EM, Sandor P , Ruiz I, Rob-erts EA, Janecek E, Domecq C, Greenblatt DJ. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981; 30: 239 – 245.

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