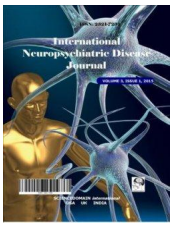

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Bilateral Pedal Oedema Associated with Intramuscular Haloperidol – A Rare Observation

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Authors' contributions

This work was carried out in collaboration between both authors who saw and managed the patient together. Author OO designed the study and wrote the first draft of the manuscript. Author NT carried out the literature searches. Both authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Background: Cases of peripheral oedema associated with antipsychotic medication have been reported, especially with the atypical types of antipsychotics. The exact cause is not known.
Aim: Our purpose is to bring to the medical world that though peripheral oedema is more reported with atypical antipsychotics than the typical counterparts, rarely it occurs following typical antipsychotic medication such as haloperidol.
Presentation of Case: We report a case of pedal oedema following intramuscular injection of haloperidol to a 35-year old female doctor diagnosed with delusional disorder. Withdrawal of the drug led to immediate resolution of oedema but subsequent re-administration of the drug provoked a re-occurrence of oedema which again resolved quickly on the suspension of the haloperidol.
Discussion: Every antipsychotic, especially the second-generation antipsychotics, has the potential to cause peripheral oedema. The cause of the oedema is not very certain but its occurrence can cause embarrassment to patients and family leading to fear, unnecessary investigations, and poor medication adherence.
Conclusion: Clinicians are reminded that while peripheral oedema is known to be associated more

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with second-generation antipsychotics than the first generation antipsychotics like haloperidol, the latter occasionally cause a similar side-effect. Hence, routine enquiries of the side effect should be in all patients not only on those taking atypical antipsychotics.

Keywords: Pedal oedema, haloperidol, typical antipsychotic, withdrawal, resolution.

1. INTRODUCTION

Haloperidol is a typical (first-generation) antipsychotic agent belonging to the chemical class of butyrophenones. It is a potent dopamine-receptor antagonist with few effects at other neurotransmitter receptors that influence its adverse-effect profile [1].

Haloperidol is useful in the treatment of psychotic conditions like schizophrenia and also to control motor and verbal tics as well as aggressive behaviours, among other conditions.

Peripheral oedema following the use of antipsychotics has been reported mostly with the atypical group of antipsychotics, such as risperidone [2,3,4], olanzapine [5,6], ziprasidone [7,8], quetiapine [9], and clozapine [10].

Only very few cases of typical antipsychotic-induced peripheral oedema have been reported and these include those due to trifluoperazine [11] and haloperidol [12]. Our extensive literature search showed no report of such a side effect in relation to haloperidol from Nigeria, a country that has been using the drug for decades.

Angioedema is characterized by oedema of the deep dermal and subcutaneous tissues [4]. Several pathophysiological mechanisms for the development of pedal oedema have been listed [5,13] though the mechanism(s) by which antipsychotics lead to this oedema is not very clear [3,9,10].

Peripheral oedema is not listed on the manufacturer's list of adverse effects of haloperidol supporting the rarity of such side effect [14].

2. PRESENTATION OF CASE

We report a case of a 35-year old medical practitioner and mother of four with features suggestive of delusional disorder who had been receiving care from another hospital in another geopolitical zone of the country before she presented to our facility for the first time in September 2017 following her official work transfer to Ebonyi state. She was very aggressive when she was brought into our emergency unit necessitating her being given a stat dose of intramuscular haloperidol, 5mg (given in the left buttock) plus intravenous diazepam, 10mg. These were repeated 12 hours later. The following day, she was calm and relatively more co-operative but developed bilateral pedal oedema – up to the knees, slightly pitting, non-itching, and non-tender (Fig. 1).

Fig. 1. Day 1 after injection haloperidol administration

She reported that she had received injection haloperidol only in one occasion about 3 years earlier but it was stopped because she developed facial puffiness and swelling of the lips then.

We stopped the haloperidol; replaced it with intramuscular chlorpromazine which was also stopped after the first dose of 100mg because of a rapid drop of the blood pressure that warranted resuscitation. She was then continued on oral risperidone (which she said she was using from her previous healthcare provider) and benzodiazepine. The cardiology and nephrology specialists were invited. Both reviewed thoroughly with extensive laboratory workup which results were unremarkable. By the third day of haloperidol withdrawal, the oedema was almost completely relieved (Fig. 2).

She continued to make progress on risperidone and benzodiazepines. However, on the sixth day into admission, she quarreled with a co-patient

over a trivial issue. After the nurses on duty had separated them into different rooms, she went further to the co-patient's room and poured her a cup of water while the latter was sleeping. Attention of the resident doctor on-call (who was not in our team) was drawn and he administered to patient intramuscular haloperidol 10mg and her usual oral lorazepam, 2 mg. Incidentally, by the following morning, the two legs were found swollen again.

Fig. 2. Day 3 of haloperidol withdrawal

There was no associated history of fever, chills, skin rash, hives, dizziness, trauma, or upper respiratory symptoms, and no history of hypertension. She was not known to be allergic to any food and was not on any other medication, be it herbal or orthodox. She had remained stable and side-effect free on risperidone for over six months as at the time of writing this report.

3. DISCUSSION

There is a paucity of reports on this rare side effect caused by haloperidol. Indeed, our literature search revealed only one report of haloperidol-related angioedema [12].

The onset of oedema in the case we reported following intramuscular administration of the haloperidol was abrupt. This is similar to an American report of a case of a 29-year old male adult with no known allergies in whom angioneurotic oedema with tongue swelling and protrusion developed four hours after the administration of a single intramuscular dose of haloperidol [12].

Our patient was reviewed by both a cardiologist and a nephrologist. Each of these physicians reported back that the blood pressure was normal and that all the haematological parameters - full blood count (FBC), serum electrolyte, urea, and creatinine (SEUCr), immunoglobulin E antibody (IgE), fasting blood sugar (FBS), thyroid function test, liver function test, and serum proteins - were within normal range. Radiological investigations carried out (chest X-ray, x-ray of the lower limbs, and abdominopelvic ultrasound) and electrocardiogram showed normal results. Hence, no physical or other possible aetiological agent was implicated. This is similar to earlier reports with antipsychotics such as haloperidol [12], risperidone [2], and many others.

Though immune reactions have been implicated in the mechanism of drug-induced oedema [7], no immunological abnormality was remarked in this patient, a similar finding by some other researchers [15]. Though the exact mechanism behind oedema formation following haloperidol medication is not clear, our patient has some risk factors already established to be of those that commonly develop oedema while using haloperidol–female gender and age 40–49 years [16].

Our patient reacted in the same manner when there was a rechallenge with the same drug. This is similar to the experiences reported with some other antipsychotics [2,9].

Surprisingly, this patient was earlier on risperidone – an atypical antipsychotic known to cause pedal oedema [2,3,4] far more than typical antipsychotics but she never developed any peripheral oedema with risperidone. This goes a long way to suggest that there are different individual factors contributing to the development of this adverse side effect of different medications.

When assessed with the Naranjo Algorithm or Adverse Drug Reaction Probability Scale (a 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) [17] she scored 9, suggesting definite probability of the oedema being as a result of the haloperidol medication. This score of 9 recorded in our patient is high, compared to some other reports [18], lending more credence to the susceptibility of the oedema being due to the intramuscular haloperidol.

The temporal relationship between the onset of oedema with the administration of injection haloperidol, the eventual caesation of the oedema on withdrawal of the drug, and the re-occurrence of the oedema on re-administration (re-challenge) of haloperidol strengthens our belief that the pedal oedema experienced by our patient was related to haloperidol medication.

4. CONCLUSION

Peripheral oedema is not a common side effect associated with typical antipsychotics, especially haloperidol. To note that this side effect could occur, its rarity notwithstanding is very important. Clinicians and other prescribers are advised to look out for oedema in all their patients on antipsychotics, not only on those using atypical antipsychotics but also on those using typical antipsychotics like haloperidol as early identification and prompt management could prevent a lot of negative consequences.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

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We acknowledge the acceptance by both patient and her husband to allow photographs of the patient's legs be taken during and after the leg swelling and also their approval that the case be reported in an international journal with the photographs included in the report.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Cowen P, Harrison P, Burns T. Shorter oxford textbook of psychiatry. Oxford University Press. 2012;522.
2. Obayi NOK, Igwe MN, Ndukuba AC, Achor JU, Adagam G, Ojiako IS, et al. Risperidone-related pedal oedema: Report of two cases from Nigeria. Nigerian Journal of Psychiatry. 2016;14(2):48 – 53.
3. Thippaiah SM, Singh VK. Pedal oedema associated with atypical antipsychotics. Progress in Neurology and Psychiatry. 2010;30-32.
   Available:www.progressnp.com
4. Hosseini SH, Ahmadi A. Peripheral oedema occurring during treatment with risperidone combined with citalopram. Case reports in Medicine. Article ID 540732. 2012;3.
   Available:http://dx.doi.org/10.1155/2012/540732-3
5. Yalug I, Ozten E, Evren Tufan A, Alemdar M, Cerit C. Bilateral pedal edema associated with olanzapine use in manic episode of bipolar disorder: report of two cases. Progress in Neuropsychopharmacol and Biological Psychiatry. 2007;31:1541–1542.
6. Umar MU, Abdullahi AT. Self-limiting atypical antipsychotics-induced oedema: Clinical cases and systematic review. Indian J Psychol Med. 2016;38(3):182–188.
   Doi: 10.4103/0253-7176.183089
7. Ku HL, Su TP, Chou YH. Ziprasidone-associated pedal edema in the treatment of schizophrenia. Progress in Neuro-psychopharmacol and Biological Psychiatry. 2006;30:963–964.
   DOI: 10.1016/j.pnpbp.2006.01.020
8. Mohan T, Bastiampillai T, Dhillon R. Ziprasidone-induced angioedema: A case report. Journal of Clinical Psychiatry. 2009; 70(7):1054.
9. Koleva HK, Erickson MA, Vanderlip ER, Tansey J, Mac J, Fiedorowicz JG. 3 case reports of oedema associated with quetiapine. Annals of Clinical Psychiatry. 2009;21(2):77-80.
10. Mishra B, Sahoo S, Sarkar S, Akhtar S Clozapine-induced angioneurotic edema. General Hospital Psychiatry. 2007;29:78–80.
    DOI: 10.1016/j.genhosppsych.2006.10.014
11. Osman M, Edwards D, Kilduff M. Trifluoperazine-induced angioedema. Case reports in Psychiatry. Article ID 140329. 2014;3.
    Available:http://dx.doi.org/10.1155/2014/140329.

12. Kahlon S, Lee C, Chirugi R, Hassen GW. Angioneurotic oedema associated with haloperidol. Case Reports in Emergency Medicine. Article ID 725461. 2012;2.
DOI:10.1155/2012/725461
13. Steyl C, Van Zyl-Smith R. Mechanisms of oedema formation: The minor role of hypoalbuminaemia. South African Medical Journal. 2009;99(1):57–59.
14. MPR (The Right Dose of Information). Haldol injection by Janssen Pharmaceuticals Inc.
Available:http://www.empr.com/haldol-injection/drug/367/
15. 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 Neuro-psychopharmacol Biol Psychiatry. 2009;33:1551–2.
DOI: 10.1016/j.pnpbp.2009.07.030
16. E Health Me. Haldol and Swelling - from FDA reports. 2018.
Available:https://www.ehealthme.com/ds/haldol/swelling/
17. 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.
Available:https://doi.org/10.1038/clpt.1981.154
18. Mathan K, Muthukrishnan V, Menon V. Olanzapine-induced tender pitting pretibial oedema. J Pharmacol Pharmacother. 2015;6(2):114-115.
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