

CASE REPORT

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Olanzapine-induced bilateral pedal and pretibial edema: A case report

Behice Han Almis¹, Mehmet Hamdi Orum²

¹Adiyaman University Training and Research Hospital, Psychiatry, Adiyaman, Turkey

²Adiyaman University Faculty of Medicine, Department of Psychiatry, Adiyaman, Turkey

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Abstract

Olanzapine is a second generation antipsychotic which has antagonistic action on serotonergic, histaminergic, dopaminergic, and muscarinic receptors. The most common seen side effects of olanzapine are weight gain, dry mouth, dizziness, and constipation. There are case reports with olanzapine especially as peripheral edema. Herein, we present a female patient who developed bilateral pedal and pretibial edema after treatment with olanzapine added to sertraline. In this case, the systemic causes of edema were ruled out. The edema resolved completely one week after cessation of the treatment. The patient was managed by aripiprazole and sertraline and the same side effect was not seen with this medication.

Keywords: Olanzapine, edema, side effect, antipsychotic

Introduction

Olanzapine is a second generation antipsychotic with affinity for D1-D4 (dopaminergic), 5-HT_{2,3,6} (serotonergic), M1-5 (muscarinic), α-1 (adrenergic) and H1 (histaminergic) receptors [1]. Although it is generally used in the treatment of psychiatric disorders such as schizophrenia, bipolar disorder, low dose is used in depression, anxiety disorders and obsessive-compulsive disorder. Extrapyramidal symptoms are less important than first-generation antipsychotic drugs, while they cause significant weight gain such as some other second-generation antipsychotics and impair glucose metabolism. It is a significant advantage that extrapyramidal symptoms are caused more rarely than first-generation antipsychotic drugs [2,3]. However, as some other second-generation antipsychotics cause significant weight gain and impair glucose metabolism, they are the disadvantages of patients' poor compliance to treatment. Common side effects include weight gain, constipation, postural hypotension, akathisia, sedation, weakness, headache, abdominal and limb pain, fatigue, dry mouth, tremors [2]. Peripheral edema is frequently associated

with the use of beta blockers, calcium channel blockers, non-steroidal anti-inflammatory drugs and some hormones [3]. It has been shown that 1% of the placebos are caused by peripheral edema, whereas 3% of those using olanzapine experience this side effect and are therefore considered to be a rare side effect [4]. In this case report, we discussed a female patient who developed peripheral edema after olanzapine use and resolved edema after switching from olanzapine to aripiprazole.

Case Presentation

Our case, a 38-year-old, single, female patient was undergoing psychiatric treatment for 10 years with the diagnosis of major depressive disorder with psychotic features. The patient was admitted to the psychiatric outpatient unit with the complaints of reference delusions. In the past, there was a history of use of risperidone and sertraline perioral (PO) and was still using sertraline 50 mg/day PO for three years. She was diagnosed with major depressive disorder with mood-congruent psychotic features according to Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) [5] and was treated with olanzapine 10 mg/day PO in addition to sertraline 50 mg/day PO. One week addition of olanzapine to the sertraline, the patient developed significant edema in both lower extremities, especially in the pedal and pretibial region. She had no family history. She had no history of alcohol, smoking or substance abuse. The patient stated that

*Corresponding Author: Mehmet Hamdi Orum, Adiyaman University Faculty of Medicine, Department of Psychiatry, Adiyaman, Turkey,
E-mail: mhorum@hotmail.com

there was no change in dietary and fluid intake in recent days. The patient had no drug use other than sertraline and olanzapine. She had no systemic disease such as hypertension or diabetes mellitus. Physical examination was unremarkable. Urea and electrolyte, hemogram, creatinine, urine analysis, liver function tests, fasting blood glucose, protein level and lipid profile were within normal limits. Chest X-ray, electrocardiogram, renal ultrasonography, and lower extremity doppler ultrasonography gave normal results. There was no diurnal variation of edema and thyroid function tests showed normal results. Edema was attributed to olanzapine use; therefore olanzapine was stopped, sertraline 50 mg/day was continued and aripiprazole 5 mg/day PO was added to the sertraline. Three days after, edema began to decrease and aripiprazole dose was increased to 10 mg/day. 5 days after cessation of olanzapine, edema disappeared. No additional treatment was applied for the reduction of edema. No similar side effects were reported during the follow-up of the patient. Psychiatric complaints decreased significantly. The patient and his relatives were warned of edema due to olanzapine use and informed consent was obtained from them for their knowledges. Naranjo Adverse Drug Reaction Probability Scale (NADRPS) score of the patient was 5 [6].

Discussion

This case report was evaluated as a case of peripheral edema due to olanzapine. Because there was a temporal relationship between them, the side effect began with the addition of the drug and completely cured after discontinuation of the drug. In addition, other examinations were normal. The NADRPS score indicates a probable association between drug use and side effect [6]. The exact mechanism of edema associated with olanzapine is not known, but this is thought to be associated with the receptor profile. Some hypotheses are proposed to explain this relationship [7]. First, olanzapine causes alpha-1 adrenergic blockade, resulting in peripheral vasodilatation and decreased vascular resistance. Secondly, the post receptor mechanisms for muscarinic1, histaminic1 and serotonergic 5-HT2. These olanzapine-induced receptor blockages inhibit the physiological increase of inositol triphosphate (IP3), down regulate adenosine triphosphate-dependent calcium pump and reduce smooth muscle contractility resulting in vasodilatation and edema. Third, olanzapine-induced 5-HT2 receptor blockade increases cyclic adenosine monophosphate, relaxing vascular smooth muscles through myosin light chain kinase phosphorylation. Fourth, the use of olanzapine-induced dopaminergic blockade is thought to result in edema by disrupting renal regulation of fluid and electrolytes. Yalug et al. [7] suggested that the side effect of creating olanzapine edema was dose-dependent. However, we found it appropriate to change the drug, which is thought to cause side effects in our study. On the other hand, edema cases related to aripiprazole use have been found in the literature, but this side effect was not seen in our case [8]. This was attributed to the fact that both drugs had different receptor profiles. Ng et al. [9], in their study examining

olanzapine-induced edema cases, they suggested that the condition was independent of sex but that the severity of edema and age were positively correlated. Our case was in the middle age group. When edema occurs, the patient's general medical condition should be reassessed and other organic conditions that may cause edema should be excluded. Dose can be reduced or the drug can be changed. Leg elevation, varicose vein stockings, diuretics can be used in the management of edema [10]. In our patient, there was no need for them, and when the drug was stopped, the edema disappeared.

Conclusion

As a result; olanzapine is an antipsychotic commonly used in psychiatric clinical practice. In addition to the important advantages, some side effects may impair the compliance of the patients. We think that this case report will be useful for clinicians to be careful about the edematous side effects of olanzapine and to question the patients in this respect.

Competing interests

The authors declare that they have no competing interest.

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Behice Han Almis ORCID: 0000-0002-9440-2451

Mehmet Hamdi Orum ORCID: 0000-0002-4154-0738

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