Olanzapine-induced eosinophilia: A case report.

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Many adverse effects of antipsychotic drugs have been described, among which hematologic adverse effects stand out. Classically, blood dyscrasias have been associated with the use of olanzapine. In this paper, we will focus on an uncommon adverse reaction: eosinophilia in a patient diagnosed with paranoid schizophrenia, who had been using olanzapine. There have been just a few reported cases of eosinophilia secondary to the use of olanzapine, which makes this an infrequent, rarely known, and even less studied adverse reaction.

Keywords: *Olanzapine, adverse effects, eosinophilic disorders*

Introduction

Among hematological adverse reactions associated with the use of atypical antipsychotics, those related to clozapine are the most well-known. These are described as having a 7% risk of blood dyscrasias[1]. Although neutropenia and eosinophilia[2] are associated with the use of this drug, the most feared manifestation is agranulocytosis because it is life-threatening. While the mechanism by which clozapine causes agranulocytosis is unknown, a 1 to 2% chance of presenting this complication in patients who have been undergoing treatment with clozapine for a year, and who have not had any risk factors apart from significant bone marrow suppression concomitant with the initiation of therapy, has been documented.

The use of other atypical antipsychotics has not shown a large quantity of hematological adverse reactions. After clozapine, risperidone is the atypical antipsychotic with the most reported hematological reactions. Descriptions of cases from the use of leukopenia[3], neutropenia[4], and lymphopenia[5] have been found as well. Another case described immuno-allergic hepatitis associated with eosinophilia with the use of risperidone, which was reversed when this drug was discontinued[6].

Only a handful of cases of hematologic adverse reactions, such as neutropenia[7] and leucopenia[8], have been described regarding olanzapine. Although the chemical structure of olanzapine is similar to that of clozapine, few cases of agranulocytosis secondary to the use of olanzapine have been reported, possibly due to the requirement of lower doses than those of clozapine[9,10]. Some cases of eosinophilia associated with the use of olanzapine have also been described[11]. Three possible cases of eosinophilic myocarditis and a case of eosinophilic pleural effusion stand out[14,15]. This paper will describe a case of asymptomatic eosinophilia, secondary to the use of olanzapine in a patient with paranoid schizophrenia.

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Clinical Case

34-year-old patient, male and single. Diagnosed with a difficult to treat paranoid schizophrenia 11 years ago. Undergoing treatment with 200 mg of sertraline and 20 mg of olanzapine. The latter drug was chosen because of a history of rhabdomyolysis when using risperidone and haloperidol. He was referred from the Emergency Department to be hospitalized in the Short Stay Unit of Hospital Barros Luco-Trudeau due to a suicide attempt by the ingestion of nine lithium pills, related to an intensification of psychotic symptoms, which were characterized by psychotic polydipsia, delirious paranoid ideas, and pseudo-obsessions regarding diet. The subject was uncooperative during the mental examination of the hospital admission interview. His appearance was according to age; he was attentive, alert, lucid, and oriented in time and space. He showed a few accessory movements, highlighting facial mimicry and poor gesturing. He did not show catatonic postures, walked normally, and was euthymic with affective flattening. His speech was monotonous and with average speed and tended towards looseness of ideas with morbid rationalism phenomena, language affectation, and non-sequitur answers. The content of his speech focused on pseudo-obsessive ideas concerning his self-image and the continuous ingestion of water, together with ideas of harm. The lack of sense of reality was impressive. There were no alterations in sensory perception. He denied suicidal ideation upon his admission. The physical exam did not show any relevant findings. His admission exams results were within normal ranges. A gradual optimization of olanzapine until reaching up to 30 mg (day 13 in the table) was decided. In a routine check of laboratory exams, after seven days from the last adjustment of the olanzapine dose, a 26450 leukocytosis with 57% of eosinophils was observed, without symptoms or associated somatic signs. A complete blood count was repeated. It was reported by a hematologist, and it showed leukocytosis of 27000 with 65% of eosinophils. Thus, a hematologic evaluation was requested, as well as a decrease of olanzapine to 25 mg (day 20 in the table). The possibility of parasitism was ruled out because of non-compatible manifestations (patient did not show gastrointestinal alterations nor blood in stools without the intake of high-risk food). When examined by Hematology, the possibility of hematological neoplasm was also ruled out, since the exam only showed eosinophilia, which is not characteristic of this group of pathologies. The hematology consultant evaluated a probable reaction to olanzapine, suggesting a gradual decrease of the drug together with serial blood counts informed by a hematologist. Throughout the laboratory check-ups, leukocytosis and eosinophil levels progressively decreased, as shown in the following table. This decrease in the hematological parameters coincided with the gradual decrease of olanzapine.

Discussion

Eosinophilia refers to the presence of >500/L of eosinophils. It is a reactive phenomenon in which origin is neoplastic or secondary to different conditions, such as allergies and parasitoses. Regarding these allergic reactions, it is essential to mention drug allergies, among which atypical antipsychotics can be noted, mainly due to their extensive use in various psychotic disorders[11].

Moreover, olanzapine is an atypical antipsychotic first approved by the FDA in 1996 for use in bipolar disorder and schizophrenia. Some of its common adverse effects are: metabolic syndrome (hyperglycemia, hyperlipidemia, and weight gain), xerostomia, dizziness, and some less common hematologic reactions such as leukopenia, neutropenia, and agranulocytosis.

In the reported case, a rise in the white blood cells stands out with frank eosinophilia in conjunction with the increase of the olanzapine dose in a patient that had reported adverse reactions (rhabdomyolysis) to antipsychotic drugs before. Having ruled out the most common differential diagnoses to which eosinophilia (mainly parasitosis) could guide us, we decided to decrease the dose of the drug slightly. As described, this caused a decrease in the hematological alteration.

There are few reported cases of eosinophilia secondary to olanzapine. Thus, the relevance of this case lies mainly in the illustration of a rare adverse reaction. Its rarity does not mean it is not as relevant as other cases. This is a possibi-

Table 1. Progression of white blood cell and eosinophils count.

Day	White Blood Cell Count (/uL)	Eusinophils Count (/uL)
0	9580	No count
6	-	-
13	-	-
16	**26350**	**15019**
17	**27600**	**17940**
20	**17650**	**8295**
23	14800	9176
30	9700	2716
34	10100	1919
37	7800	1482
42	7200	1080
50	8600	860

lity that must be taken into account when prescribing this antipsychotic. At the same time, it is a differential diagnosis that must be ruled out in a patient that shows this disturbance when treated with olanzapine.

In conclusion, even though the use of olanzapine in psychiatric conditions such as schizophrenia and psychotic mania can be of great utility, its many adverse metabolic effects, such as changes in glucose homeostasis and weight gain, should be considered. At the same time, rare yet relevant adverse hematologic effects, such as eosinophilia, should also be considered.

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