

## Olanzapine-Associated Thrombocytopenia: A Case Report and Review of the Literature

H. Chebli<sup>1\*</sup>, H. Berrada<sup>1</sup>, S. Belbachir<sup>1</sup>, A. Ouanass<sup>1</sup>

<sup>1</sup>University Psychiatric Hospital Arrazi in Sale, Faculty of Medicine and Pharmacy in Rabat, Mohammed V University, Rabat, Morocco

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\*Corresponding author: H. Chebli

University Psychiatric Hospital Arrazi in Sale, Faculty of Medicine and Pharmacy in Rabat, Mohammed V University, Rabat, Morocco

### Abstract

### Case Report

Olanzapine is an atypical antipsychotic with proven efficacy in the treatment of schizophrenia and bipolar disorder. This molecule is known for its metabolic side effects, but it is considered the safest with regard to haematological toxicity. The case of our 28 year old patient, who has been followed anarchically for 5 years for schizophrenia and who presented a thrombocytopenia of  $99,000/\text{mm}^3$  within a week of being put on olanzapine without any other associated signs, is one of nine cases published in the literature illustrating this association which is rare but encourages clinicians to institute close haematological monitoring to prevent any life threatening effects.

**Keywords:** Olanzapine, schizophrenia, bipolar disorder, haematological toxicity, Thrombocytopenia.

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## INTRODUCTION

Thrombocytopenia is defined as a platelet count  $< 150,000/\text{mm}^3$ . It is a common adverse effect of drugs such as NSAIDs, diuretics, and heparin but is rarely reported with psychotropic drugs. In the literature there are only a few articles that have reported the association of thrombocytopenia with olanzapine.

We will describe here the case of a patient hospitalised at the Arrazi psychiatric hospital in Salé, Morocco, for schizophrenia, who was put on olanzapine and presented a thrombocytopenia diagnosed during a platelet count monitoring.

This case gave us the opportunity to study this rare adverse effect of olanzapine and its management.

## CLINICAL CASE

Mr A. M is a 28 year old patient, admitted to our training centre for agitation and verbalization of delusions in the context of a schizophrenia that has been evolving for 5 years.

The onset of the symptomatology seems to date back to about 5 years ago with the progressive installation of behavioural disorders of isolation and withdrawal with verbalization of delusions of

persecution. The patient would have benefited from a medical consultation and would have been put on olanzapine. The evolution was marked by unsatisfactory compliance with the treatment. The patient did not take his treatment regularly and stopped it after a few days.

Our patient's condition only worsened but was tolerated by his family for 5 years.

One week before his admission to the hospital, the patient became aggressive towards his family and friends, and had several agitated episodes, verbalising delusions of persecution with soliloquy and a tendency to wander, hence his hospitalisation for better care.

His history included problematic use of cannabis and organic solvents. The examination on admission revealed a delusional syndrome, a hallucinatory syndrome with impaired judgment and insight.

The patient was put on olanzapine 10 mg/d. His check-up, which was carried out the week of his admission, showed an isolated thrombocytopenia of  $106,000/\text{mm}^3$ ; the check-up was repeated 2 days later and came back in favour of a platelet count of  $99,000/\text{mm}^3$ .

Platelet count on citrate tube confirmed the thrombocytopenia. The patient had a ferritin, vitamin B9 and B12 assay and a smear test which came back without any particularities.

All medication was stopped and the platelet count was closely monitored. After normalization of the balance sheet, the reintroduction of olanzapine was attempted and a platelet count was done 48 hours later, which showed a reappearance of thrombocytopenia.

After normalization of the workup, after 2 weeks of stopping Olanzapine the patient was put on Aripiprazole. The patient's condition improved and he was discharged from hospital 3 weeks later.

## DISCUSSION

Thrombocytopenia is defined as a platelet count of less than 150,000/mm<sup>3</sup> and may be of central origin due to lack of production or of peripheral origin due to consumption, distribution abnormalities or immunological destruction.

Drug-induced thrombocytopenia is secondary to the presence of an antibody capable of binding to the platelet membrane only in the presence of the drug in question [1].

In order to conclude that thrombocytopenia is drug related, the following criteria must be met:

- The introduction of the drug in question must precede the thrombocytopenia, with complete and consistent recovery after cessation of treatment.
- The drug in question is the only one used before the onset of thrombocytopenia, or treatments that were continued or reintroduced after the candidate drug was discontinued did not affect the platelet count.
- Other causes of thrombocytopenia were excluded
- Reintroduction of the candidate drug results in recurrence of thrombocytopenia [2].

Antipsychotic-related thrombocytopenia is rare and has been reported with some second-generation antipsychotics such as Clozapine [3], Olanzapine [4, 5] and Risperidone [6]. It usually occurs 5-15 days after the start of drug treatment, sometimes earlier if the patient has already been on the same treatment, and the platelet count returns to normal within a week of stopping the drug.

Olanzapine is a 5HT<sub>2A</sub> and D<sub>2</sub> receptor antagonist. It is indicated for the treatment and prevention of relapse in schizophrenia and bipolar mania, and in combination with fluoxetine in bipolar depression and resistant depression. A study published in 2014 assessed the relationship between the effect of olanzapine on serotonin metabolism and the decrease in

platelet count through its effect on platelet structure [13].

There are no exact data on the association of thrombocytopenia and olanzapine. In the PubMed search, only 9 cases of thrombocytopenia associated with Olanzapine were found.

The case reported in 1998 by Bachmann *et al.* was of a 30 year old female patient who had idiopathic thrombocytopenic purpura and the use of 20mg/d olanzapine had worsened her thrombocytopenia [4].

Of the reported cases, five had other haematological abnormalities such as pancytopenia, neutropenia and leukopenia [8-12].

Carillo *et al.*, reported on a 78-year-old patient who died from complications of thrombocytopenia that occurred 3 weeks after initiation of 10 mg/d olanzapine. Olanzapine plasma levels were 10 times the therapeutic dose [7].

Olanzapine is an atypical antipsychotic known to have a high risk of metabolic side effects, but it has been considered the agent with the lowest risk of haematological side effects. Olanzapine-associated thrombocytopenia, although rare, can be fatal in some cases [7]. The clinician must therefore recognise this side effect early when it develops and take immediate steps to stop the process, while maintaining the patient's psychiatric stability. These steps could include stopping the offending drug, switching to a drug with a different chemical structure and starting corticosteroid therapy if necessary [14].

As in the case presented above, our management was to discontinue olanzapine with close monitoring of platelet counts. Two weeks after discontinuation, our patient's platelet count was normal without the use of steroids.

Discontinuation of olanzapine was the rule in all reported cases, with the use of steroids in two patients [4, 5, 11].

## CONCLUSION

Although rare, Olanzapine-associated thrombocytopenia should be known to the clinician. Our case presented below highlights the need for haematological monitoring of patients on Olanzapine, as well as discontinuation of treatment if this effect is confirmed.

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