CASE REPORT

Thrombocytopenia associated with olanzapine: A case report and review of literature

Swapnajeet Sahoo, Himanshu Singla, M. Spoorty, Pankaj Malhotra, Sandeep Grover
Departments of Psychiatry and Internal Medicine, Post Graduate Institute of Medical Education and Research, Chandigarh, India

ABSTRACT

There is limited literature on olanzapine-associated thrombocytopenia. In this report, we present a case of a 32-year-old female, suffering from persistent delusional disorder who had thrombocytopenia (46,000/mm³) with the use of olanzapine 25 mg/day, 6 weeks after starting medication. Blood film did not reveal any evidence of any dysplastic cells, disturbance in the count of other cell lines, and autoimmune workup including antinuclear antibodies and anti-neutrophil cytoplasmic antibodies were found to be negative. Given no other etiology, olanzapine was gradually tapered, and platelet counts were monitored. Reduction in the dose of olanzapine led to an improvement in platelet counts which reached the normal range after complete stoppage of olanzapine. In view of continued psychotic symptoms, she was started on clozapine and which was gradually increased to 200 mg/day with biweekly monitoring of total platelet counts before each increment in the dose of clozapine. Thrombocytopenia did not recur with use of clozapine. With clozapine, her psychosis improved by nearly 60%. A review of literature revealed only eight case reports supporting the association of olanzapine and thrombocytopenia.

Key words: Blood dyscrasias, olanzapine, thrombocytopenia

INTRODUCTION

Thrombocytopenia, i.e., platelet count of <150,000/µl is a rare side effect of psychotropic medications.[1] However, in terms of clinical significance, a platelet count of <50,000/µl is considered to be thrombocytopenia which requires emergency treatment.[2] Thrombocytopenia is a rarely reported side effect of antipsychotic medications. Among the typical antipsychotic medications, the incidence of thrombocytopenia has been reported to be more with phenothiazines when compared to haloperidol.[3] Among the atypical antipsychotics, it is more often reported with clozapine,[4-6] although there are few case reports pointing to the association of olanzapine,[7-10] risperidone,[11,12] and quetiapine[13-15] with thrombocytopenia.

In view of limited literature on the association of olanzapine and thrombocytopenia, we present a case of olanzapine-induced thrombocytopenia and review the existing literature.

CASE REPORT

Miss. A, a 32-year-old, graduate, hailing from an urban background, with no family history of mental illness, presented with an insidious onset of continuous psychotic symptoms.

Address for correspondence: Dr. Sandeep Grover, Department of Psychiatry, Postgraduate Institute of Medical Education and Research, Chandigarh - 160 012, India. E-mail: drsandeepg2002@yahoo.com

How to cite this article: Sahoo S, Singla H, Spoorty M, Malhotra P, Grover S. Thrombocytopenia associated with olanzapine: A case report and review of literature. Indian J Psychiatry 2016;58:339-41.
illness of 12 years duration. The illness was characterized by well-formed and systematized delusion of love involving one of her male colleagues. Initially, the delusional beliefs were limited to love only, but later, these extended to being persecutory delusions too. These symptoms led to marked socio-occupational dysfunction as the patient did not take up any job despite having multiple job offers and became homebound. She was treated with adequate doses of amisulpride and trifluperazine for an adequate duration (each trial lasting for at least 3 months) with no improvement.

At the time of initial assessment, her physical examination did not reveal any abnormality and her mental status examination revealed delusion of persecution. Based on the history, a diagnosis of persistent delusional disorder (as per the International Classification of Diseases, Revision 10) was considered. Routine investigations including hemogram did not reveal abnormality at the initial evaluation and her platelet count was 3.5 lakhs/mm$^3$. She was started on tablet olanzapine which was gradually increased to 25 mg/day over 6 weeks, with no significant improvement. Following this, it was planned to start clozapine, and during the preclozapine evaluation (during the 7th week of olanzapine therapy), she was found to have an evidence of low platelet count (46,000/mm$^3$) without any clinical manifestations of thrombocytopenia. There was no reduction in the blood cells of other lines. She was thoroughly evaluated for thrombocytopenia. There was no history of any fever, signs and symptoms suggestive of any local or systemic infection and intake of any other medications. Physical examination did not reveal any evidence of hepato-splenomegaly. Blood film did not reveal any evidence of dysplastic cells, disturbance in the count of other cell lines, and autoimmune workup including antinuclear antibodies and anti-neutrophil cytoplasmic antibodies were found to be negative. Over the next 2 months, multiple hemograms showed platelet counts to vary from 40,000 to 70,000/$\mu$L with no abnormalities in the other cell counts and clinical manifestations of thrombocytopenia. Given persistent thrombocytopenia and persistent psychopathology, the patient was admitted for a detailed evaluation. Olanzapine was gradually tapered off along with monitoring of platelet count. Serial monitoring revealed an increase in the total

| Author, year | Patient’s characteristics: age and diagnosis | Dose (mg) | Duration in days after the initiation of olanzapine when thrombocytopenia developed (days) | TPC before and after olanzapine | Other blood cells abnormalities | Treatment received |
|--------------|---------------------------------------------|----------|-----------------------------------------------------------------------------------|-------------------------------|--------------------------------|-------------------|
| Bachmann et al., 1998$^{[7]}$ | A 30-year-old female with comorbid idiopathic thrombocytopenic purpura and paranoid schizophrenia | 20       | 17                                                                                | 137-10/µL                    | -                              | Stoppage of olanzapine followed by the administration of human gamma globulins and prednisolone |
| Bogunovic and Viswanathan, 2000$^{[9]}$ | A 38-year-old female, schizoaffective disorder | 10       | 30                                                                                | 224 × 10$^3$-20 × 10$^3$/L    | -                              | Stoppage of olanzapine followed by treatment with chlorohydrate and prednisolone |
| Onofrj and Thomas, 2001$^{[10]}$ | A 67-year-old male, Parkinson’s disease with psychosis | 10       | 35                                                                                | 155,000-120,000               | Pancytopenia                    | Stoppage of olanzapine improved pancytopenia and thrombocytopenia in 2 weeks |
| Carrillo et al., 2004$^{[11]}$ | A 78-year-old male, dementia with behavioral problems | 10       | 21                                                                                | 4000/mm$^3$ (no baseline data available) | -                              | Death due to internal bleed |
| Rai et al., 2004$^{[12]}$ | A 40-year-old male, paranoid schizophrenia | 15       | 7                                                                                 | Normal counts (exact details not mentioned) to 96,000/mm$^3$ | Pancytopenia                    | Stoppage of olanzapine improved blood counts in 4 days |
| Mehta and Sanitato, 2005$^{[13]}$ | A 83-year-old female, major depression and dementia | 2.5      | 1                                                                                 | Reduced to 145 × 10$^3$/L (baseline data not available) | Neutropenia                     | Stoppage of all medications, isolation and administration of G-CSF and antibiotics |
| Maurier et al., 2010$^{[14]}$ | A 56-year-old male, chronic psychotic illness | 20       | Around 100                                                                         | 39 × 10$^3$/L (baseline data not available) | Pancytopenia with severe folate deficiency | Stoppage of olanzapine and management of folate deficiency |
| Grover et al., 2012$^{[15]}$ | A 23-year-old male, paranoid schizophrenia | 7.5      | 14                                                                                | 2,000,000-20,000/dL | Leukopenia (2700/dL) | Stoppage of olanzapine, addition of lithium |

TPC – Total platelet counts; G-CSF – Granulocyte colony-stimulating factor
platelet count while olanzapine was being tapered and platelet count reached to the normal range (160,000/μl) after complete stoppage of olanzapine. Following this, a possibility of olanzapine-induced thrombocytopenia was considered. Later on, clozapine was started which was gradually increased to 200 mg/day with biweekly monitoring of the total platelet count before each increment in the dose of clozapine. No decline in platelet count was noted while the patient was on clozapine. With clozapine, her psychotic symptoms improved by 60%. Over the next 6-month follow-up period, her platelet counts remained within normal limit while on clozapine.

**DISCUSSION**

In the index case, olanzapine-associated thrombocytopenia was detected accidentally. In fact, it was never considered, despite the presence of low platelet count for 3 months. Thrombocytopenia has rarely been reported to be associated with the use of olanzapine, and there are no exact data on the incidence of thrombocytopenia with the use of olanzapine. In PubMed search, we could find only eight published case reports on the association of thrombocytopenia with olanzapine. As shown in Table 1, in many of these reports (five case reports), thrombocytopenia was associated with disturbances in the blood cells of other lines too.[10,16-19] Further, in one of the cases, thrombocytopenia could be attributed to folate deficiency.[10] Some of these reports also suggest that patients who experienced thrombocytopenia with olanzapine also experienced the same with the use of other medications such as benztropinemesylate[6] and neutropenia with clozapine.[19,20] In contrast to these reports, the index case tolerated clozapine without any complications. One of the previous case reports also suggests that sequential use of olanzapine and clozapine does not suggest that if a patient develops thrombocytopenia with one drug, the patient is definitely going to develop thrombocytopenia with the second drug.[17] Our case also supports this assertion. In the index case, the Naranjo probability score[21] was 9 indicating a definite association of thrombocytopenia with olanzapine in the index case.

Our case adds to the limited existing literature of olanzapine-induced thrombocytopenia and suggests that whenever a patient receiving olanzapine has an objective evidence of thrombocytopenia, olanzapine must be suspected as a cause and clinical evaluation must include the stoppage of medication as one of the strategies for the evaluation of thrombocytopenia.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. George JN, Raskob GE, Shah SR, Rizvi MA, Hamilton SA, Osborne S, et al. Drug-induced thrombocytopenia: A systematic review of published case reports. Ann Intern Med 1998;129:886-90.
2. What Is Thrombocytopenia? – NHLBI, NIH Internet. Available from: http://www.nhlbi.nih.gov/health/health-topics/topics/thcp. [Last cited on 2016 Feb 04].
3. Holt RJ. Neuroleptic drug-induced changes in platelet levels. J Clin Psychopharmacol 1984;4:130-2.
4. Kate N, Grover S, Aggarwal M, Malhotra P, Sachdeva MS. Clozapine associated thrombocytopenia. J Pharmacol Pharmacother 2013;4:149-51.
5. Abanmy NO, Al-Jaloud A, Al-Jabr A, Al-Ruwaisan R, Al-Saeed W, Fatani S. Clozapine-induced blood dyscrasias in Saudi Arab patients. Int J Clin Pharm 2014;36:815-20.
6. Lee J, Takeuchi H, Fervaha G, Powell V, Bhalaoo A, Bies R, et al. The effect of clozapine on hematological indices: A 1-year follow-up study. J Clin Psychopharmacol 2015;35:510-6.
7. Bachmann S, Schröder J, Pantel J, Mundt C, Zorn M, Witzens M, et al. Olanzapine-induced thrombocytopenia in association with idiopathic thrombocytopenic purpura. Br J Psychiatry 1998;173:352.
8. Bogunovic O, Viswanathan R. Thrombocytopenia possibly associated with olanzapine and subsequently with benzotropine mesylate. Psychosomatics 2000;41:277-8.
9. Carrillo JA, González JA, Gervasini G, López R, Fernández MA, Núñez GM. Thrombocytopenia and fatality associated with olanzapine. Eur J Clin Pharmacol 2004;60:295-6.
10. Maurier F, Petitpain N, Guichard JF, Javlot L, Tréchot P. Olanzapine and pancytopenia with severe folate deficiency. Eur J Clin Pharmacol 2010;66:531-3.
11. Assion HJ, Kolbinger HM, Rao ML, Laux G. Lymphocytopenia and thrombocytopenia during treatment with risperidone or clozapine. Psychopharmacology 1996;29:227-8.
12. Sembra J, Okui S. Risperidone-induced thrombocytopenia: A case report. Gen Hosp Psychiatry 2009;31:97-8.
13. Cowan C, Oakley C. Leukopenia and neutropenia induced by quetiapine. Prog Neuropsychopharmacol Biol Psychiatry 2007;31:292-4.
14. Fan KY, Chen WY, Huang MC. Quetiapine-associated leukopenia and thrombocytopenia: A case report. BMC Psychiatry 2015;15:110.
15. Lalli A, Michel B, Georget S, Bouillot C, Mangin A, Javelot H. Thrombocytopenia with quetiapine: Two case reports, one with positive rechallenge. Rev Bras Psiquiatr 2015;37:351.
16. Onofri M, Thomas A, One further case of pancytopenia induced by olanzapine in a Parkinson’s disease patient. Eur Neurol 2001;45:56-7.
17. Rai S, Chakrabarti S, Lobana A. Pancytopenia on switching from clozapine to olanzapine: A case report and some unresolved issues. Indian J Pharmaco 2004;36:186-7.
18. Mehta A, Sanitato J. A case of neutropenia and thrombocytopenia shortly after initiating olanzapine. Psychiatriy (Edgmont) 2005;2:18-9.
19. Grover S, Hegde A, Agarwal M, Sachdeva MS. Olanzapine-associated leukopenia and thrombocytopenia managed with lithium in a patient who developed leukopenia with olanzapine in the past: A case report. Prim Care Companion CNS Disord 2012;14 pii: PCC.1201367.
20. Benedetti F, Cavallaro R, Smeraldu E. Olanzapine-induced neutropenia after clozapine-induced neutropenia. Lancet 1999;354:567.
21. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;30:239-45.