Olanzapine-Associated Leukopenia and Thrombocytopenia Managed With Lithium in a Patient Who Developed Leukopenia With Clozapine in the Past: A Case Report

To the Editor: There are very few case reports of thrombocytopenia associated with olanzapine.[1–7] We present a case of a man who developed leukopenia with clozapine and later had recurrence of leukopenia with olanzapine. Additionally, the leukopenia that developed during olanzapine treatment was accompanied by thrombocytopenia.

Case report. Mr A, a 23-year-old man, presented with an illness of 3 years' duration suggestive of paranoid schizophrenia (*DSM-IV*) along with sustained neck dystonia due to paliperidone use. He had partial response to an adequate trial of quetiapine and a course of electroconvulsive therapy (ECT); as a result, clozapine was considered. Prior to consideration of clozapine, hemogram revealed no abnormality. Clozapine was started at 12.5 mg/d and was increased by 12.5 mg/d at each increment after 3 or 4 days depending on tolerability. When the dosage of clozapine was increased to 87.5 mg/d, hemogram revealed, for the first time, evidence of leukopenia without thrombocytopenia. As a result, clozapine was stopped, and illness was managed only with lorazepam. After clozapine was stopped, hemogram normalized. Over the next 3 weeks, repeated hemogram revealed no abnormality.

In view of the patient's past history of extrapyramidal side effects (neck dystonia) and of his partial response to quetiapine, olanzapine was chosen. Prior to his starting olanzapine, his total leukocyte count was 6,900/dL and platelet count was 200,000/dL. Two weeks after start of olanzapine at a dosage of 7.5 mg/d, hemogram revealed, for the first time, leukopenia (total leukocyte count, 2,700/dL), which was accompanied by thrombocytopenia (platelet count, 20,000/dL).

There was no evidence of fever, skin rash, or any infective focus or history of intake of any other medications other than lorazepam preceding either incidence, ie, when he developed leukopenia with clozapine and when he developed leukopenia and thrombocytopenia with olanzapine.

Olanzapine was stopped. The possibility of drug-induced leukopenia and thrombocytopenia was considered. Following this, he was started on treatment with lithium, which was gradually increased to 600 mg/d to manage his agitation and low blood counts. Within a few days, his total leukocyte count recovered to 4,600/dL and his platelet count was 140,000/dL. In the next 2 weeks, his total leukocyte count and platelet count increased to 7,000/dL and 220,000/dL, respectively.

After the risk of recurrence of hematologic abnormalities was explained and the pros and cons were weighed, an informed decision was made to restart olanzapine along with continuation of lithium (600 mg/d). Gradually, olanzapine was increased to 7.5 mg/d. With this combination, he achieved remission without recurrence of hematologic abnormalities.

Thrombocytopenia is defined as platelet count less than 150,000/dL. In our literature search, we could find only 7 case reports of olanzapine-associated thrombocytopenia (see Table 1).[1–7] In 2 of the 7 case reports, thrombocytopenia was seen in the background of idiopathic thrombocytopenic purpura, and in 1 case report, thrombocytopenia was seen in the presence of folate deficiency. In all cases, thrombocytopenia improved after removal of the offending agent. Additionally, prednisolone in 1 case report and folic acid supplementation in another were used to manage thrombocytopenia. Besides these case reports, Tu and Yang[8] reported an interesting case of olanzapine-induced ethylenediaminetetraacetic acid–dependent pseudothrombocytopenia.[8]

Previous reports have shown that subjects who develop blood dyscrasias with clozapine can have recurrence of blood dyscrasias[9] or can have prolonged deranged blood counts[10–12] when started on olanzapine treatment. Structural similarities in clozapine and olanzapine have been hypothesized as a possible reason of development of hematologic abnormalities in subjects initially treated with clozapine and subsequently treated with olanzapine.[13] Fortunately, in our case, rechallenge with olanzapine while the patient was on lithium treatment did not result in recurrence of thrombocytopenia.

Our case reflects that, in rare cases, especially in those who develop leukopenia with clozapine treatment, olanzapine can lead to leukopenia and thrombocytopenia; hence, close hematologic monitoring should be considered in such cases.

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Table 1. Case Reports of Olanzapine-Induced Thrombocytopenia

Report	Medical History	Challenge With Other Agent	Associated Hematological Disturbances	Management Done
Bachmann et al[1]	Idiopathic thrombocytopenic purpura	…	…	…
Bogunovic and Viswanathan[2]	None	Developed thrombocytopenia with benztropine mesylate	…	Prednisolone
Onofrj and Thomas[3]	…	…	Pancytopenia	…
Carrillo et al[4]	History of idiopathic thrombocytopenic purpura	…	…	…
Rai et al[5]	…	…	Pancytopenia	…
Mehta and Sanitato[6]	…	…	Neutropenia	…
Maurier et al[7]	Folate deficiency	…	Pancytopenia Megaloblastic anemia	Folic acid

Symbol: … = not specified in report.

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