

Thrombocytopenia and Spontaneous Intracranial Hemorrhage After Olanzapine Therapy

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The use of atypical antipsychotics in the United States has increased over the past decade, since atypical antipsychotics such as olanzapine and clozapine were introduced. Of the adverse effects associated with olanzapine, bone marrow suppression is one of the most common, but spontaneous intracranial hemorrhage secondary to thrombocytopenia is rare. The present case report describes an 88-year-old man who presented with an intracranial hemorrhage after taking olanzapine for 2 weeks. This case emphasizes the importance of monitoring the potential adverse effects associated with olanzapine and other antipsychotics, especially in elderly patients.

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The use of atypical antipsychotics has increased 5 to 6 times in the United States over the past decade.¹ In the elderly population with schizophrenia, long-term treatment with atypical antipsychotics has been shown to be effective.¹ These positive results have been traced back to the 1990s, when atypical antipsychotics such as olanzapine and clozapine were introduced, because they were found to be more effective and involve fewer adverse effects than typical antipsychotics. However, atypical agents have been associated with notable adverse effects, including the potential for weight gain, myocardial infarction, extrapyramidal symptoms, stroke, and sudden death.¹

We discuss the case of an elderly man who presented with a change in mental status after being prescribed olanzapine. The patient was found to have a spontaneous intracranial hemorrhage secondary to thrombocytopenia. Although cases of patients with thrombocytopenia caused by olanzapine have been reported,^{2,3,10} as well as patients presenting with a spontaneous hemorrhage due to thrombocytopenia,¹³ to our knowledge, there are no reported cases of patients with thrombocytopenia caused by olanzapine in addition to a subsequent spontaneous intracranial hemorrhage.

Report of Case

An 88-year-old man with a history of hypertension and hypercholesterolemia presented to the emergency department 6 hours after family members and staff at the nursing home where he resided noticed a change in his mental status. According to family members, before the change in mental status, the patient was fairly independent, verbal, able to ambulate, and had no history of dementia. On arrival to the emergency department, he was nonverbal, would only move to withdraw from pain, and was not able to follow commands. It was reported that the patient was evaluated by his primary care

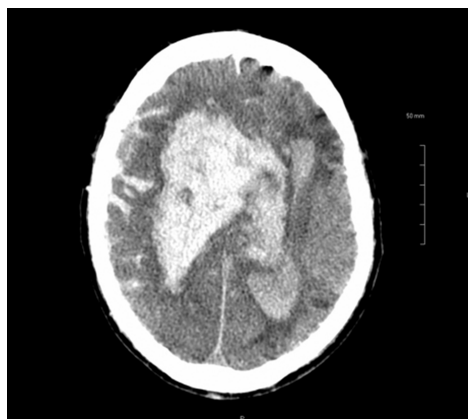


Figure 1.
Computed tomographic scan of the brain showing intracranial hemorrhage in an elderly patient who began olanzapine therapy 2 weeks prior.

physician 2 weeks previously, received a diagnosis of depression, and was given a prescription for olanzapine, 20 mg/d.

The patient's vital signs at the time of presentation were as follows: temperature, 99.1°F; oxygen saturation while breathing room air, 94%; heart rate, 120/min; blood pressure, 134/68 mm Hg; and respiration rate, 32/min. Although he was breathing independently, in an effort to protect and maintain his airway, the patient was intubated immediately. Aside from requiring intubation, the patient's physical examination results were unremarkable, as were cardiovascular and respiratory examination results. The patient was well nourished and did not have any signs of trauma to the head, body, or extremities. His medications included lisinopril and simvastatin in addition to the newly prescribed olanzapine. The nursing home staff reported that the patient's blood pressure was well maintained.

Results of laboratory tests, including a basic metabolic panel, troponin level, white blood cell count, hemoglobin level, and hematocrit level, were normal. The patient had a prothrombin time of 12 seconds, international normalized ratio of 1.1, and activated partial thromboplastin time of 26 seconds. His platelet count was below the reference range, at $4 \times 10^3/\mu\text{L}$,

which had dropped from $166 \times 10^3/\mu\text{L}$ as recorded by his primary care physician 2 weeks before. A computed tomographic scan of his brain revealed a spontaneous intracranial bleed (**Figure 1**). His medical records showed a normal computed tomographic scan of the brain 1 year before admission.

The patient remained intubated and was admitted to the intensive care unit on the day of presentation because of a massive intraparenchymal, intraventricular, subarachnoid, and subdural hemorrhage with impending herniation. After discussion with family members and the hospital's palliative care team about the patient's prognosis, the family withdrew care, and the patient died 48 hours after admission.

Discussion

Physicians should be cautious when prescribing atypical antipsychotics to elderly patients, and they should consider polypharmacy, potential drug interactions, and age-related changes such as decreased creatinine clearance, changes in volume of distribution, and prolonged effects of medication due to slower metabolism. Olanzapine and clozapine are both complex-structured atypical antipsychotics that contain aromatic hydrocarbons (**Figure 2**). Medications with such configurations have been found to be associated with bone marrow suppression.^{4,5} Whereas clozapine has been shown to lead to hematopoietic effects, especially neutropenia and thrombocytopenia, olanzapine has been deemed as a safe alternative for patients who

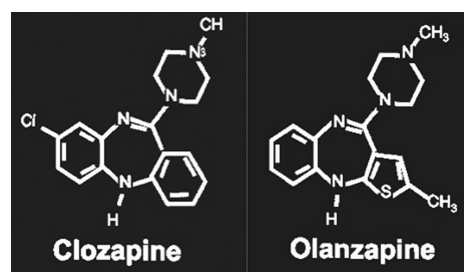


Figure 2.
Chemical structures of clozapine and olanzapine.

have had hematologic side effects from other antipsychotics.² The incidence of hematopoietic suppression, including leukopenia and thrombocytopenia, is lower with olanzapine than with clozapine,^{2,3} but physicians should still be cautious when prescribing it to elderly patients.

Cases of patients with thrombocytopenia caused by compounds consisting of aromatic rings are well documented.^{4,5} Studies have evaluated the serotonin metabolism effects of olanzapine on platelet structure, which leads to decreases in platelet count.⁶⁻⁸ Several case reports detail the relationship of such platelet count changes over a short period, ranging from a few days to several months.⁹⁻¹² Additionally, when platelet levels are below 10 to $20 \times 10^3/\mu\text{L}$, the risk for spontaneous bleeding, particularly intracranial hemorrhage, increases.¹³ The patient in the current case did not have trauma and was not taking other medications known to cause thrombocytopenia. Before presentation, the patient was in good health and had no history of infection or low platelet count. The differential diagnosis for this patient's intracranial hemorrhage included trauma and hypertensive emergency, but these conditions were ruled out after reviewing the patient's medical history and completing a physical examination.

Conclusion

Cases of thrombocytopenia secondary to olanzapine have been noted in the literature, but there is no previous record, to our knowledge, of spontaneous intracranial hemorrhage secondary to thrombocytopenia caused by olanzapine. It is important for physicians to be mindful of the potential adverse effects of bone marrow suppression and thrombocytopenia when prescribing antipsychotics and other medications containing aromatic compounds.

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