

Olanzapine-Associated Neutropenia: A Case Report

Amine Achak^{1*}, S. Bahetta¹, H. Nafaa¹, M. Sabir¹

¹Women's Unit A, Ar-Razi University Psychiatric Hospital, Salé, Ibn Sina University Hospital, Morocco

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*Corresponding author: Amine Achak

Women's Unit A, Ar-Razi University Psychiatric Hospital, Salé, Ibn Sina University Hospital, Morocco

Abstract

Case Report

Background. Olanzapine-associated neutropenia is rare but potentially serious and is less widely recognized than clozapine-associated neutropenia. Routine hematological monitoring is not required for every patient receiving olanzapine. **Case presentation.** A 27-year-old woman with no known hematological history was admitted with cannabis-induced psychotic disorder after a suicide attempt by jumping from a height in a delusional context. A complete blood count obtained four months earlier showed an absolute neutrophil count (ANC) of 1,550/mm³. Olanzapine 10 mg/day had been started approximately two weeks before admission. On July 22, 2026, an increase to 20 mg/day was prescribed before laboratory results became available; the ANC was subsequently found to be 900/mm³. It reached a nadir of 700/mm³ on July 24, prompting permanent discontinuation of olanzapine. The patient remained afebrile and had no clinical signs of infection. C-reactive protein was negative, and peripheral blood smear, vitamin B12, folate, renal, liver, thyroid, HIV, hepatitis B, hepatitis C, and syphilis testing did not disclose an alternative cause. Aripiprazole was started at 15 mg/day on July 26 and increased to 30 mg/day on August 3. The ANC recovered to 1,950/mm³ by July 31 and remained normal at outpatient follow-up on August 17 (1,947/mm³). **Conclusion.** The temporal relationship, negative etiological work-up, and recovery after withdrawal constitute a positive dechallenge and support a probable association between olanzapine and neutropenia. Baseline blood counts and targeted early monitoring should be considered in patients with low or borderline pretreatment leukocyte or neutrophil counts.

Keywords: Olanzapine; neutropenia; antipsychotic; pharmacovigilance; case report.

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INTRODUCTION

Neutropenia is generally defined as an absolute neutrophil count below $1.5 \times 10^9/L$. A value between 0.5 and $1.0 \times 10^9/L$ is usually classified as moderate neutropenia, whereas a value below $0.5 \times 10^9/L$ defines severe neutropenia and is often termed agranulocytosis in the pharmacovigilance literature [1,2]. The risk of infection increases with the depth and duration of neutropenia.

Antipsychotic-related blood dyscrasias are primarily associated with clozapine, but they have also been reported with other agents. In the AMSP pharmacovigilance program, 124 cases of neutropenia or agranulocytosis were reported among 333,175 psychiatric inpatients exposed to antipsychotics, corresponding to 0.37 cases per 1,000 patients. Seven cases attributed to olanzapine alone were identified among 54,822 exposures, corresponding to 0.13 cases per 1,000 patients [1]. Most events occurred during the first three months of treatment.

Official prescribing information recognizes leukopenia, neutropenia, and agranulocytosis as class effects. It recommends frequent complete blood count monitoring in patients with a preexisting low white blood cell count or a history of drug-induced neutropenia, and discontinuation of olanzapine when the absolute neutrophil count falls below 1,000/mm³ [3]. We report rapidly reversible isolated neutropenia after olanzapine withdrawal in a young woman with no known hematological history.

CASE PRESENTATION

Patient information and clinical findings

A 27-year-old woman was admitted to an inpatient psychiatric unit on July 20, 2026, after a suicide attempt by jumping from a height in a delusional context. Psychiatric examination showed delusions, hallucinations, impaired judgment and insight, and insomnia. The final diagnosis was cannabis-induced psychotic disorder.

Her history included problematic cannabis and tobacco use. She had no known medical, surgical, or

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hematological history. A complete blood count obtained on March 10, 2026, before olanzapine exposure, showed a leukocyte count of 5,000/mm³, an ANC of 1,550/mm³, hemoglobin of 13.4 g/dL, and a platelet count of 382,000/mm³.

Drug exposure and hematological course

Olanzapine had been started at 10 mg/day approximately two weeks before admission, around July 6, 2026. Diazepam, the only concomitant medication, was started on admission at 30 mg/day, progressively tapered, and completely discontinued on August 7, 2026.

On July 22, an increase in olanzapine to 20 mg/day was prescribed before the laboratory results became available. The complete blood count obtained that day subsequently showed isolated neutropenia, with an ANC of 900/mm³ and a leukocyte count of

4,600/mm³. Repeat testing on July 24 showed further deterioration, with an ANC nadir of 700/mm³ and a leukocyte count of 4,700/mm³. Olanzapine was then permanently discontinued. Neither granulocyte colony-stimulating factor nor antibiotic treatment was administered.

The ANC increased to 900/mm³ on July 25. In view of this favorable trend and the need to maintain antipsychotic treatment, aripiprazole was started at 15 mg/day on July 26 under hematological monitoring. Leukocyte count and ANC were 3,900/mm³ and 1,000/mm³ on July 27, 4,500/mm³ and 1,200/mm³ on July 28, and 6,880/mm³ and 1,950/mm³ on July 31, respectively. Aripiprazole was increased to 30 mg/day on August 3. The patient was discharged on August 10 on aripiprazole 30 mg/day.

Table 1: Timeline of treatment and hematological findings

Date	Event/treatment	Leukocytes (/mm ³)	ANC (/mm ³)
10 Mar 2026	CBC before olanzapine exposure	5,000	1,550
Approx. 6 Jul	Olanzapine 10 mg/day started	—	—
20 Jul	Admission; diazepam 30 mg/day	—	—
22 Jul	Olanzapine increased to 20 mg/day before CBC result	4,600	900
23 Jul	Report submitted to pharmacovigilance center	—	—
24 Jul	Nadir; olanzapine permanently discontinued	4,700	700
25 Jul	Recovery after withdrawal	4,100	900
26 Jul	Aripiprazole 15 mg/day started	—	—
27 Jul	Hematological monitoring	3,900	1,000
28 Jul	Hematological monitoring	4,500	1,200
31 Jul	ANC normalized	6,880	1,950
3 Aug	Aripiprazole increased to 30 mg/day	—	—
7 Aug	Diazepam completely discontinued	—	—
10 Aug	Discharged on aripiprazole 30 mg/day	—	—
17 Aug	Outpatient CBC: Hb 13.4 g/dL; platelets 275,000/mm ³	5,500	1,947

Abbreviations: ANC, absolute neutrophil count; CBC, complete blood count; Hb, hemoglobin.

Etiological evaluation

Throughout the episode, the patient remained afebrile and showed no clinical signs of infection. C-reactive protein was negative. Serological tests for HIV, hepatitis B, hepatitis C, and syphilis were negative. Vitamin B12 and folate concentrations were normal, as were renal, liver, and thyroid function tests. The peripheral blood smear was normal. Because hemoglobin and platelet counts were preserved, the abnormality was classified as isolated neutropenia. No hematological consultation or bone marrow examination

was performed because of the rapid improvement after drug withdrawal.

Follow-up and outcome

An outpatient complete blood count obtained on August 17, 2026, confirmed sustained recovery: leukocytes 5,500/mm³, ANC 1,947/mm³, hemoglobin 13.4 g/dL, and platelets 275,000/mm³. No infectious signs were reported, and aripiprazole was well tolerated. Olanzapine was contraindicated for this patient. The suspected adverse drug reaction was reported to the pharmacovigilance center on July 23, 2026.

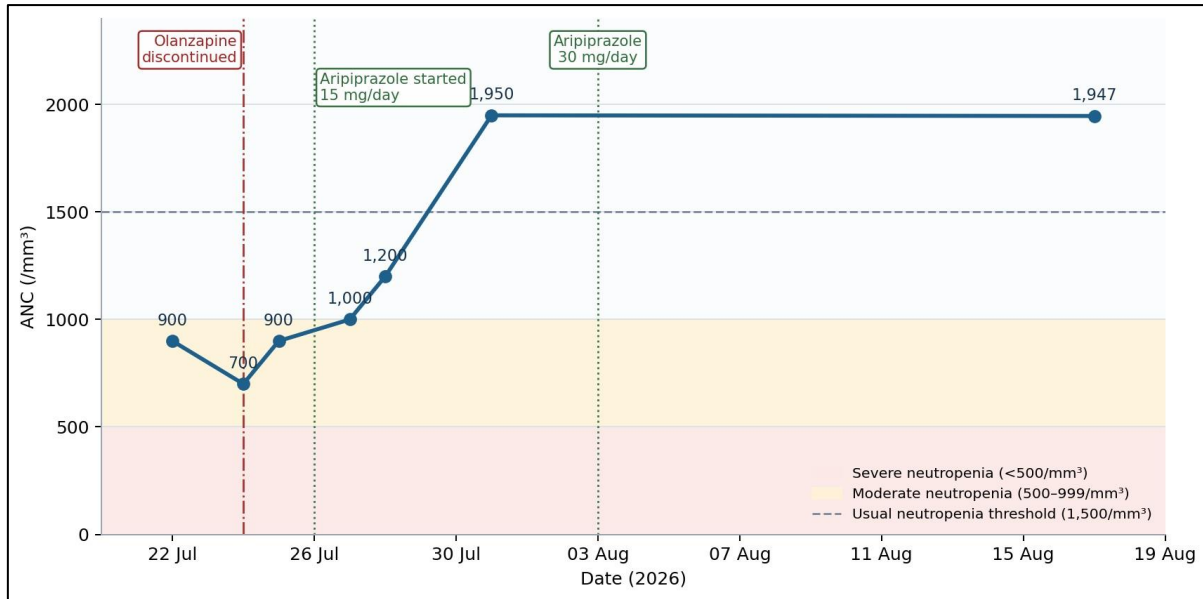


Figure 1: Absolute neutrophil count after olanzapine withdrawal and switch to aripiprazole

The previous CBC obtained on March 10, 2026 (ANC 1,550/mm³), is not shown to preserve the readability of the acute phase.

DISCUSSION

This case is compatible with olanzapine-associated isolated neutropenia. The temporal sequence is suggestive: onset after approximately two weeks of exposure, a decline to 700/mm³, and progressive recovery after permanent discontinuation. This timing falls within the early risk period reported for drug-induced and antipsychotic-associated neutropenia [1,2]. Comparable cases of reversible olanzapine-associated neutropenia have been published, with variable onset times, doses, and confounding factors [4,5].

Causality is supported primarily by the positive dechallenge, repeated objective laboratory findings, and the absence of an identified infectious, nutritional, or

visceral cause. Diazepam was the only concomitant medication; it was started after the initial exposure to olanzapine and continued while the ANC recovered, making its involvement less likely. Persistent normalization during aripiprazole treatment also supports, without independently proving, an olanzapine-specific effect.

Using the Naranjo algorithm, the conservative score was 5, corresponding to a probable adverse drug reaction [6]. Alternative causes were rated as uncertain rather than absent because no bone marrow, autoimmune, copper, or genetic investigations were performed. Rechallenge was not attempted and would not have been ethically justified given the ANC nadir below 1,000/mm³.

Table 2: Conservative causality assessment using the Naranjo algorithm

Criterion	Response	Score
Previous reports of this reaction with olanzapine	Yes	+1
Event occurred after drug administration	Yes	+2
Improvement after drug withdrawal	Yes	+1
Recurrence after rechallenge	Not performed	0
Alternative cause could explain the event	Uncertain	0
Recurrence with placebo	Not performed	0
Toxic drug concentration	Not measured	0
Dose-response relationship	Uncertain	0
Previous similar reaction	Unknown	0
Objective confirmation	Yes: serial CBCs	+1
Total	Probable causality	5

The precise mechanisms of olanzapine-associated neutropenia remain undetermined. As with other drug-induced neutropenias, direct toxicity to the myeloid lineage and peripheral immunemediated destruction have been proposed [1,2]. The structural

similarity between olanzapine and clozapine and the possible formation of reactive metabolites have also been investigated, although the level of risk associated with clozapine cannot be extrapolated to olanzapine [7].

The pretreatment ANC of 1,550/mm³ was at the usual lower limit. It may reflect constitutional individual variability. Duffy-null status, which is associated with lower circulating neutrophil counts without a demonstrated increase in infection risk, was not assessed [8]. This possibility represents a vulnerability factor or differential diagnosis, but it does not independently explain the acute decline to 700/mm³ followed by recovery toward the usual value after olanzapine withdrawal.

Olanzapine prescribing information recommends discontinuation when the ANC is below 1,000/mm³ and monitoring until recovery [3]. The management adopted permanent discontinuation, clinical monitoring for fever, and serial complete blood counts was therefore consistent with these recommendations. The absence of fever, infection, or profound agranulocytosis explains why antibiotics and granulocyte colony-stimulating factor were not administered. Cautious initiation of another antipsychotic with close monitoring was necessary because of the acute psychiatric symptoms.

Limitations

This report has the inherent limitations of a single case. The exact date of the first olanzapine dose was estimated as approximately two weeks before admission. No complete blood count was available immediately before exposure; the latest previous count dated from March 10, 2026. Several rare causes of neutropenia were not investigated, including autoimmune disease, copper deficiency, and Duffy-null status. No hematological consultation or bone marrow examination was performed because of the rapid recovery. Finally, the absence of rechallenge prevents establishment of certain causality, although rechallenge would not have been justified.

CONCLUSION

Neutropenia may occur early during olanzapine treatment, even in patients without a known hematological history. In this case, the ANC nadir of 700/mm³, the negative available etiological work-up, and rapid normalization after withdrawal support probable causality. A baseline complete blood count and targeted monitoring early in treatment appear particularly relevant when the pretreatment leukocyte or neutrophil

count is low or borderline. Early recognition, withdrawal of the suspected drug, and pharmacovigilance reporting may reduce the risk of progression to a serious infectious complication.

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