

Methimazole-Induced Agranulocytosis

Tellagorla Bharathi, Siram Teja Manikanta*, Viswanadhapalli Jaswanth Raju, Katragadda Pradeepthi, Ghanta Vijayakumar, Ghanta Vijaya Kumar

Department of Pharmacy Practice, KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada, Andhra Pradesh, INDIA.

ABSTRACT

The antithyroid drug methimazole is used to treat patients with hyperthyroidism. Agranulocytosis is a rare and life-threatening adverse effect of the drug, characterized by a reduced circulating white blood cell count, which increases the risk of infections. We present the case of a 49-year-old male patient with a known history of hyperthyroidism for 10 years who was on tablet methimazole 10 mg three times daily. He presented with complaints of high-grade fever associated with chills for 2 days, sweating, body myalgias, difficulty in speaking due to neck swelling and palpitations. Laboratory investigations revealed severe neutropenia along with a thyrotoxic crisis. The patient's symptoms and laboratory abnormalities resolved after withdrawal of the drug, and he was managed with broad-spectrum antibiotics, propranolol, hydrocortisone, and cholestyramine. His neutrophil count normalized within 1 week. This case report highlights the importance of early identification of methimazole-induced agranulocytosis. Clinicians should maintain a high index of suspicion for rare life-threatening complications, of antithyroid drugs in patients presenting with infectious symptoms. Management of methimazole-induced agranulocytosis mainly involves discontinuation of the drug for preventing mortality associated with ATD-induced agranulocytosis.

Keywords: Agranulocytosis, Methimazole, Hyperthyroidism, Thyrotoxic crisis.

Correspondence:

Mr. Siram Teja Manikanta

Department of Pharmacy Practice, KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada, Andhra Pradesh, INDIA.

Email: tejamanikantasiram@gmail.com

Received: 24-09-2025;

Revised: 07-11-2025;

Accepted: 12-01-2026.

INTRODUCTION

Antithyroid Medications (ATDs) are frequently used to treat hyperthyroidism (Sun *et al.*, 2009). Hyperthyroidism is a complex endocrine disorder characterized by an abnormally elevated metabolic rate due to excessive thyroid hormone secretion (Blick *et al.*, 2025). Methimazole, a frequently prescribed ATD, lowers thyroid hormone production by inhibiting thyroperoxidase, and essential enzyme involved in the synthesis of Thyroxine (T4) and Triiodothyronine (T3). Methimazole, a frequently prescribed ATD, lowers the production of thyroid hormones. Methimazole helps restore normal thyroid function by lowering thyroid hormone levels. It may also lessen thyrotoxicosis-related complications like bone loss (Sun *et al.*, 2025).

Up to 5% of patients experience mild side effects from Antithyroid Medications (ATDs), including fever, arthralgia, and skin rash. These reactions typically resolve spontaneously or after switching to an alternate ATD. Hepatotoxicity and agranulocytosis are major and uncommon but dangerous side effects that affect 0.2–0.3% of adults. Agranulocytosis is defined as an Absolute

Neutrophil Count (ANC) of less than 500/mm³ and it usually appears during the initial weeks to months of treatment. Fever, malaise, and sore throats are common initial symptoms; in more severe cases, deep tissue infections, sepsis, or septic shock may develop (MacKay *et al.*, 2023).

Furthermore, the risk of agranulocytosis with methimazole is dose-dependent (Sun *et al.*, 2009).

CASE REPORT

A 49-year-old male patient with a known history of hyperthyroidism for 10 years presented to general medicine with a high-grade fever with chills, excessive sweating, and generalized myalgia for 2 days. He also reported a productive cough with whitish sputum and neck swelling for 1 week. He also reported palpitations for the past 5 years and recent difficulty in speaking.

The patient had previously used tablet Thyronorm 100 mcg for 4-5 years, which was discontinued in February-2023. He was then started on tablet Neomercazole 10 mg, which was stopped one year later, following which methimazole 10 mg three times daily was initiated in June 2025 and continued regularly. Past surgical history includes incision and drainage of a gluteal abscess, 10 years ago.

On admission, he appeared toxic and febrile. His vital signs were: heart rate 110/min, blood pressure 130/80 mmHg, respiratory rate 25/min, and temperature 105°F. Physical examination revealed thyroid swelling, mild tenderness in the neck region, and bilateral



DOI: 10.5530/ijopp.20260688

Copyright Information :

Copyright Author (s) 2026 Distributed under Creative Commons CC-BY 4.0

Publishing Partner : Manuscript Technomedia. [www.mstechnomedia.com]

coarse breath sounds on auscultation. Cardiovascular, abdominal, and neurological examinations were otherwise unremarkable.

Laboratory evaluation demonstrated severe leukopenia, with a TWBC count of $2.4 \times 10^3/\mu\text{L}$, and neutrophil count 11%. Hemoglobin was 10.3 g/dL, platelets $2.7 \times 10^5/\text{L}$, and ESR 27 mm/hr. Serum electrolytes were within normal limits (Na^+ 136 mEq/L, K^+ 4.0 mEq/L). Thyroid function tests revealed a TSH level of $< 0.01 \text{ ug/mL}$.

➤T3: -5.15 ng/mL.

➤T4: -26.19 ug/dL.

USG NECK: -Both the lobes of the thyroid and the isthmus are enlarged in size.

➤RT lobe: -4.7 x 4.2 x 4.0 cm.

➤LT lobe: -4.0 x 3.1 x 3.0 cm.

Both lobes of the thyroid are bulky with altered echotexture and mildly increased vascularity.

Considering the presence of fever, neutropenia, long-term methimazole use, and biochemical thyrotoxicosis, a diagnosis of methimazole-induced agranulocytosis precipitating thyrotoxic crisis was made.

Serial hematological parameters during hospitalization are summarized in Table 1.

Methimazole was immediately discontinued. The patient was started on broad-spectrum antibiotics, Granulocyte Colony-Stimulating Factor (G-CSF), propranolol, cholestyramine and hydrocortisone. For symptomatic control of thyrotoxicosis. Serial complete blood counts showed a progressive improvement in leukocyte and neutrophil counts over the next several days, accompanied by resolution of fever and respiratory symptoms.

The patient continued to improve clinically and was discharged in stable condition fever and tachycardia had resolved and neutrophil counts had improved.

DISCUSSION

Agranulocytosis, a serious reduction in white blood cells, can occur with the use of Antithyroid Drugs (ATDs) such as Methimazole. It usually presents within the first 2 to 3 months of treatment, however, delayed onset after several months or even one to two years of therapy has also been reported (Menino *et al.*, 2025).

This condition can occur through multiple mechanisms. The drug or its metabolites may directly damage the bone marrow, where white blood cells are produced. They may also trigger immune-mediated destruction of these cells. These drugs affect the bone marrow by interfering with oxygen and glucose utilization by white blood cells, which are essential for their survival and function. Typically, these toxic effects develop insidiously after 20-40 days of continuous exposure and are generally dose and concentration-dependent. However, the present case does not follow this typical pattern. Additionally, ATDs may damage stem cells or granulocytic precursors in the bone marrow, impairing granulocyte differentiation while leaving the existing peripheral neutrophil pool largely unaffected (Sun *et al.*, 2009).

Thyrotoxicosis occurs when there is an excess of thyroid hormone, primarily T3 and T4, in the body. This condition results from elevated circulating hormone levels, leading to an increase metabolic state (Sun *et al.*, 2025).

Patients treated with Granulocyte Colony-Stimulating Factor (G-CSF), demonstrated hematological recovery within 3 to 13 days. All patients fully recovered from agranulocytosis. Based on these findings, we suggest that: (1) routine complete blood count monitoring can aid in early detection of agranulocytosis; (2) patient education regarded typical symptoms may enable timely diagnosis; (3) G-CSF therapy is associated with a favourable outcome; and (4) monitoring for potential cross-reactivity between antithyroid drugs is essential to prevent recurrence (Yang *et al.*, 2012).

Table 1: Serial hematological parameters during hospitalization.

Day	TWBC ($\times 10^3/\mu\text{L}$)	Neutrophils (%)	Hb (g/dL)	MCV (fL)
On admission	0.3	2	10.0	55
Day 1	0.43	4	11.0	55
Day 2	1.0	8	11.0	59
Day 3	1.45	11	12.0	65
Day 4	2.0	25	11.5	70
Day 5	2.43	30	11.0	68
Day 6	3.0	38	11.0	68.3
Day 7	3.2	45	12.0	69.1
Day 8	4.10	50	12.5	70.3
At discharge	4.10	58	13.0	85

Agranulocytosis caused by methimazole is a rare but potentially life-threatening drug reaction and is estimated to have an incidence of between 0.2 and 0.5, and it is stated to be dose dependent. Though the majority of the cases happen in the first months of therapy, delayed onset of the process has also been reported in the treatment of long-term course. Wary signs of fever and sore throat should be noted early on in order to be diagnosed in time. The withdrawal of the offending drug is the mainstay of management that should be done immediately. Granulocyte Colony-Stimulating Factor (G-CSF) adjunctive treatment has also been found to hasten neutrophil recovery and shorten the length of stay, and the majority of patients recover hematologically in 3-13 days. The case is associated with a favorable outcome and a clinical course, which is consistent with the literature published earlier, and the necessity to introduce early intervention and provide proper supportive care.

CONCLUSION

A rare but potentially life-threatening effect of Antithyroid Drug (ATD) therapy is agranulocytosis. Recognizing early symptoms such as fever is essential. Regular blood monitoring and patient education warning symptoms are crucial for early detection.

If agranulocytosis occurs, the offending drug must be discontinued immediately, intravenous broad-spectrum antibiotics should be initiated and Granulocyte-Colony Stimulating Factor (G-CSF) may be consideration to accelerate neutrophil recovery.

This case highlights the importance of careful monitoring during antithyroid drug therapy is so particularly with Methimazole (MMI), due to the risk of agranulocytosis.

ABBREVIATIONS

ATD: Antithyroid drug; **ANC:** Absolute Neutrophil Count; **G-CSF:** Granulocyte Colony-Stimulating Factor; **MMI:** Methimazole; **TSH:** Thyroid-Stimulating Hormone; **T3:** Triiodothyronine; **T4:** Thyroxine; **TWBC:** Total White Blood Cell Count.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient, and institutional permission was granted by the hospital for publication of this anonymized case report.

REFERENCES

- Bai, X. S., Liu, J. H., & Xiao, S. M. (2014). A patient with agranulocytosis following the discontinuation of methimazole treatment for 4 months: A case report. *Experimental and Therapeutic Medicine*, 8(3), 823–825. <https://doi.org/10.3892/etm.2014.1817>
- Blick, C., Nguyen, M., & Jialal, I. (2025). Thyrotoxicosis. *StatPearls*. StatPearls Publishing.
- El-Shareif, H. J. (2023). Agranulocytosis: A rare complication of the thionamides. *The Egyptian Journal of Internal Medicine*, 35, 1–5. <https://doi.org/10.1186/s43162-023-00245-w>
- MacKay, M., Clewis, M. C., & Sweet, P. (2023). Antithyroid drug-induced agranulocytosis: A case report. *Cureus*, 15(11), e48264. <https://doi.org/10.7759/cureus.48264>
- Menino, J., Meira, I., Gonçalves, J., Ribeiro, S., Pedro, J., & Queirós, J. (2025). Methimazole-induced agranulocytosis: A clinical case report. *Endocrinology Insights*, 20(2), 112–115. <https://doi.org/10.1159/000546313>
- Sun, M. T., Tsai, C. H., & Shih, K. C. (2009). Antithyroid drug-induced agranulocytosis. *Journal of the Chinese Medical Association*, 72(8), 438–441. [https://doi.org/10.1016/S1726-4901\(09\)70402-2](https://doi.org/10.1016/S1726-4901(09)70402-2)
- Sun, Y., Wang, S., & Zhou, X. (2025). Adverse events of the thyroid peroxidase inhibitor methimazole in the treatment of hyperthyroidism: A comprehensive analysis. *Frontiers in Endocrinology*, 16, 1680281. <https://doi.org/10.3389/fendo.2025.1680281>
- Yang, J., Zhong, J., Zhou, L. Z., Hong, T., Xiao, X. H., & Wen, G. B. (2012). Sudden onset agranulocytosis and hepatotoxicity after taking methimazole. *Internal Medicine*, 51(16), 2189–2192. <https://doi.org/10.2169/internalmedicine.51.7845>

Cite this article: Bharathi T, Manikanta ST, Raju VJ, Pradeepthi K, Vijayakumar G, Kumar GV. Methimazole-Induced Agranulocytosis. *Indian J Pharmacy Practice*. 2026;19(3):435-7.