

Thyroid Ablation As Graves' Disease Treatment Modality in Methimazole-Induced Drug-Induced Liver Injury

Putri Cinthya Ismihari^{1,2}, Hermina Novida^{3,4*}, Arfika Wida Ekacitta^{5,6}

¹Internal Medicine Specialist Study Program, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia (<https://orcid.org/0009-0009-9485-3779>)

²Internal Medicine Specialist Study Program, Department of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia (<https://orcid.org/0009-0009-9485-3779>)

³Division of Endocrinology, Diabetes and Nutrition, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia (<https://orcid.org/0000-0001-5899-1589>)

⁴Division of Endocrinology, Diabetes and Nutrition, Department of Internal Medicine, Universitas Airlangga Hospital, Surabaya, Indonesia (<https://orcid.org/0000-0001-5899-1589>)

⁵Department of Internal Medicine, Sumberrarjo Regional Hospital, Bojonegoro, Indonesia (<https://orcid.org/0000-0002-2114-7840>)

⁶Department of Internal Medicine, Temayang Regional Hospital, Bojonegoro, Indonesia (<https://orcid.org/0000-0002-2114-7840>)

*Corresponding Author: Hermina Novida, Division of Endocrinology, Diabetes, and Nutrition, Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga – Universitas Airlangga Hospital, Surabaya, Indonesia, +62 813-3152-6625, Email: hermina-n@fk.unair.ac.id

Abstract

Methimazole (MMI)-related drug-induced liver injury (DILI) in Graves' Disease (GD) patients is rare and the other antithyroid drugs (ATD) also have DILI risk as MMI. This case report illustrated DILI disease course in the patient and explored the other therapeutic modality option. A 39-year-old woman came to emergency room (ER) due to yellowish color and itching in all of her body for one week. She also complained nauseous, bloating, tea colored urine and putty colored stool. She was diagnosed GD 3 months prior and received MMI as her treatment. Her sclera was icteric and her liver function test increased in both transaminase (Aspartate Aminotransferase (AST) 118, Alanine Aminotransferase (ALT) 187) and hyperbilirubinemia (total bilirubin 10.56, direct bilirubin 6.54). Per exclusion, she was diagnosed MMI-related DILI. Therefore, her MMI treatment was stopped and thyroid ablation was received. Two days after her ablation, she showed significant clinical improvement and was discharged. MMI-related DILI in GD patients is rare but life threatening. Thyroid ablation is a therapeutic modality option in GD management.

Keywords: human and health, hyperthyroidism, Graves' Disease, Drug-Induced Liver Injury, antithyroid agents, methimazole, ablation.

Introduction

Drug-related hepatotoxicity or Drug-Induced Liver Injury (DILI) is a severe drug adverse event, including antithyroid drugs (ATD) such as methimazole (MMI) and propylthiouracil (PTU).¹⁻³ The prevalence of ATD-related DILI is 2.5%, by means of 1.4% is MMI-related and 6.3% is PTU-related.⁴ This condition often occurred in women and the complication risk was bigger.⁵ This was caused by the drug sensitivity and metabolism are different in men and women resulting in immune response and inflammation-related to sex hormones, leading to drug-induced autoimmune reactions and liver injury in women.⁶ Thyroid ablation is one of Graves' Disease (GD) safe therapeutic options for women.⁷

Thyroid ablation is minimally invasive treatment modality for thyroid nodule.⁸ This technique uses a radiofrequency catheter inserted into the target nodule, therefore inducing irreversible tissue damage and necrosis. Some of ablation benefits are higher precision, minimally invasive, speedy recovery, less traumatic, more cost effective and more cosmetically appealing.⁹ Despite thyroid ablation is covered by insurance in Indonesia, its usage as GD treatment is still rare due to hospital facility. Hence, this case report describes benefits of thyroid ablation as GD therapeutic options.¹⁰

This case report describes a 39-year-old GD woman having DILI due to MMI consumption. It aims to illustrate DILI disease course due to MMI and explore the other therapeutic modality options. This case report will hopefully assist clinicians determine a safe and appropriate therapeutic modality for GD patients.

Case Presentation

A 39-year-old woman came to ER due to yellowish color and itching in all over her body for one week. She also complained bloating and nauseous. After four days, yellowish color was all over her body. She also had tea colored urine and putty colored stool. There was no fever or no abdominal pain. She was diagnosed GD 3 months prior. At the time, she had a protrusion in her left eye and double vision for 3 weeks. She had weight loss and palpitation.

There was no history of diabetes mellitus or tuberculosis. She worked at car cable factory. She had 3 children. Moreover, she received MMI since her GD was diagnosed.

On physical examination, her blood pressure was 110/80 mmHg. She had icteric sclera and distended abdomen. There was no tachycardia, no hepatomegaly, no exophthalmos and no abdominal pain.

Liver function test showed increased levels of both her transaminase (Aspartate Aminotransferase (AST) 118, Alanine Aminotransferase (ALT) 187) and hyperbilirubinemia (total bilirubin 10.56 and direct bilirubin 6.54). Her hepatitis viral markers were negative. Her thyroid function test was normal. Her abdominal ultrasound showed slightly contracted gall bladder (GB), impressing there were no gall stones. Her abdominal Magnetic Resonance Imaging (MRI) showed a possibility of chronic cholecystitis in contracted GB; biliary duct was not widening but there was a cut off in common bile duct (CBD) with slight enlargement in head of pancreas. Her thyroid uptake and scan (Fig. 1) resulted in diffuse struma within normal uptake condition. Her complete blood count and electrolyte, including calcium were normal. Her chest x-ray was normal.

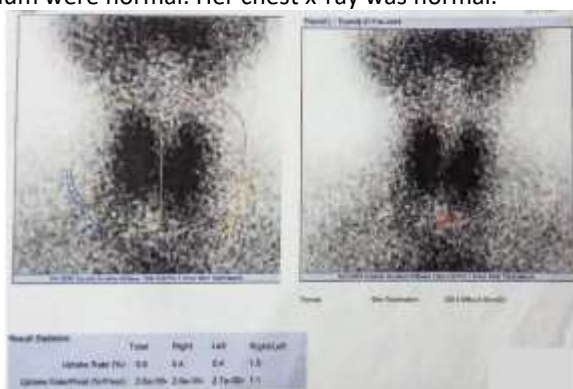


Fig. 1: Thyroid uptake and scan of the patient

Her initial therapy was her ATD drug was continued, that is MMI, propranolol and hepatoprotection agent. She was admitted to the hospital for further observation. On the 4th day of treatment, she had severe nausea and she was suggested to have liver biopsy and thyroid ablation. Then, she was diagnosed MMI-related DILI and her ATD is stopped. She had her thyroid ablation on her 6th day of treatment. She was discharged on her 8th day of treatment. At that time, she was clinically improved and her liver function test both transaminase (AST 27 and ALT 24) and bilirubin (total bilirubin 0.73 and direct bilirubin 0.34) were normal. At her follow-up, one week later, she had no nausea, no icteric and no itching. She never received her ATD since.

Discussion

This case report highlights a patient with ATD-related DILI, that is MMI. She had yellowish color and itching all over her body. Her liver function tests increase, both transaminase (AST 118 and ALT 187) and bilirubin (total bilirubin 10.56 and direct bilirubin 6.54). Whereas, her viral hepatitis markers were negative. Jaundice is a change in tissue color from normal to yellow due to bilirubin deposition. This condition becomes a liver disorder marker. According to the algorithm for diagnosing the cause of jaundice and her liver function test abnormalities, the jaundice occurring in the patient is cholestatic jaundice.¹¹ This type of jaundice consists of three type, pure cholestasis, hepatitis cholestasis and acute cholestasis. Furthermore, drugs consumption could also cause cholestasis to occur.^{12,13} A prior case report shows MMI consumption could cause acute liver injury.¹⁴ Another case report shows chronic consumption of MMI induces DILI needing total thyroidectomy. Therefore, DILI occurring in the patient needs special attention and precision in order to determine a safer and more appropriate treatment.¹⁵

In this case, the patient has idiosyncratic type of DILI, that could not be predicted and is not dose dependent. This type occurs randomly and hard to predict in patients without prior allergic history or certain risk factor.^{13,16} Although hepatotoxicity is one of MMI side effect, its prevalence is low, that is 2.5%.^{3,4} MMI causes cholestatic or mixed type of hepatotoxicity, often occurring within 2–12 first weeks of its consumption. This is in accordance to patient's duration of MMI consumption.¹ Besides, DILI is prone to occur and has worse outcomes in women as the evaluation and monitoring should be more careful. Thereof, the MMI consumption is stopped.⁵

The patient's thyroid uptake and scan were diffuse struma within normal uptake condition. This shows her hyperthyroid has been controlled by ATD consumption. ATD consumption is one of interfering factors in this procedure.¹⁷ The selection of thyroid ablation for this patient related to DILI occurring. Thyroid ablation is minimally invasive treatment modality that may become an alternative to surgery in patients with benign thyroid nodule. Prior study shows thyroid ablation is effective in eradicating GD.^{8,18} Another study reports thyroid ablation has high tolerability, safety and efficacy. Consequently, this technique could be considered as one of GD therapeutic options.⁹ This case report has several limitations. First, lack of definitive diagnosis tools such as alkaline phosphatase, inhibited the assessment of RUCAM score in DILI patient. Second, the patient's follow-up data was not available, due to her routine follow-up in another hospital. Nonetheless, this case encourages clinicians to be more aware of hepatotoxicity or DILI that could occur in GD patients consuming MMI.

Conclusion

This case report illustrates MMI-related DILI in GD patient. Type of DILI in this patient was mixed cholestatic type and prone to severe complication risk. Consequently, the conservative therapy has been done, that is stopping MMI consumption. Another therapeutic option for GD, the thyroid ablation, has been done to control its activity. This case was hoped to give consideration to thyroid ablation therapy in GD patients, especially in the patients who prone to have ATD-related hepatotoxicity or DILI.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent form. In the form, patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil

Conflict of interest

The authors declare no conflict of interests

Author contribution

Conceptualization, PCI, HN; Methodology, HN, AWD; Validation, HN; Data Curation, PCI, HN, AWD; Writing – original draft preparation, PCI, AWD; reviewing and editing, PCI, HN, AWD; Supervision, HN; Project Administration, AWD

Data availability

The data supporting this case report are available from corresponding author upon reasonable requests.

References

1. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012 [cited 2025 Sept 12]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK547852/>
2. Chalasani NP, Maddur H, Russo MW, Wong RJ, Reddy KR, Practice Parameters Committee of the American College of Gastroenterology. ACG Clinical Guideline: Diagnosis and Management of Idiosyncratic Drug-Induced Liver Injury. *Am J Gastroenterol*. 2021 May 1;116(5):878–98. DOI:10.14309/ajg.0000000000001259.
3. Salsabila A, Kholili U, Novida H. Drug-Induced Liver Injury (DILI) related to Propylthiouracil (PTU) in hyperthyroidism with liver cirrhosis. *Bali Med J*. 2023 May 11;12(2):1594–600. DOI: 10.15562/bmj.v12i2.4206.
4. Khan AA, Ata F, Aziz A, Elamin H, Shahzad A, Yousaf Z, et al. Clinical Characteristics and Outcomes of Patients With Antithyroid Drug–Related Liver Injury. *J Endocr Soc*. 2023 Dec 1;8(1):bvad133. DOI: 10.1210/endo/bvad133.

5. Chalasani N, Björnsson E. Risk factors for idiosyncratic drug-induced liver injury. *Gastroenterology*. 2010 June;138(7):2246–59. DOI: 10.1053/j.gastro.2010.04.001.
6. Sun X, Zhang X, Liu M. Increased attention to women with drug-induced liver injury: Risk factors and early intervention. *iLIVER*. 2024 Dec;3(4):100125. DOI: 10.1016/j.iliver.2024.100125.
7. Eliyanti A. The Safety of Radioiodine Therapy for Women of Reproductive Age. *J Midwifery*. 2019 Sept 18;4(1):1. DOI: 10.25077/jom.4.1.1-6.2019.
8. Kim JH, Baek JH, Lim HK, Ahn HS, Baek SM, Choi YJ, et al. 2017 Thyroid Radiofrequency Ablation Guideline: Korean Society of Thyroid Radiology. *Korean J Radiol*. 2018;19(4):632. DOI: 10.3348/kjr.2018/19/4/632.
9. Cai G, Luo B, Wang M, Su J, Lin L, Li G, et al. Efficacy and safety of ultrasound-guided thermal ablation of graves' disease: a retrospective cohort study. *Thyroid Res*. 2024 June 3;17(1):10. DOI: 10.1186/s13044-024-00198-4.
10. Mandaya M. Metode Pengobatan Kanker Tiroid, Kanker yang Dapat Disembuhkan dengan Nuklir. Mandaya [Internet]. 2024 Apr 30; Available from: <https://mandayahospitalgroup.com/id/metode-pengobatan-kanker-tiroid/#:~:text=Layanan%20ablasi%20nuklir%20sendiri%20belum,pasien%20bisa%20berhenti%20minum%20obat>.
11. John S, Pratt DS. Jaundice. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, et al., editors. *Harrison's Principles of Internal Medicine*. 22nd ed. New York: Mc Graw Hill; 2025. p. 320–6.
12. David S, Hamilton JP. Drug-induced Liver Injury. *US Gastroenterol Hepatol Rev*. 2010 Jan 1;6:73–80.
13. Chen M, Suzuki A, Borlak J, Andrade RJ, Lucena MI. Drug-induced liver injury: Interactions between drug properties and host factors. *J Hepatol*. 2015 Aug;63(2):503–14. DOI: 10.1016/j.jhep.2015.04.016.
14. Niveditha K, Menon AS, Kumar H, Eapen M, Gopalakrishna R. A case of acute liver injury induced by methimazole. *Thyroid Res Pract*. 2021 Jan;18(1):34–6. DOI: 10.4103/trp.trp_73_20.
15. Pekmezian A, Cobb W, Portoghese J. Antithyroid Drug-Induced Hepatotoxicity From Chronic Methimazole Consumption Requiring Total Thyroidectomy. *J Endocr Surg*. 2024;24(3):85. DOI: 10.16956/jes.2024.24.3.85.
16. European Association for the Study of the Liver. EASL Clinical Practice Guidelines: Drug-induced liver injury. *J Hepatol*. 2019 June;70(6):1222–61. DOI: 10.1016/j.jhep.2019.02.014.
17. Iqbal A, Rehman A. Thyroid Uptake and Scan. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Sept 14]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK555978/>
18. Nwatssock JF, Taieb D, Tessonier L, Mancini J, Dong-A-Zok F, Mundler O. Radioiodine thyroid ablation in graves' hyperthyroidism: merits and pitfalls. *World J Nucl Med*. 2012 Jan;11(1):7–11. DOI: 10.4103/1450-1147.98731.