PERINATAL JOURNAL

Original Article

Perinatal Journal 2025; 33(2):257-264

https://doi.org/10.57239/prn.25.03320029

Comprehensive management of refractory Graves 'disease with multiple radioiodine ablations: A case report

Vania Petrina[1], Hermina Novida[2]*

[1]Department Internal Medicine Universitas Airlangga
[2]Department Internal Medicine Dr. Soetomo Teaching Hospital

Abstract

Graves' Disease (GD) is a prominent autoimmune thyroid disorder predominantly characterized by the overproduction of thyroid hormones, known as hyperthyroidism, triggered by autoantibodies that target the thyroidal TSH receptor, leading to increased synthesis and secretion of thyroid hormones. The management of Graves' disease presents a notable challenge, primarily due to the contentious nature of selecting an appropriate primary therapy. The UK National Institute for Health and Care Excellence (NICE) has shifted its guidelines to recommend radioiodine as the first-line treatment in the UK, citing its cost-effectiveness and efficacy relative to thioamides. This case report presents the management of Graves' disease with radioiodine ablation. The case illustration was a 52-year-old female patient who presented primarily with palpitations. The patient had been diagnosed with Graves' disease and had undergone three radioiodine ablations on July 11, 2022, July 12, 2023, and November 7, 2023, each using a 10 mCi dose of NaI-131. The result shows that multiple radioiodine ablations illustrate the necessity of a tailored approach in achieving effective disease control. The progressive reduction in thyroid gland activity through repeated radioiodine treatments leads to stable hypothyroidism managed with levothyroxine. This case demonstrates that radioiodine therapy remains a pivotal option for patients with severe or resistant Graves' disease, emphasizing the need for continuous monitoring and adjustment of treatment strategies to optimize patient outcomes and improve quality of life.

Keywords: Hyperthyroidism, TSH, Thyroid gland, NICE

Introduction

Diffuse toxic goiter (DTG), also known as Graves' disease or thyrotoxicosis, is characterized by a diffuse enlargement of the thyroid gland and represents a prevalent autoimmune thyroid disorder [1]. This condition is triggered by autoantibodies that target the thyroidal TSH receptor, leading to increased synthesis and secretion of thyroid hormones. Graves' disease is the predominant cause of hyperthyroidism in iodine-sufficient populations, exhibiting a prevalence of 2% among women and 0.5% among men [2,19]. Additionally, the incidence of Graves' disease varies significantly, ranging from 30 to 200 cases per 100,000 individuals annually [3], with other reports indicating an incidence rate of 20-40 cases per 100,000 people per year [4,5].

The management of Graves' disease presents a notable challenge, primarily due to the contentious nature of selecting an appropriate primary therapy. Three established treatments—antithyroid drugs, radioiodine therapy, and thyroidectomy—have been in use for decades, each recognized for their respective efficacies and limitations [6]. Ablative options, such as radioiodine or thyroidectomy, offer higher cure rates and address the issue of non-compliance associated with thionamides; however, they necessitate lifelong levothyroxine replacement therapy [7,8]. While radioiodine is the preferred initial treatment in the United States, it is often designated as a secondary option in Europe and most of Asia, reserved for patients who do not respond adequately to initial thionamide therapy [9]. Recently, the UK National Institute for Health and Care Excellence (NICE) has shifted its guidelines to recommend radioiodine as the first-line treatment in the UK, citing its cost-effectiveness and efficacy relative to thionamides [10,18]. In this case report, we present the management of Graves' disease with radioiodine ablation conducted in our center.

Experimental

Case illustration

A 52-year-old female patient presented primarily with palpitations.

Assessment and management

The patient had been diagnosed with thyrotoxicosis

Correspondence: Hermina Novida Cetinel, Department Internal Medicine Dr. Soetomo Teaching Hospital, **e-mail:** : hermina-n@fk.unair.ac.id, **Received:** July 20, 2025 **Accepted:** September 19, 2025

due to diffuse toxic goiter (Graves' disease) and had undergone three radioiodine ablations on July 11, 2022, July 12, 2023, and November 7, 2023, each using a 10 mCi dose of NaI-131.

Result and Discussion

Anamnesis

A 52-year-old female patient, unmarried, previously diagnosed with Graves' disease, was referred from a private hospital, presenting primarily with palpitations. She reported no instances of shortness of breath or leg swelling. The patient described an intolerance to hot environments, excessive sweating, and general fatigue. She also noted a persistent neck lump that had been present for 19 years. The neck lump, which moved during swallowing, was painless but caused mild difficulty swallowing.

Additionally, the patient reported unintended weight loss despite increased appetite, frequent tremors, and hair loss. Her menstrual cycles were regular and unproblematic. She experienced soft bowel movements two to three times daily and had no urinary complaints. Moreover, the patient had no history of chronic conditions such as diabetes mellitus, hypertension, or renal or hepatic disorders, and there were no similar health complaints in her family history.

The patient had been under the care of an internal medicine specialist in Semarang for the same durations, initially treated with thyrozol 10 mg t.i.d. p.o., which showed minimal effectiveness. The patient still frequently experienced palpitations, tremors, weight loss, and heat intolerance. The thyroid function tests also did not show improvement. The patient had been treated with thyrozol 20 mg t.i.d, p.o., and underwent various dose adjustments. In May 2023, the thyrozol dosage was reduced from 10 mg t.i.d. to an alternating regimen of 10 mg q.d. on odd dates and 10 mg b.i.d. on even dates. However, her symptoms of palpitations reemerged whenever the medication dosage was decreased.

Physical examination

Her overall health appeared stable, with a body weight of 53 kg and a height of 155 cm, resulting in a body mass index of 22.1 kg/m2, classified within the normal weight range. Her vital signs were within normal limits, including blood pressure at 120/70 mmHg, heart rate at 80 beats per minute, respiratory rate at 20 breaths per minute, body temperature at 36.8°C, and oxygen saturation at 98% on room air. Physical examination revealed a bilaterally diffused enlargement of the thyroid gland approximately the size of a tennis ball, which moved upon swallowing, as can be seen in Figure 1. There was no tenderness or bruit observed. No other abnormalities were detected during the physical examination.

Figure 1. Physical appearance of the patient. The bilateral enlargement was found in the neck of the patient

Ancillary examinations

Ultrasonography on September 3, 2021 at Biotest Clinic Surabaya, as can be seen in Figure 2 revealed bilateral thyroid enlargement with right lobe size 3.84 x 3.29 x 8.42 cm (vol 55cc), echo parenchym decreased heterogeneously, vascularisation increased, and left lobe size 3.95 x 3.16 x 9.06 cm (vol 58 cc), echo parenchym decreased heterogeneous, respectively, suggesting bilateral diffuse toxic goiter.

The ultrasound also detected a left thyroid nodule measuring 0.65 x 0.63 cm. There was no right or left colli lymphadenopathy on ultrasonography. A thyroid scintigraphy performed on July 12, 2022, as can be seen in Figure 3, showed uniform radioactive uptake in both thyroid lobes without any areas of reduced activity, suggesting diffuse toxic goiter.

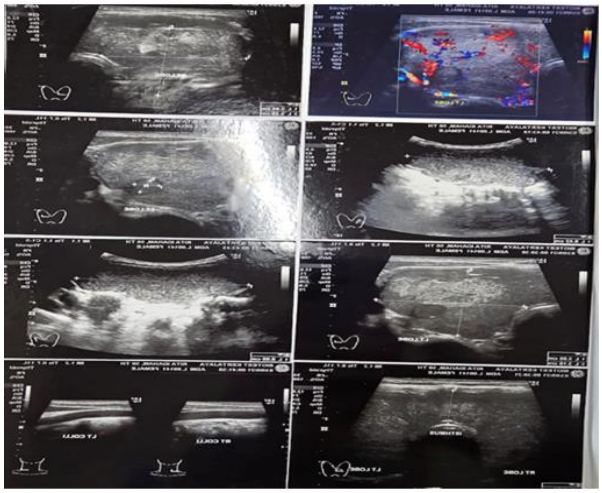

Figure 2. Ultrasonography on September 3, 2021, at biotest clinic surabaya

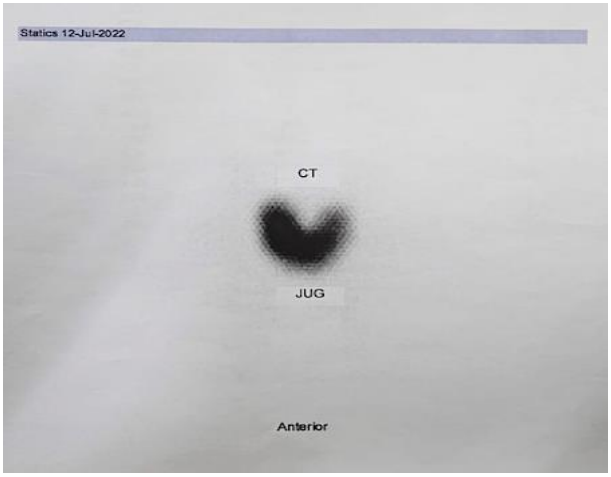

Figure 3. Thyroid scintigraphy on July 12, 2022, at Dr. Soetomo HospitalThe thyroid function test was held in two different institutions. It is shown in Table 1 at Biotest Clinic Surabaya and Table 2 at Dr. Soetomo Hospital

Table 1. Thyroid function test results at Biotest Clinic Surabaya

	Normal Range	27 Jul 21	13 Dec 22	31 May 23	10 Jul 23
T3 (Total) ng/mL	0.80-1.95	>6.51	-	-	4.01
Free T4 ng/dL	0.93-1.70	24.8	1.71	3.02	>7.77
TSH µIU/mL	0.27-4.20	<0.005	<0.005	<0.005	<0,005

Table 2. Thyroid function test results at Dr. Soetomo Hospital

	Normal Range	5 Jul 22	5 Jul 23	5 Oct 23	6 Nov 23	27 Dec 23
T3 (Total) ng/mL	0.35-1.93	1.49	20.8	11.44	3.46	0.3
Free T4 ng/dL	0.70-1.48	0.89	52.5	7.37	0,77	0.42
TSH µIU/mL	0.55-4.78	0.007	<0.0083	0.007	0,005	2.211

A complete blood count showed no significant findings except for a slight increase in the percentage of monocytes (14.6% on October 5, 2023, and 10.3% on December 27, 2023). Serum electrolyte and d-dimer tests were normal. A thyroid receptor antibody (TRAb) test conducted on December 13, 2022, showed increased antibody levels of 320.8 IU/L (normal ≤ 1.75 IU/L). Thyroid function tests indicated elevated free T4 and T3 levels from July 27, 2021, to November 6, 2023, with relatively lower levels noted on July 5, 2022, and December 27, 2023. TSH levels remained extremely low until December 27, 2023, when the TSH level finally rose to 2.211 µIU/mL, falling within the normal range. This graph of thyroid function test over time, with normal ranges, can be seen in Figure 4

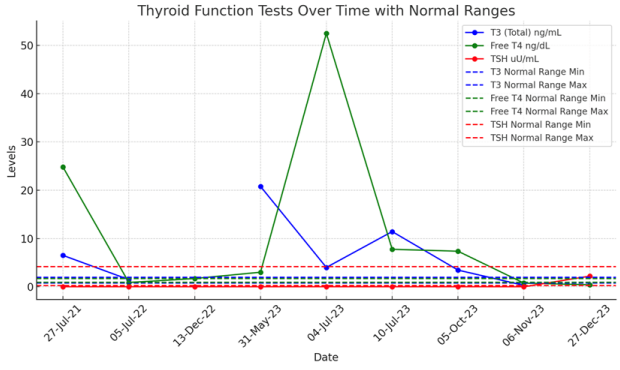

Figure 4. Thyroid function test results over time

Significant fluctuations in T3 (Total) and Free T4 peaked on July 4, 2023, followed by a gradual

decrease, reaching slightly below the normal range by December 27, 2023. TSH levels remained very low throughout the period. However, by December 27, 2023, TSH increased to within the normal range, suggesting that thyroid function may be stabilizing due to treatment.

Graves' Disease (GD) is a prominent autoimmune thyroid disorder predominantly characterized by the overproduction of thyroid hormones, known as hyperthyroidism. Graves' disease is a syndrome that may consist of hyperthyroidism, goiter, thyroid eye disease (TED; Graves' orbitopathy), and occasionally a dermopathy. It is the most common cause of hyperthyroidism in iodine-sufficient regions, with a notable incidence of 20-40 cases per 100,000 annually [4]. The disease exhibits a significant female predilection, being 5-10 times more common in women than in men, particularly between the ages of 30 and 60 [11]. The pathophysiology involves the generation of autoantibodies against the thyroid-stimulating hormone receptor (TSH-R), which stimulates the thyroid gland to produce excessive thyroid hormones [12]. Genetic predispositions influence this autoimmune reaction, account for approximately 75% of the disease risk, and environmental factors, contribute the remaining 25% [13]. Common clinical presentations of GD include palpitations, increased sweating, heat intolerance, and goiter. Other symptoms that GD patients may experience were insomnia, weight loss, and anxiety [4]. In this patient's case, she complained of palpitations, increased sweating, heat intolerance, and goiter, all of which are common manifestations of GD.

The management of long-standing Graves' disease exemplifies the complex interplay of therapeutic efficacy and patient-specific responses, especially reflected in treating a case of chronic autoimmune thyroid disorder. The inability to achieve remission with Thionamide Antithyroid Drugs (ATDs) is repeatedly noted in current literature where a significant proportion of patients experience recurrence of hyperthyroidism post-treatment. It is known that a critical aspect of Graves' disease management is the potential for ATDs to fail in providing long-term euthyroidism without recurrence, particularly in patients with severe or resistant forms of the disease [14]. In the presented case, the patient was initially managed with thyrozol. Despite 19 years of treatment, she continued to experience persistent symptoms. Additionally, she suffered from recurrent palpitations whenever the dosage of the medication was reduced.

It should stem directly from the data presented and no extra material should be introduced. It should be consistent with the introduction in fulfilling any promise made therein to the reader. The conclusion should also include negative results and recommendations based on the results. In such cases where the study has led to clearcut finding, it is preferable to give the conclusions in the form of a series of numbered points.

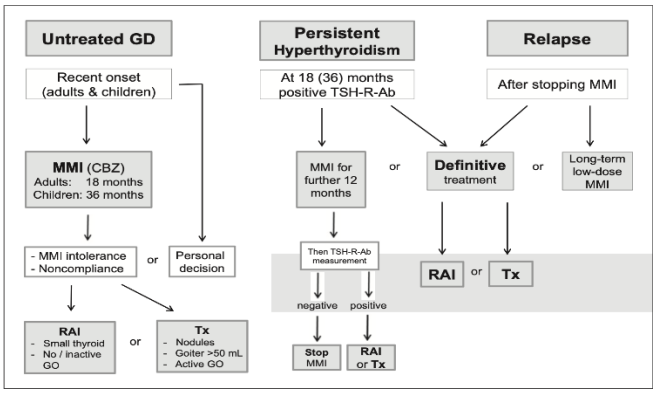

Figure 4. Algorithm for the management of a patient with Graves' hyperthyroidism. GD, Graves' Disease; MMI, methimazole; CBZ, carbimazole; GO, Graves' Orbitopathy; RAI, Radioactive Iodine; Tx, Total Thyroidectomy (Kahaly et al., 2018)

Transitioning to radioiodine therapy was a pivotal decision influenced by the patient's history of non-compliance, intolerance, and the suboptimal control of hyperthyroid symptoms with ATDs. For patients with Graves' disease who relapse into hyperthyroidism after completing an initial course of Antithyroid Drug (ATD) Therapy, definitive treatment with Radioactive Iodine (RAI) or thyroidectomy is typically recommended. However, for those who do not achieve remission and prefer a non-invasive approach, the option of long-term low-dose methimazole (MMI) therapy may be considered as an alternative. Radioiodine is recognized for its efficacy in permanently reducing thyroid function, thus addressing the autoimmune overactivity in Graves' disease. However, this treatment strategy

also introduces the necessity for lifelong thyroid hormone replacement due to resultant hypothyroidism—a significant change in the patient's management plan that aligns with documented outcomes and expert recommendations. This shift from a conservative to a more definitive treatment approach underscores the importance of personalized medicine in endocrinology, where treatment modalities are adapted based on individual patient responses and the balance between disease control and quality of life. The choice of radioiodine, influenced by its superior cost-effectiveness and lower relapse rates compared to ATDs, as noted in current guidelines, reflects a strategic approach to managing challenging cases of Graves' disease, prioritizing long-term stability over the reversible control offered by ATDs [6,14,15].

In the management of Graves' disease, radioiodine ablation plays a pivotal role, especially when patients exhibit resistance or relapse following initial antithyroid drug therapy (ATD). Multiple radioiodine interventions may be necessary to achieve a more definitive resolution of hyperthyroid symptoms by progressively reducing thyroid gland activity. This strategy aligns with findings that suggest a dose-response effect in achieving thyroid ablation and clinical remission [7]. In this case, the patient experienced persistent hyperthyroidism despite receiving ATD, supported by positive TSH receptor antibodies, indicating a complex case in which standard therapies required augmentation. For this reason, there was consideration for performing radioiodine ablation on the patient.

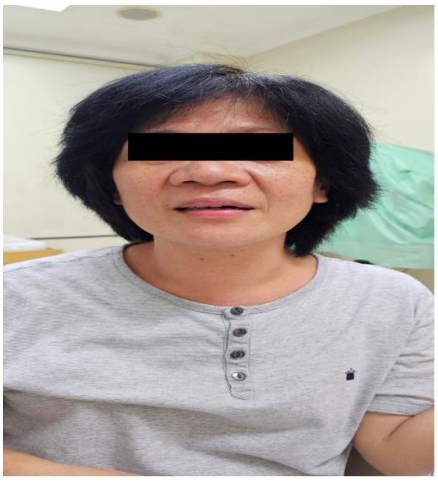

Figure 5. Physical appearance of the patient after several radioiodine ablations

The process and outcomes of radioiodine therapy in such recurrent cases underscore the balance clinicians must maintain between effective thyroid ablation and the avoidance of overtreatment. Each administration of radioiodine intends to incrementally ablate thyroid tissue sufficient to control the disease while minimizing the risk of inducing other complications, such as worsening of Graves' orbitopathy [16]. The decision for repeated radioiodine treatments, as seen with this patient, often follows evidence of persistent thyroid activity or relapse, which can be common in patients with larger thyroid volumes.

Monitoring and long-term management of Graves' disease post-radioiodine therapy involve rigorous follow-up with thyroid function tests and assessments of thyroid-stimulating hormone receptor antibody levels. These metrics provide essential insights into the thyroid's functional status and the autoimmune activity underlying the disease. This adaptive management approach ensures that therapy is responsive to the disease's progression and the patient's changing physiological needs, thereby aiming to stabilize thyroid function and improve quality of life over the long term [17]. In this patient’s case, continuous monitoring was essential, as adjustments to the therapeutic approach were guided by the test results. The tests include thyroid function tests and TSH receptor antibody assessments. The goal in managing such cases is to tailor the intervention to achieve euthyroidism or, more commonly after ablation, to manage hypothyroidism through hormone replacement therapy.

The management of challenging cases of Graves' disease, as exemplified by the discussed patient, elucidates several crucial lessons and underscores the importance of personalized, patient-centered care. The patient’s journey through initial Treatment With Antithyroid Drugs (ATDs) and subsequent multiple radioiodine therapies highlight the necessity for adaptive treatment strategies tailored to individual patient responses and disease dynamics. This case demonstrates that while ATDs may be effective initially, they can fail to maintain long-term

remission, particularly in severe or resistant forms of Graves' disease, necessitating definitive treatments such as radioiodine. The transition to radioiodine, driven by its efficacy in permanently reducing thyroid function and lowering relapse rates, reflects a strategic pivot toward more definitive management aimed at achieving stable disease control. Furthermore, this case reinforces the critical role of continuous monitoring, including regular assessments of thyroid function and autoantibody levels, to guide therapeutic adjustments and manage induced hypothyroidism effectively. From this, it is evident that a flexible approach, responsive to evolving clinical presentations and informed by ongoing patient feedback, is essential in managing complex autoimmune thyroid disorders.

Conclusion

In conclusion, this case report underscores the complexities involved in managing refractory Graves' disease, particularly in patients unresponsive to conventional antithyroid drugs. The patient's journey through multiple radioiodine ablations illustrates the necessity of a tailored approach in achieving effective disease control. The progressive reduction in thyroid gland activity through repeated radioiodine treatments, leading to stable hypothyroidism managed with levothyroxine, highlights the importance of personalized, patient-centered care. This case demonstrates that radioiodine therapy remains a pivotal option for patients with severe or resistant Graves' disease, emphasizing the need for continuous monitoring and adjustment of treatment strategies to optimize patient outcomes and improve quality of life. The findings support the strategic use of radioiodine as a cost-effective and efficacious alternative when conventional therapies fail, reinforcing its role in the evolving landscape of Graves' disease management.

References

[1]. A. D. Shukurullaevich, E. R. Kosim, S. D. Salim, E. N. Ziyadulla, *Vestn. Nauki Obrazov.*, 2021, *60*, 80–87..

[2]. S. Y. Lee, E. N. Pearce, *JAMA*, 2023, *330* (15), 1472–1483. https://doi.org/10.1001/jama.2023.19052.

[3]. E. A. Ospanbekov, T. T. Aitasov, A. Kairatuly, D. V. Ismailov, G. Partizan, D. S. Kerimbekov, *IOP Conf. Ser. Mater. Sci. Eng.*, 2020, *862* (2). https://doi.org/10.1088/1757-899X/862/2/022063.

[4]. T. F. Davies, S. Andersen, R. Latif, Y. Nagayama, G. Barbesino, M. Brito, A. K. Eckstein, A. Stagnaro-Green, G. J. Kahaly, *Nat. Rev. Dis. Prim.*, 2020, *6* (1). https://doi.org/10.1038/s41572-020-0184-y.

[5]. H. F. Nyström, S. Jansson, G. Berg, *Clin. Endocrinol. (Oxf).*, 2013, *78* (5), 768–776. https://doi.org/10.1111/cen.12060.

[6]. G. J. Kahaly, L. Bartalena, L. Hegedüs, L. Leenhardt, K. Poppe, S. H. Pearce, *Eur. Thyroid J.*, 2018, *7* (4), 167–186. https://doi.org/10.1159/000490384.

[7]. O. E. Okosieme, P. N. Taylor, C. M. Dayan, *Thyroid Res.*, 2020, *13* (1), 1–7. https://doi.org/10.1186/s13044-020-00077-8.

[8]. D. S. Ross, H. B. Burch, D. S. Cooper, M. C. Greenlee, P. Laurberg, A. L. Maia, S. A. Rivkees, M. Samuels, J. A. Sosa, M. N. Stan, M. A. Walter, *Thyroid*, 2016, *26* (10), 1343–1421. https://doi.org/10.1089/thy.2016.0229.

[9]. P. N. Taylor, D. Albrecht, A. Scholz, G. Gutierrez-Buey, J. H. Lazarus, C. M. Dayan, O. E. Okosieme, *Nat. Rev. Endocrinol.*, 2018, *14* (5), 301–316. https://doi.org/10.1038/nrendo.2018.18.

[10]. National Institute for Health and Care Excellence. Thyroid Disease: Assessment and Management. NICE 2019, November.

[11]. A. Antonelli, S. M. Ferrari, F. Ragusa, G. Elia, S. R. Paparo, I. Ruffilli, A. Patrizio, C. Giusti, D. Gonnella, A. Cristaudo, R. Foddis, Y. Shoenfeld, P. Fallahi, *Best Pract. Res. Clin. Endocrinol. Metab.*, 2020, *34* (1). https://doi.org/10.1016/j.beem.2020.101387.

[12]. A. Kotwal, M. Stan, *Ophthal. Plast. Reconstr. Surg.*, 2018, *34* (4), S20–S27. https://doi.org/10.1097/IOP.0000000000001052..

[13]. T. H. Brix, L. Hegedüs, *Clin. Endocrinol. (Oxf).*, 2012, *76* (4), 457–464. https://doi.org/10.1111/j.1365-2265.2011.04318.x.

[14]. L. Bartalena, L. Chiovato, C. Marcocci, P. Vitti, E.

Piantanida, M. L. Tanda, *J. Endocrinol. Invest.*, 2020, *43* (8), 1149–1151. https://doi.org/10.1007/s40618-020-01293-7.

[15]. G. J. Kahaly, *J. Clin. Endocrinol. Metab.*, 2020, *105* (12), 3704–3720. https://doi.org/10.1210/clinem/dgaa646.

[16]. J. Kim, J. Park, Association between Blood Vitamin D Levels and Regular Physical Activity in Korean Adolescents, 2022, 1–10 Adolescents. 2022, 1–10.

[17]. D. S. Ross, *Radioiodine Treatment in Patients with Graves' Disease*, In *Graves' Disease: A Comprehensive Guide for Clinicians*; Springer US: New York, 2015; pp 83–98.

[18] Abbas, M., Khan, T. I., & Jam, F. A. (2025). Avoid Excessive Usage: Examining the Motivations and Outcomes of Generative Artificial Intelligence Usage among Students. Journal of Academic Ethics, 1-20.

[19]Moghavvemi, S., & Jam, F. A. (2025). Unraveling the influential factors driving persistent adoption of ChatGPT in learning environments. Education and Information Technologies, 1-28.

Appendix

Graphical Abstract

Comprehensive Management of Refractory Graves' Disease with Multiple Radioiodine Ablations: A Case Report

Vania Petrina, Hermina Novida