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CASE REPORT

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Graves' disease diagnosed nearly six months after microwave ablation of benign thyroid nodules: a case report

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Abstract

Background Microwave ablation is a new, minimally invasive technique for the treatment of thyroid nodules. Hyperthyroidism due to destructive thyroiditis is a known risk of microwave ablation, though it occurs in only a minority of cases. We report a rare case of a patient diagnosed with Graves' disease nearly six months after undergoing microwave ablation of a thyroid nodule.

Case presentation On July 31, 2022, a 43-year-old male patient presented to our hospital with symptoms of pyrexia, excessive sweating, and palpitations lasting for 15 days. History inquiry revealed that the patient had undergone microwave ablation of right-sided thyroid nodule nearly five months ago at another hospital. The patient's thyroid ultrasound suggested bilateral diffuse thyroid lesions, with a moderately echogenic mass observed on the right side of the thyroid gland, potentially indicative of thyroid nodule ablation. The patient had elevated serum thyroid hormone levels, decreased thyroid-stimulating hormone levels and positive associated thyroid antibodies. To control the symptoms of hyperthyroidism, the patient opted for oral antithyroid medication, and thyroid hormonal levels returned to normal after 3 months of treatment. The patient is now under regular follow-up.

Conclusions In this case, we presented the onset of Graves' disease following microwave ablation in a patient with subclinical thyroid autoimmunity. While the causal relationship between microwave ablation and Graves' disease remains unproven, this case suggests that preexisting autoimmune thyroid conditions may increase susceptibility to postoperative thyroid dysfunction. Procedural factors, such as thermal injury to surrounding tissues and potential involvement of the autonomic nervous system, are also potential contributors to the development of Graves' disease following microwave ablation.

Keywords Case report, Thyroid nodules, Hyperthyroidism, Microwave ablation, Graves' disease, Complications

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Background

Thermal ablation is a minimally invasive interventional oncology technology that includes radiofrequency ablation (RFA), microwave ablation (MWA), and laser ablation (LA) [1]. Thermal ablation was first clinically used in the early 21st century to treat benign thyroid nodules (BTN). Ultrasound-guided MWA is advantageous due to its minimal trauma, rapid recovery, and low complication rates. It has been widely used to treat BTN, low-risk papillary thyroid microcarcinoma (PTMC) and metastatic lymph nodes in the neck. While MWA has been used to treat primary hyperthyroidism, it can lead to intraoperative complications such as nerve damage, vascular injury as well as skin and peripheral tissue burns. Postoperative complications include nodule rupture, liquefactive necrosis and abnormal thyroid function [2]. These complications have limited its use in smaller and special site nodules. Hyperthyroidism due to destructive thyroiditis is a known risk of MWA, which occurs in only a minority of cases [2–5], generally within three months after the procedure, and is self-limiting. The condition is probably due to thermal injury during the procedure and the subsequent release of thyroid hormone.

Herein, we report a case of a middle-aged male patient who was diagnosed with Graves' disease(GD) nearly six months after thyroid MWA. His thyroid hormone metabolism was restored to normal levels after three months of antithyroid medication. To the best of our knowledge, this is the first case report of hyperthyroidism symptoms secondary to GD after MWA of BTN.

Case presentation

The patient was found to have multiple thyroid nodules during a physical examination at a primary care hospital in September 2021, however, we did not abtain the thyroid ultrasound results at that time. Later, the patient visited our outpatient clinic on September 29, 2021, and was advised to undergo blood test and a thyroid ultrasound. Given the patient's difficulty in accessing medical care and their urgency to understand the underlying cause, the outpatient doctor also ordered thyroid antibody tests during the same visit. Blood test data is detailed in (Table 1). The results showed that the patient's free triiodothyronine (FT3) was 0.74 uIU/mL [5.33 pmol/L] (0.43–0.95 uIU/mL; 3.10–6.80 pmol/L) and anti-thyroid peroxidase antibody (TPOAb) was 166.2 IU/L (0–34 IU/L), indicating a potential presence of autoimmune thyroiditis and mild hyperthyroidism. The ultrasound at that time (Fig. 1) showed diffuse bilateral thyroid lesions with enlargement. The patient's right and left lobes showed multiple nodules, with the largest nodule on the right-side measuring approximately 3.36×1.72 cm. The nodule was heterogeneous, with a regular shape, well-rounded margin, and was horizontal growth. Color Doppler flow imaging (CDFI) revealed a small amount of blood flow within and around the nodule. Given the potential for an adenomatous nodular goiter on the patient's right side, a fine needle aspiration biopsy of the thyroid was recommended, which the patient declined. Instead, the patient was instructed to avoid iodine and to undergo thyroid ultrasound evaluations every six months, along with thyroid function assessments every six to 12 months.

On July 31, 2022, the patient consulted the Department of Endocrinology at our hospital again, reporting symptoms including heat intolerance, excessive sweating, and palpitations for more than 15 days. The patient informed us that he had undergone MWA for thyroid nodules at another hospital in February 2022. However, it was unclear whether the patient had undergone preoperative puncture cytology biopsy, and the specific surgical procedures were unavailable. Physical examination showed that the patient's thyroid gland was enlarged to degree I (based on the World Health Organization (WHO) goiter classification criteria) [6], with no thyroid gland tenderness and no proptosis. The patient had a heart rate of 100 beats/min, clear respiratory sounds, a rhythmic heartbeat, and no tremor in the upper extremities. Thyroid ultrasound (Fig. 2) revealed bilateral diffuse thyroid lesions, with a moderately echogenic mass observed on the right side of the thyroid gland, potentially indicative of thyroid nodule ablation. The mass was oval in shape,

Table 1 FT3, FT4, TSH, TRAb, and TPOAB levels of the patient during the follow-up period

Date	FT3/(pmol/L)	FT4/(pmol/L)	TSH/(μIU/mL)	TRAb/(IU/L)	TPOAB/(IU/L)
2021.09.29 (pre-MWA)	5.33	18.34	1.2	0.80	166.2
2022.07.31 (6 m after MWA)	25.45	83.37	0	2.38	579.3
2022.09.11 (12 days post-dose)	12.43	38.46	0	——	——
2022.09.30	6.65	21.28	0	3.88	——
2022.11.26	5.15	16.22	1.87	4.60	437.1
2023.04.22	4.51	15.19	3.14	1.80	——
2023.08.15	——	——	——	0.80	——
2023.10.22	4.89	17.04	2.21	1.34	——

Abbreviations: FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyroid-stimulating hormone; TRAb, thyrotrophin receptor antibody; TPOAb, thyroid peroxidase antibodies

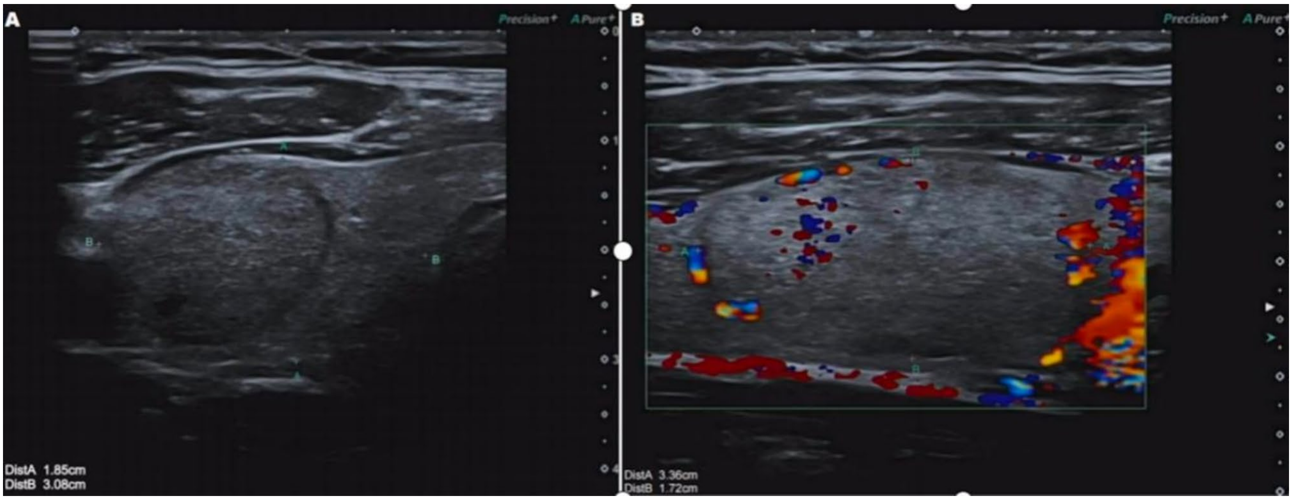

Fig. 1 Thyroid ultrasound image 4 months before microwave ablation of the right nodule. Right thyroid lobe (**A**) and right thyroid nodule in cross section (**B**)

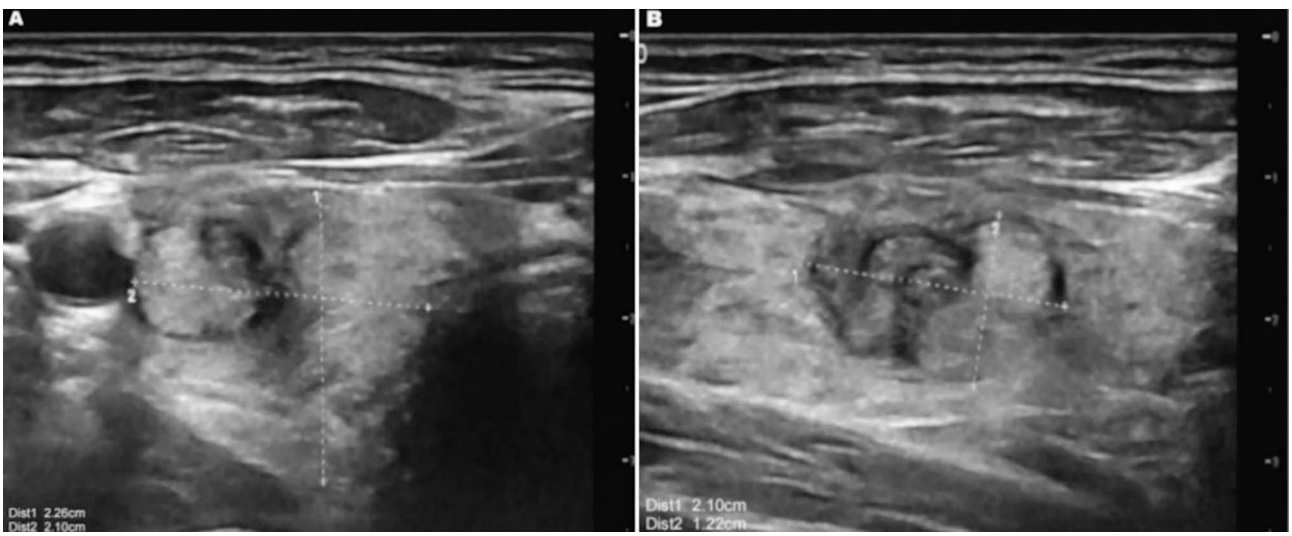

Fig. 2 Ultrasonogram of the thyroid gland 6 months after microwave ablation of the right nodule. Right thyroid lobe (**A**) and right thyroid nodule in cross section (**B**)

measuring approximately 2.10×1.22 cm, with clear borders and no significant calcification or hyperechogenicity. The CDFI revealed blood flow signals present within and surrounding the mass, while no evident abnormal lymph nodes were observed in the bilateral neck regions. Thyroid and thyroid-stimulating hormonal metabolism and antibody measurements showed that FT3 was 3.54 uIU/mL [25.45 pmol/L] (0.43–0.95 uIU/mL; 3.10–6.80 pmol/L), free thyroxine (FT4) was 11.59 uIU/mL [83.37 pmol/L] (1.67–3.06 uIU /mL; 12–22 pmol/L), thyrotropin-stimulating hormone (TSH) was <0.005 uIU/ml [<0.036 pmol/L] (0.3–5.5 uIU/ml; 2.15–31.46 pmol/L), thyrotropin receptor antibody (TRAb) was 2.38 IU/L (0–1.75 IU/L), anti-thyroglobulin antibody (TgAb) was 553.40 IU/L (0–135 IU/L) and TPOAB was 579.3 IU/L (0–34 IU/L). The patient's liver function, biochemistry and lipids were not significantly abnormal. Based on the the clinical manifestations and auxiliary examinations, the patient was diagnosed with GD. The outpatient doctor recommended that the patient take antithyroid medication, which he refused. Therefore, the doctor advised him to have a follow-up visit in one week and emphasized that he should seek immediately emergency care if symptoms worsened.

On September 11, 2022, the patient was rechecked at our hospital and reported that he had taken Methimazole 10 mg bid, Risperdal tablets 20 mg tid, Propranolol 10 mg tid and JiaKangLingJiaoNang (a traditional Chinese medicine primarily composed of Eclipta prostrata, Dioscorea opposita, Salvia miltiorrhiza, Fossilized bone, Prunella vulgaris, and Oyster shell. This medication is primarily used for the treatment of hyperthyroidism.) 2 g tid orally on his own for 12 days, and the symptoms of heat intolerance, excessive sweating, and palpitation had improved. The patient underwent blood tests again. The routine blood and liver function tests showed no significant abnormalities. Thyroid and thyroid-stimulating hormonal metabolism were as follows: FT3 was 1.73 uIU/mL [12.43 pmol/L] (0.43–0.95 uIU/mL; 3.10–6.80 pmol/L), FT4 was 5.35 uIU/mL [38.46 pmol/L] (1.67–3.06 uIU/mL; 12–22 pmol/L) and TSH was < 0.005 uIU/ml [< 0.036 pmol/L] (0.3–5.5 uIU/ml; 2.15–31.46 pmol/L). Following consultation with the outpatient doctor regarding the relevant treatments for hyperthyroidism (including antithyroid medication, radioactive ^{131}I and surgery), the patient chose to continue treatment with oral antithyroid medication (Methimazole 10 mg bid + JiaKangLingJiaoNang 2 g tid) and regular follow-ups. After three months of hyperthyroid medication, his thyroid and thyroid-stimulating hormonal metabolism had almost normalized, while thyroid-related antibodies (TRAb, TPOAB) remained alavated. We documented the levels of thyroid hormones, TSH, TRAb and TPOAb from the patient's first visit to our hospital on 29 September 2021 to the last follow-up on 22 October 2023 (Table 1). The patient continues to opt for drug treatment (Methimazole 5 mg bid + JiaKangLingJiaoNang 2 g tid) and active monitoring. We will continue to follow up with the patient.

Discussion

MWA is a minimally invasive treatment for BTN and PTMC, with established efficacy and safety [7–9]. Compared with thyroid surgery, MWA preserves thyroid gland physiology, is better tolerated, and results in lower postoperative inflammation [10]. Adverse effects, including hematoma, transient or permanent voice changes, and intolerable pain, have been reported, with incidence rates of 3.8%, 4.6%, and 2.2%, respectively [7]. Although abnormal thyroid function is not a common adverse effect, this case highlights the potential for GD following MWA.

GD is an autoimmune thyroid disorder (AITD) with a complex etiology that involves genetic, environmental, and immunological factors. Genetic studies implicate Tlymphocyte-associated antigen 4(CTLA-4), TSH-R, Tg, CD40, protein tyrosine phosphatase-22 (PTPN 22), human leukocyte antigen (HLA), and CD25 in GD development, with approximately 70% of the involved genes linked to T-cell activity [12, 13]. Environmental factors, such as smoking, stress, iodine exposure, and infections, are also known triggers [14]. Immunologically, a predominance of Th1 responses and thyroid-stimulating antibodies (TSAb) produced by B-cell clones infiltrating the thyroid are key mechanisms in GD [13]. Furthermore, gut microbiota dysbiosis has been linked to GD pathogenesis [15].

This case involves a middle-aged male patient who exhibited hypermetabolic symptoms such as heat intolerance, hyperhidrosis, and palpitations nearly six months following MWA. These symptoms are consistent with hyperthyroidism [11]. The patient had a history of smoking and a stressful lifestyle, which are known risk factors for GD. While MWA is a localized treatment, it has the potential to induce transient immune fluctuations or exacerbate thyroid tissue damage. Studies have shown that short-term elevations in FT3, FT4, TgAb, TPOAb and TRAb levels occur following MWA, although these levels often stabilize after a few months of treatment [16, 17]. This raises the question of whether MWA could serve as a triggering factor in susceptible individuals.

Previous studies have shown that the immune system plays a key role in the pathogenesis of GD. In this case, the preoperative elevation of TPOAb in the patient suggests a possible subclinical thyroid autoimmune state, which may predispose him to developing GD postoperatively. A retrospective analysis explored the changes in relevant antibodies before and after ablation of thyroid nodules and found that MWA for thyroid nodules had little effect on thyroid hormones. However, TgAb, TPOAB, and TRAb were elevated beyond the normal range after MWA, a result that may be related to the higher levels of TgAb and TPOAB prior to ablation [17]. Changes in TgAb, TPOAb, and TRAb levels observed in this case may reflect immune dysregulation induced by postoperative tissue repair processes. This hypothesis aligns with findings from cases of GD following percutaneous ethanol injection or radiofrequency ablation, where most symptoms appeared within two to three months and were transient [2].

Some clinical evidence of diffuse hyperthyroidism, however, does not support the hypothesis that immune mechanisms are the primary drivers of GD pathophysiology. Clinical case studies have suggested that autonomic nervous system (ANS) overactivation can independently or synergistically contribute to the onset and progression of GD by regulating thyroid blood flow and hormone production [18]. In particular, in cases of "mild hyperthyroidism" characterized by normal TSHR-Ab levels but slight increases in FT3 and FT4, ANS overactivation likely plays a crucial role in the pathogenesis of GD, with immune dysregulation serving as a secondary factor [19]. During MWA, the location of the nodule and improper use of isolation fluid may affect the dissipation of thermal energy, potentially disrupting surrounding autonomic nerve tissues through thermal or mechanical injury. Such injuries could significantly increase neuronal excitability, which may subsequently affect thyroid hormone levels and immune status, contributing to the development of GD. However, whether MWA increases susceptibility to GD via excessive ANS activation warrants further investigation.

While these proposed mechanisms are plausible, the precise etiology of GD following MWA remains speculative. In our case, the patient underwent MWA at another hospital, and due to the lack of intraoperative data, we were unable to assess key procedural factors, such as nodule location and the use of isolation fluid, which may have exacerbated thermal injury to adjacent tissues. Furthermore, the absence of immediate postoperative thyroid hormonal levels prevents the identification of early thyroid dysfunction or transient subclinical hyperthyroidism.

In conclusion, this case suggests that MWA may predispose patients with subclinical autoimmune thyroid disease to GD, and that any stimuli, including microsurgical procedures, may trigger GD by excessively activating the autonomic nervous system. Although a causal relationship between MWA and GD has not been established, this case highlights the importance of preoperative thyroid antibody screening and close postoperative monitoring. Future studies should further explore the immunological and neurogenic mechanisms linking thermal ablation and autoimmune thyroid diseases to guide clinical decision-making and improve patient outcomes.

Conclusion

In this case, we presented the onset of GD following MWA in a patient with subclinical thyroid autoimmunity. While the causal relationship between MWA and GD remains unproven, the case suggests that preexisting autoimmune thyroid conditions may increase susceptibility to postoperative thyroid dysfunction. Procedural factors, such as thermal injury to surrounding tissues and potential involvement of the autonomic nervous system, are also potential contributors to the development of GD following MWA.

To mitigate such risks, it is essential to assess preoperative thyroid antibody levels as potential predictors of postoperative thyroid abnormalities. Large-scale studies are needed to evaluate the connection between procedural parameters and thyroid autoimmune activation, and to establish evidence-based protocols for patient selection, preoperative evaluation, and postoperative monitoring. These efforts will enhance the safety and efficacy of MWA and guide clinical decision-making to improve patient outcomes.

Abbreviations

RFA	Radiofrequency ablation
MWA	Microwave ablation
LA	Laser ablation
BTN	Benign thyroid nodules
GD	Graves' disease
FT3	Free triiodothyronine
FT4	Free thyroxine
TSH	Thyrotropin-stimulating hormone
TRAb	Thyrotropin-receptor antibody
TgAb	Anti-thyroglobulin antibody
TPOAB	Anti-thyroid peroxidase antibody
GDFI	Color Doppler flow imaging
AITD	Autoimmune thyroid disorder
CTLA-4	Tlymphocyte-associated antigen 4
PTPN-22	Protein tyrosine phosphatase-22
HLA	Human leukocyte antigen
PTMC	Papillary thyroid microcarcinoma
TSAb	Thyroid stimulating antibody
ANS	Autonomic nervous system

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None.

Author contributions
XH: Writing - review & editing, Data curation. YG and RC: Writing - original draft, Data curation, Formal Analysis, Writing - review & editing. MC, XJ and LW: Data collection.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The human subjects involved in this study were approved by the Ethics Committee of Changzhou First People's Hospital. The study was conducted in accordance with local legal and institutional requirements. Participants provided written informed consent to participate in this study. Written informed consent was obtained from the person concerned for the publication of any identifiable images or data included in this article.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the journal editor.

Competing interests
The authors declare no competing interests.

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