Letter to the Editor

Ultrasound-guided microwave ablation combined with Lugol's solution for preoperative preparation in the treatment of refractory pediatric hyperthyroidism: a description of two cases

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Introduction

Hyperthyroidism is a pathological condition primarily caused by Graves disease (85%) and is characterized by increased synthesis and secretion of thyroid hormones (1). Elevated thyroid hormone levels in the bloodstream result in a clinical syndrome involving heightened metabolism and increased sympathetic nervous system activity (2). Children with hyperthyroidism often experience more severe consequences including accelerated growth and bone maturation and a decline in academic performance (3). Similar to that for adults, the initial treatment for hyperthyroidism in children is medication. If the treatment response is poor or the medication produces known side-effects including liver abnormalities, surgical or iodine-131 treatment should be considered. However, surgery often entails high risks of bleeding and infection and can lead to complications such as hypoparathyroidism (4). Iodine-131 treatment usually leads to permanent hypothyroidism and sometimes fails to control the hyperthyroidism (5-7). The European Thyroid Association guidelines state that patients under 5 years old are an absolute contraindication, while patients between 5 and 10 years old are a relative contraindication (8). Hence, identifying other safe and effective treatment modalities is crucial for managing pediatric hyperthyroidism.

In recent years, ultrasound-guided microwave ablation, as a minimally invasive technique, has been successfully used in the treatment of thyroid diseases (9,10). The principle of microwave ablation involves targeting lesion tissue under real-time ultrasound guidance, inserting ablation needles percutaneously into the lesion, using the localized heating effect of microwaves, generating a large amount of heat within the lesion tissue in a short period to induce necrosis of the lesion tissue, and thus achieving the effect of disease treatment. Due to its good safety, minimally invasive nature, and repeatability, ablation has become one of the standard treatment modalities for thyroid-related diseases. However, research on ablation for adult hyperthyroidism is still in its early stages (2,11,12), and reports on ablation for pediatric hyperthyroidism are particularly scarce (13) (*Table 1*). Therefore, this study aimed to investigate the safety and effectiveness of ablation in the treatment of pediatric hyperthyroidism.

Iodine solution is commonly used as preoperative medication in surgery for hyperthyroidism (14). The most frequently used types are Lugol's solution and potassium iodide solution, with our institution primarily employing Lugol's solution. Preoperative administration of iodine serves three principal purposes: (I) it causes the thyroid gland to shrink and become harder and less brittle, thus facilitating surgical maneuvers. (II) It reduces arterial congestion in the thyroid gland, thereby minimizing intraoperative bleeding. (III) It decreases the release of thyroid hormones, lowering the risk of thyroid crises during surgery (15,16). Based on our experience and the guidelines for adult hyperthyroidism ablation therapy (12), we have concluded that ablation for hyperthyroidism also requires the routine use of iodine solution. Apart from the mentioned effects, Lugol's solution can also reduce

Table 1 Summary of patient characteristics and treatment outcomes in the literature on ablation therapy for hyperthyroidism

Subject	Ref. (11), 2021	Ref. (13), 2022	Ref. (2), 2023									
			Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Normal range
Gender	Female	Female	Female	Female	Female	Female	Male	Female	Female	Male	Female	
Age (years)	28	13	14	33	34	55	55	36	32	39	34	
Illness duration (years)	0.5	4					–					
FT3 (pmol/L)	3.33 (2.8–6.3)	5.88 (3.30–8.25)	6.84	8.34	6.9	5.69	19.4	9.23	8.76	6.57	6.58	3.5–6.5
FT4 (pmol/L)	1.81 (10.5–24.4)	7.98 (8.37–29.60)	17.16	26.1	25	17.6	56.4	28.9	27.7	19.7	18.3	11.5–22.7
TSH (mIU/L)	0.021 (0.38–4.34)	0.03 (0.40–4.00)	0.01	<0.005	<0.005	0.193	<0.005	<0.005	<0.005	<0.005	<0.005	0.25–5
TR-Ab (IU/L)	38.74 (<1.75)	5.27 (<1.75)	>40	2.46	1.9	2.18	18.4	35.6	1.02	11.7	35.3	0–2.57
Types of medication taken	Methimazole	Propylthiouracil	Methimazole	Methimazole	Methimazole, metoprolol	Propylthiouracil	Methimazole	Methimazole	Propylthiouracil, metoprolol	Methimazole	Methimazole, metoprolol	
Dose	20 mg qd po	100 mg qd po	15 mg qd po	15 mg qd po	20 mg qd po; 47.5 mg qd po	50 mg tid po	10 mg qd po	10 mg qd po	100 mg qd po; 25 mg bid po	10 mg tid po	10 mg bid po; 12.5 mg bid po	
Postablation dose	0 (5 weeks postprocedure)	0 (9 months postprocedure)					Reduced to 31.25% (3 months postprocedure)					
Ablation proportion	–	30%					30–50%					
Follow-up time	5 weeks	10 months					3 months					

Data are presented as patient's value (normal range). FT3, free triiodothyronine 3; FT4, free thyroxine 4; TSH, thyroid-stimulating hormone; TR-Ab, thyrotropin receptor antibody.

the blood flow in thyroid tissues, minimizing the heat-sink effect during the ablation process, thus expanding the ablation area (17).

Cases presentation

All procedures performed in this study were conducted in accordance with the ethical standards of the Ethics Committee of The Affiliated Hospital of Qingdao University (approval No. QYFYWZLL 28239) and with the Declaration of Helsinki (as revised in 2013). The requirement for patient consent for the publication of this article and accompanying images was waived by the Ethics Committee of tThe Affiliated Hospital of Qingdao University.

Two children with hyperthyroidism visited The Affiliated Hospital of Qingdao University due to failed drug treatments. After multidisciplinary consultations involving pediatric endocrinologists, thyroid surgeons, nuclear medicine specialists, and ultrasound physicians, we recommend that the patients undergo ultrasound-guided microwave ablation. Upon admission, we conducted thyroid ultrasound examinations, thyroid function tests, and other standard assessments.

Similar to thyroid surgery for hyperthyroidism, we requested patients continue their antithyroid drugs and other medications related to hyperthyroidism before ablation. Alongside these medications, approximately seven days before ablation, the patients began taking Lugol's solution.

Before ablation, we measured the length, width, and thickness of both lobes of the thyroid gland. We designated the point slightly anterior to the intersection of the three diameters as the ablation center. This avoids damage to structures behind the thyroid, such as the recurrent laryngeal nerve. Since near-total thyroidectomy often leads to a high incidence of hypothyroidism, we set the ablation volume to 50–60% of the thyroid volume. Additionally, we slightly increased the ablation proportion on the visibly enlarged side of the thyroid in order to achieve a more symmetrical appearance after ablation. The following the thyroid volume formula was used: volume (unilateral lobe) = length × width × thickness × 0.479 (18). To achieve the 50–60% ablation proportion, we set the ablation range to around fourth-fifths of each diameter.

The ablation procedure was performed in the interventional operating room and was conducted by two experienced ultrasound interventional physicians. An anesthesiologist and a pediatric endocrinologist were also present to address any emergent situations. The patients were in a supine position with the neck hyperextended. We conducted routine disinfection of the surgical area, and local anesthesia with 1% lidocaine was administered. Under the guidance of an ultrasound probe, a sterile syringe was used to inject isolating fluid between the thyroid lobe and the surrounding critical structures. Subsequently, a microwave ablation needle was inserted into the central part of the thyroid lobe, activating the ablation switch. After the ablation of the planned area, contrast-enhanced ultrasound was performed to assess the ablation volume and aid in determining whether the ablation time should be extended.

For one year after ablation, we regularly followed up the patients to assess the changes in thyroid function, medication dosage, and thyroid volume.

Case 1

A 12-year-old boy was diagnosed with Graves disease in 2014. He had been consistently taking medications including methimazole since this diagnosis. Upon the reexamination in July 21, 2022, it was found that his hyperthyroidism was still not well controlled [free triiodothyronine 3 (FT3) 38.9 pmol/L, free thyroxine 4 (FT4) 70.8 pmol/L, thyrotropin receptor antibody (TRAb) >40.00 IU/L] by his intake of methimazole (10 mg, bid). The normal ranges for FT3, FT4, and TRAb are 3.93–7.70 pmol/L, 12.6–21.0 pmol/L, and <1.75 IU/L, respectively. On July 23, 2022, the patient was admitted to our center to undergo ultrasound-guided ablation for treatment of hyperthyroidism.

Before ablation, the patient continued taking methimazole (10 mg bid), along with other medications. Additionally, six days before ablation, the patient began using Lugol's solution beginning at 6 drops bid and gradually increasing to 10 drops bid before ablation. The patient was then instructed to discontinue Lugol's solution intake on the fourth day after surgery. According to the preoperative thyroid ultrasound, the size left and right lobes of the patient's thyroid were respectively 5.8×2.3×1.7 and 6.0×2.4×1.9 cm.

On July 28, 2022, we performed thyroid ablation on this patient. The ablation duration was 171 seconds in left lobe and 177 seconds in right lobe. Postprocedure contrast-enhanced ultrasound revealed a 4.1×2.1×1.4 cm ablation zone in left lobe and a 4.3×2.2×1.6 cm ablation zone in right lobe (*Figure 1A-1D*). The patient experienced no immediate

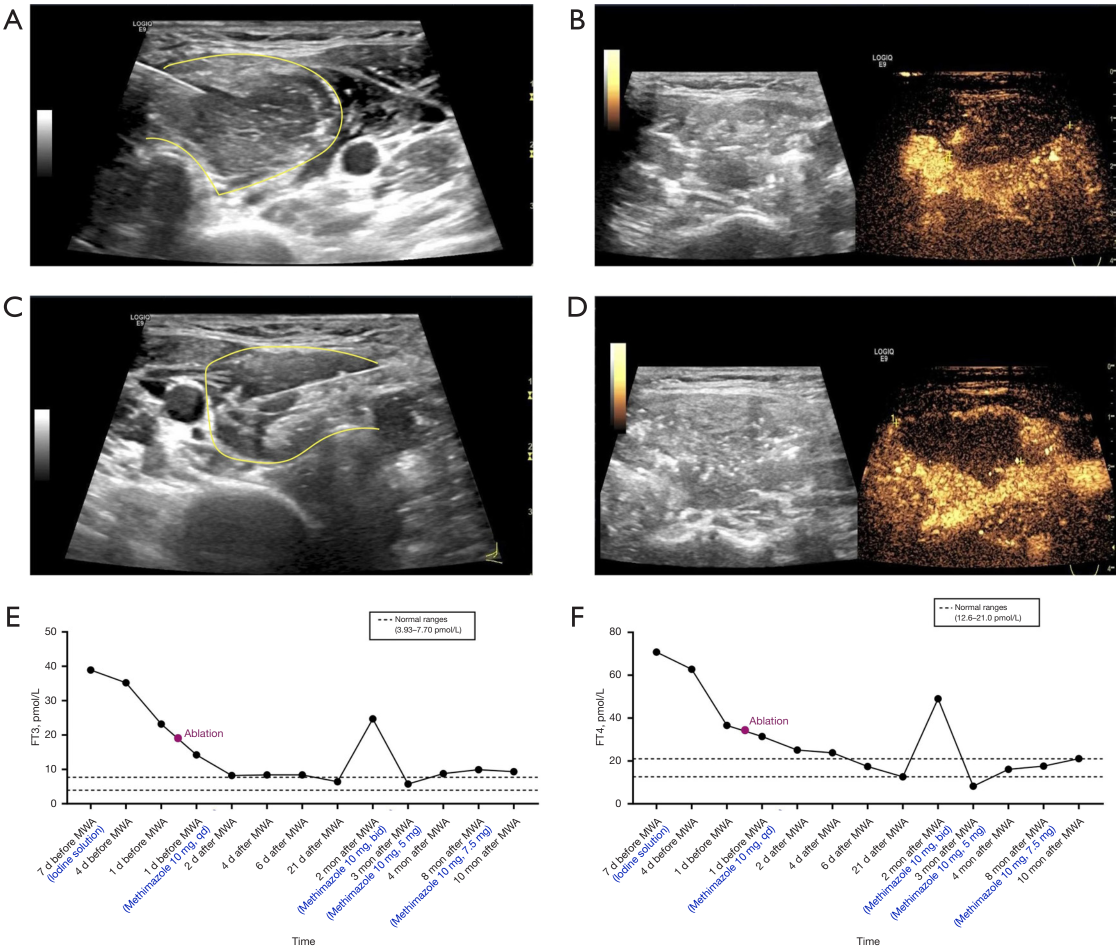

Figure 1 The ultrasound images during ablation, contrast-enhanced ultrasound, and the changes in thyroid function before and after microwave ablation for the first patient. (A) Left lobe during ablation. (B) Contrast-enhanced ultrasound evaluating the extent of left lobe ablation. (C) Right lobe during ablation. (D) Contrast-enhanced ultrasound evaluating the extent of right lobe ablation. (E) Changes in FT3. (F) Changes in FT4. FT3, free triiodothyronine 3; FT4, free thyroxine 4.

postablative complications and was discharged on the 13th day after admission.

Ten months after the procedure, ultrasound measurements indicated the left and right lobes of the thyroid were respectively 2.8×1.6×1.5 and 3.0×1.8×1.4 cm in size. The size of the residual ablation zones were 1.0×0.8×0.4 and 1.6×0.8×0.4 cm in left and right lobes. There was a notable reduction in thyroid volume compared to that measured preprocedure. The clinician reduced the methimazole dosage by half that prescribed postprocedure, changing it from 10 mg bid to 10 mg qd. However, during the reexamination two months after ablation, inadequate control of thyroid function was observed (FT3 24.7 pmol/L, FT4 49.0 pmol/L). Consequently, the dosage of methimazole was gradually adjusted from 10 mg qd to 10 mg in the morning and 7.5 mg in the evening. As of this writing, the FT3 and FT4 levels are mostly within the normal range, but the thyroid-stimulating hormone (TSH) levels still remain far below the normal range (*Figure 1E,1F*). This might be due to the long illness duration of this patient, requiring more time for TSH levels to recover.

Case 2

A 9-year-old boy required medical attention after the discovery of a neck mass. Based on thyroid function tests and other examinations, the attending doctor at a local hospital diagnosed this patient with Graves disease

(TRAb 10.40 IU/L) and treated him using the antithyroid drug methimazole. However, after taking methimazole, the boy's liver function showed abnormalities [aspartate aminotransferase (AST) 193.1 U/L, alanine transaminase (ALT) 334.3 U/L]. The normal ranges for AST and ALT are 15–40 and 9–50 U/L, respectively. Consequently, on August 25, 2022, he was admitted to our hospital for treatment. The clinician discontinued methimazole and used drugs including glutathione and magnesium isoglycyrrhizinate injection for liver protection treatment. Upon improvement in liver function, the clinician resumed treatment with methimazole. However, subsequent examinations indicated a reoccurrence of abnormal liver function. Hence, the patient's guardians ultimately opted for ablation.

Before ablation, the patient continued on the prescribed medication. Additionally, seven days before ablation, we began adding Lugol's solution (five drops bid), gradually increasing the dosage to eight drops bid before ablation. Lugol's solution was discontinued on the fourth day after surgery. Through the preoperative thyroid ultrasound, the size of the left and right lobes of thyroid in the patient were respectively 4.1×1.7×1.6 and 4.0×1.6×1.5 cm.

On September 29, 2022, we performed ablation on this patient. The duration of ablation was 122 seconds in the left lobe and 61 seconds in the right lobe. Postprocedure contrast-enhanced ultrasound revealed a 3.3×1.3×1.2 cm ablation zone in left lobe and a 3.1×1.2×1.1 cm ablation zone in right lobe (*Figure 2A-2D*). The patient had no immediate postablative complications and was discharged on the 15th day after admission.

Nine months after the procedure, ultrasound measurements showed the left and right lobes were respectively 2.6×1.4×1.3 and 2.5×1.5×1.3 cm in size. Meanwhile, the size of the ablation zones measured 1.6×1.0×0.6 cm in the left lobe and 1.4×0.8×0.7 cm in the right lobe, indicating a significant reduction in thyroid volume compared to that measured before the procedure (*Figure 2E,2F*). The patient's FT3 and FT4 levels continued to decrease after the ablation and were below the normal range by three months after procedure; meanwhile, the TSH levels had risen to 30.9 mIU/L. Consequently, the clinician added levothyroxine (Euthyrox) to the treatment regimen. By 14 months after the procedure, the patient's thyroid function remained consistently within the normal range (*Figure 2G-2I*). As of this writing, all medications used before ablation have been discontinued, and the patient is only taking levothyroxine (Euthyrox) at 25 UG qd, with a continued tapering off process.

Discussion

Compared to surgery and iodine-131 treatment, ultrasound-guided microwave ablation demonstrates significant advantages in treating pediatric hyperthyroidism. In contrast to surgery, ablation poses a lower risk of damaging vital structures around the thyroid since ablation mainly operates within the thyroid (10). Additionally, scarring and adhesions in the surgical area postsurgery make repeated operations more challenging. However, ablation therapy provides good repeatability, allowing for satisfactory treatment outcomes through multiple sessions of ablation. Compared to iodine-131 treatment, ablation reduces the risk of permanent hypothyroidism. Therefore, ablation tends to be more suitable for pediatric patients with hyperthyroidism. However, the application duration of ablation for hyperthyroidism is relatively short, and there remain other issues remain unresolved and in need of further investigation.

Currently, there are varying opinions on the ablation range for treating hyperthyroidism caused by Graves disease. The expert consensus in China is to achieve near-total ablation, comparable to the scope of near-total thyroidectomy (leaving 4–6 g of thyroid tissue) (12). However, Tang *et al.* and Song *et al.* recommend ablation ranges of 40% and 30% of the thyroid volume, respectively (2,13), reporting good results with each of these ranges. We believe that using a scope of near-total thyroidectomy carries a high risk of hypothyroidism. Compared to that in adults, hypothyroidism in children can lead to severe adverse effects, such as growth retardation and intellectual impairment (19,20). However, a too-small ablation range might result in inadequate treatment effects. Hence, we implement an ablation range of 50–60% of the thyroid volume, reaching around fourth-fifths of each diameter. Nonetheless, the proportion of ablation for pediatric patients with hyperthyroidism should be further examined.

For the two children in this case report, we planned the ablation range using the same proportions described above. However, there were variations in the postoperative thyroid function changes. After ablation, the clinician reduced the medication for the first child, but upon follow-up, it was observed that this dosage could not maintain thyroid function. The medication has since been adjusted to seven-eighths of the preoperative dosage. The second child, unable to tolerate antithyroid drugs, discontinued their use before ablation. Postoperative follow-up revealed FT3 and FT4 levels below the normal range. Consequently,

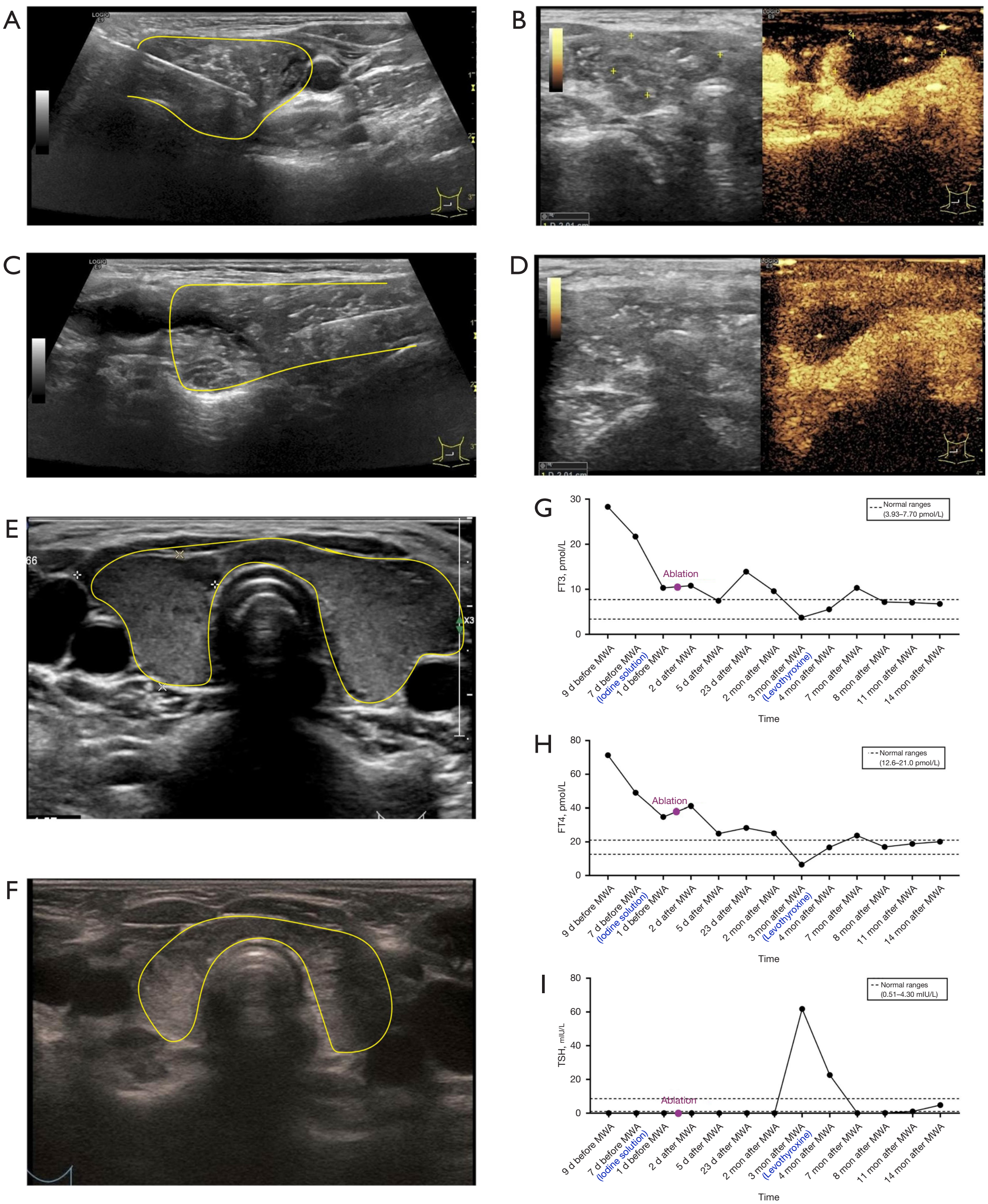

Figure 2 The ultrasound images during ablation, contrast-enhanced ultrasound, and the changes in thyroid size and function before and after microwave ablation for the second patient. (A) Left lobe during ablation. (B) Contrast-enhanced ultrasound evaluating the extent of left lobe ablation. (C) Right lobe during ablation. (D) Contrast-enhanced ultrasound evaluating the extent of right lobe ablation. (E) Preoperative thyroid transverse ultrasound image. (F) Thyroid transverse ultrasound image 9 months postoperation. (G) Changes in FT3. (H) Changes in FT4. (I) Changes in TSH. FT3, free triiodothyronine 3; FT4, free thyroxine 4; TSH, thyroid-stimulating hormone.

a temporary addition of levothyroxine (Euthyrox) was initiated to regulate thyroid function. Regarding the discrepant outcomes in these two children, we believe further research involving more cases are necessary to account for this variability. Although the preoperative TRAb levels of both patients were above the normal range, the first patient's level was significantly higher than that of the second patient. Therefore, we suspect TRAb to be one of the factors influencing the ablation outcome. Further research is needed to determine how to adjust the ablation range based on TRAb levels and to determine whether the ablation range needs to be adjusted based on the patient's illness duration, condition, preoperative medication, or other factors.

Preoperative medication preparation is an important factor affecting treatment success. The expert consensus in China is to add iodine when symptom control is difficult or when the thyroid is enlarged to grade II or above (12). In one of our cases of ablation for adult hyperthyroidism, a thyroid crisis suddenly occurred possibly due to the lack of Lugol's solution before ablation. However, a month later, when we administered Lugol's solution before ablation, the ablation proceeded smoothly. Therefore, we believe iodine solution should be routinely used for every patient with hyperthyroidism undergoing ablation. This not only reduces intraoperative bleeding and the risk of thyroid crises but also restricts the heat-sink effect by limiting congestion, thereby expanding the area that can be ablated.

Due to the impact of thyroid function on children's growth and development, we recommend a multidisciplinary consultation be conducted before ablation, with each specialist analyzing the patient's specific situation to determine if ablation is the most suitable therapy. Additionally, it is advisable to have an anesthesiologist and pediatric endocrinologist present during the ablation to address any unexpected occurrences.

Conclusions

Our experience with these two cases indicates that microwave ablation can avoid the trauma and risks associated with surgery and iodine-131 therapy and effectively treat pediatric hyperthyroidism. However, further research with additional cases is needed to establish the safety and efficacy of this method.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-24-134/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were conducted in accordance with the ethical standards of the Ethics Committee of the Affiliated Hospital of Qingdao University (approval No. QYFYWZLL 28239) and with the Declaration of Helsinki (as revised in 2013). The requirement for patient consent for the publication of this article and accompanying images was waived by the Ethics Committee of the Affiliated Hospital of Qingdao University.

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