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Therapeutic Effects of Ultrasound-Guided Percutaneous Laser Ablation for Primary Thyroid Microcarcinoma

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Abstract

Background: Ultrasound-guided percutaneous laser ablation, as a minimally invasive ablation method, has been widely used in the treatment of benign and malignant tumors. The objective of the current study is to determine the efficacy and safety of ultrasound-guided percutaneous laser ablation (PLA) for unifocal papillary thyroid micro carcinomas (PTMC).

Methods: A total of 18 patients were included in this study. Patients with a single PTMC were treated via the PLA method, and postoperative complications, tumor size and recurrence rate were followed up and recorded.

Results: Data suggested that three patients underwent a secondary ablation, and the remaining 15 patients underwent a single ablation without serious complications. No recurrence or metastasis was found among the follow-up patients, and the tumor sizes decreased significantly from 12 months following PLA treatment.

Conclusions: Ultrasound-guided PLA is a new therapeutic means that can be used as an alternative to PTMC treatment.

Background

Thyroid microcarcinoma (TMC) refers to thyroid cancer with diameter ≤ 1 cm, also known as occult thyroid cancer[1, 2]. TMC has a high prevalence in the population and a previous autopsy study on subjects who died of non-thyroidal diseases revealed latent TMC in up to 5.2% of the subjects[1, 3]. TMC is a special type of thyroid cancer in pathological classification, among which papillary thyroid microcarcinoma (PTMC) is most commonly observed and accounts for 65%-99% of cases[4]. PTMC is characterized by high incidence and slow progression, but is prone to cervical lymph node metastasis[5]. For most patients, cervical lymph node metastasis has a reduced impact on survival, but it increases the risk of recurrence[6, 7]. It is precisely due to these characteristics of PTMC that the diagnosis and treatment of PTMC have become a controversial topic in clinical work. Thus far, surgical resection is the classic and predominant treatment for PTMC, and some scholars are already aware of the problem of excessive resection[8, 9]. Early cancer detection and minimally invasive intervention have been suggested to reduce the mortality and morbidity of patients.

Percutaneous laser ablation (PLA) is a minimally invasive intervention that has been successfully used in the treatment of benign thyroid nodules in recent years, and it exhibits considerable clinical efficacy[10, 11]. Compared with radiofrequency ablation and microwave ablation, PLA has unique advantages in the treatment of cervical diseases adjacent to vital organs due to its small laser fiber needle and precise and controllable output energy[12, 13]. Some scholars have applied PLA as an alternative surgical treatment to some PTMCs, finding that PLA could effectively kill PTMC without recurrence[14]. Other studies also supported the application of PLA in the treatment of TMC cervical lymphatic metastases[15, 16]. Overall, the application of PLA in treating PTMC is still limited.

The purpose of this study is to investigate the safety and efficacy of ultrasound-guided PLA in the treatment of PTMC, and to provide a clinical basis for early intervention in patients with PTMCs.

Methods

Patients

From November 2016 to October 2018, 18 patients with solitary PTMC were included. Patient information is summarized in **Table 1**. The present study has been approved by the ethics committee of the Affiliated Suzhou Science & Technology Town Hospital of Nanjing Medical University.

A written informed consent document was obtained from all patients before the procedure.
Inclusion criteria for patients included patients with: (1) PTMC confirmed by fine-needle aspiration biopsy (FNAB); (2) A single tumor with a maximum diameter of less than 10 mm; (3) A tumor without contact or invasion of the thyroid capsule; (4) Normal cardiopulmonary function; (5) Normal blood tests, such as routine blood and coagulation function; and (5) No cervical or distant lymph node metastasis.
Exclusion criteria were as follows: (1) Patients with multiple nodules, or nodules larger than 10 mm in diameter; (2) Patients with lymph node metastasis or distant metastasis; (3) Patients with tumors that invaded the thyroid capsule or important organs; (4) Patients with severe cardiopulmonary dysfunction; and (5) Patients treated with thyroid surgery or radioiodine treatment.

Pre-pla Observation

The tumor locations, diameters, volumes and ultrasonographic characteristics were evaluated by ultrasonography (TOSHIBA Apli0500 Ultrasound Instrument, High Frequency Linear Array Probe, frequency of 10 MHz). Blood tests included serum thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free tetraiodothyronine (FT4), thyroglobulin (TG), anti-TG antibody, and routine blood and coagulation function. The tumor volume was calculated as follows: $V = \Pi \times a \times b \times c/6$ (where V is the volume, a is the maximum diameter, and b and c are the other maximum vertical diameters).

Pla Method

The patient was in a supine position, and the neck was fully exposed. Ultrasound-guided local anesthesia with 2% lidocaine was used after routine disinfection and towel laying. A 21G guided needle was then fixed in the center of the nodule. Then, a needle core was inserted with optical fibers, and the guided needle was retreated 5 mm to the tip of the optical fibers to contact the nodule directly. The laser ablation system was switched on for continuous ablation. Radiofrequency power was ablated from 4 to 6 W, and a single-point and constant ablation was performed until the high echo in the ablation area completely covered the proposed range. The ablation focus was at least 0.1 cm above the edge of the nodule. If the patient did not feel any obvious discomfort, the power could be increased slowly. A volume of 20 ml of hydro dissection solution could be used to avoid thermal damage if tumors were found to be close to the recurrent laryngeal nerve, common carotid artery or jugular vein. If patients felt obvious pain or discomfort during ablation, power was reduced or the ablation was suspended. The ablation should be ceased when nodules were completely covered by strong echoes. Contrast-enhanced ultrasonography (CEUS) was performed 5 minutes after ablation. Additional ablation was feasible if nodular enhancement signals were still present in the ablation area. The puncture area was covered with ice and compressed for 30 minutes and patients were observed in the hospital for 24 hours.

Post-pla Observation And Follow-up

Complications and tumor volumes were recorded. Patients were followed at 1, 3, 6, 12, 18, and 24 months and every six months thereafter following PLA. The lesion size, blood supply and necrosis were observed via ultrasound or CEUS. Fine needle aspiration biopsy was performed if suspected metastatic lymph nodes and suspected lesions in thyroid parenchyma were found. Blood tests including serum TSH, FT3, FT4, TG, and anti-TG antibody were examined every month.

Statistical analysis

Statistical analysis was carried out using SPSS 19.0 (Chicago, IL, USA) and quantitative variables were reported as the mean ± standard deviation (SD). A matched t-test was performed on the volume and maximum diameter at different time points. P values < 0.05 were considered to indicate statistical significance.

Results

Pre and intra-PLA measurement

In the present study, 18 nodules of 18 patients were completely ablated. CEUS showed no Doppler signal enhancement in the ablation focus after operation. Among the 18 patients, 14 were females; 11 nodules were on the left side and 7 were on the right. The maximum diameter and the volume were (7.1 ± 2.3) mm and (79.5 ± 24.6) mm^3. No thyroid hormone disorders were found among the patients, and the active time during PLA was (308.2 ± 120.6) s. In addition, of the 18 patients, 15 patients were treated with single needle and single PLA ablation, and 3 patients had a secondary ablation performed. Postoperative CEUS demonstrated that no Doppler signal enhancement was found in the ablation areas (Table 1).

Complications Post-pla

During the PLA process, 5 patients complained of neck pain during the operation and 1 patient received 5 mg of dzosin via intramuscular injection. All patients felt self-limited neck swelling to some extent. Of the 18 patients, 1 subject experienced a cough and fever during post-PLA operation and recovered 7 days later under symptomatic treatment. No cases of dysphonia, neck hematoma, surgical area infection or vital organ injury occurred during the operation. However, a 33-year-old woman was found to experience hypothyroidism 1 month post PLA operation, and the thyroid hormone level was recovered by the second month. A 55-year-old woman experienced hoarseness after surgery and was diagnosed with a recurrent laryngeal nerve injury, which recovered 3 months later. No cervical lymph node metastasis or distant metastasis of these patients was found during the ensuing follow-up (Table 1).

Follow-up Measurement

Preoperative Doppler ultrasound revealed a hypoechoic nodule (Fig. 1A/ 2A). Intraoperative ultrasound showed that irregular and strongly homogeneous gasification areas began to appear around the mass with the release of ablation energy (Fig. 1B/ 2B). Postoperative CEUS examination showed that the ablation area became a vaporized cavity after PLA (Fig. 1C/ 2C). Six months later, ultrasound showed a hyperechoic nodule in the ablation area (Fig. 1D/ 2D). The follow-up time ranged from 5.6 months to 31.1 months, with an average follow-up time of (18.6 ± 6.2) months. During the follow-up period, ultrasound dynamic examination confirmed the disappearance of blood perfusion in the ablation area. Following PLA treatment, the volume of ablation focus decreased gradually from the 6th month over time. At the last follow-up, the ablation lesions of 8 cases completely disappeared, and scar-like changes remained in 6 cases. During the follow-up period, the maximum diameter and volume of the postoperative ablation areas at 30 minutes and 1 month were significantly larger than those of the preoperative nodules. At the 3rd month and 6th month post operation, the maximum diameter and volume of the ablation areas decreased, and no significant differences were found between the post and preoperative nodules. From the 12th month, the maximum diameter and volume of ablation areas gradually decreased, which were significantly smaller than those of the preoperative nodules (Table 2).

Discussion

With the increasing incidence of PTMC in recent decades, surgical resection has become the main clinical treatment worldwide[17]. However, traditional excision may cause detachment of the thyroid gland, which may inevitably lead to varying degrees of hypothyroidism[18]. Surgical resection for PTMC often leads to excessive resection and a sense of insecurity in patients, which has been controversial for many years[19, 20]. Some scholars believe that total thyroidectomy for PTMC is unnecessary and expanding thyroidectomy does not improve surgical efficiency[21]. Some academics argue that lymph node metastasis did not affect the survival rates of PTMC patients, and preventive lymph node dissection is unnecessary for those PTMC patients without suspected lymph node metastasis[22–24]. Therefore, in the current clinical environment, an effective minimally invasive treatment of PTMC is urgently needed.

PLA was first used in the treatment of hepatic, uterine and adrenal diseases[25–27]. Pacella et al[28] preliminarily verified the efficacy of PLA to treat benign thyroid nodules. Ultrasound-guided PLA treatment, which has become a promising minimally invasive treatment for thyroid nodules, offers a series of advantages, including simple operation, minimal invasiveness, stable coagulation range, safety, and quick recovery[29]. Døssing et al.[30–32] performed PLA 3 times for 16, 30, and 78 patients with benign cold thyroid nodules and he found that the nodular volume reduction ratios 6 months after PLA were 46%, 44%, and 51%, respectively, suggesting that PLA offers excellent tumor reduction effects. In 2010, PLA was recommended as an effective and safe method for thyroid nodules according to the American Society of Clinical Endocrinologists, the Italian Society of Clinical Endocrinology, and the European Thyroid Association[33]. Therefore, the proper application of PLA in the treatment of thyroid diseases meets the needs of development of modern medicine.

Subjects with malignant thyroid tumors treated by PLA have also been reported in recent years. Lili Ji et al.[34] found that 32.4% of the primary lesions of PTMCs had disappeared, and 64.9% remained as cicatricial hyperplasia; only 2.7% of subjects had cervical lymph node metastasis during the follow-up period after PLA treatment. Zhou W et al.[35] retrospectively analyzed 30 patients with PTMC following PLA treatment and concluded that ultrasound-guided PLA is an effective and safe method for T1N0M0 PTMC treatment of patients who are ineligible for surgical resection.

In the present study, we analyzed 18 PTMC patients undergoing PLA treatment, and our data suggested that all of the nodules of the 18 patients were effectively ablated. CEUS revealed no doppler signal enhancement in the ablation focus after the operation, showing that thyroid nodules were thoroughly removed. No serious complications were found, such as bleeding, dyspnea, or thyroid crisis post-PLA treatment. In addition, no tumor recurrence, cervical lymph node metastasis or distant metastasis were found during the follow-up. To test the ablation efficiency of PLA, we measured the maximum diameter and volume of the ablation areas, and our data suggested that the maximum diameter and volume of the ablation areas at 30 minutes and 1 month after operation were significantly larger than those of the preoperative nodules. In the 3rd month and 6th month after the operation, the maximum diameter and volume of the ablation areas decreased, and no significant differences were found between the post and preoperative nodules. From the 12th month, the maximum diameter and volume of the ablation areas gradually decreased, noticeably smaller than the preoperative nodules.

These findings suggested that ultrasound-guided PLA is a new therapeutic approach that could be an alternative treatment for PTMC.

During the process of PLA treatment, attention should be paid to the following aspects: (1) Hydrodissection solution should be used when the distance between nodules and vital organs is less than 5 mm. (2) The temperatures of the thyroid and vital organs must be monitored: once the temperature is too high, energy output must be reduced. (3) If the nodule adheres to the trachea or blood vessels, the nodule can be ablated partially. (4) If one side of recurrent laryngeal nerve (RLN) is injured, the other side of RLN should be avoided during ablation to avoid asphyxia. Although PLA exhibits considerable clinical efficacy in treating PTMC in the present study, it still must be further improved. (1) More patients and long-term follow-up need to be investigated in the ensuing studies. (2) New imaging techniques, such as computerized three-dimensional stereotaxic technology, could be used to reduce the damage surrounding vital tissues during the PLA process. (3) There are few comparative studies between thermal ablation and surgical resection, which need to be further investigated.

Conclusions

ultrasound-guided PLA is a minimally invasive therapeutic approach that can be used as an alternative to PTMC treatment.

Abbreviations

PLA: percutaneous laser ablation; PTMC: papillary thyroid micro carcinomas; TMC: Thyroid microcarcinoma; FNAB: fine-needle aspiration biopsy; TSH: thyroid stimulating hormone; FT3: free triiodothyronine; FT4: free tetraiodothyronine; TG: thyroglobulin; CEUS: Contrast-enhanced ultrasonography

Declarations

Authors' contributions

FZ, ZY and XS carried out the studies, participated in collecting data, and drafted the manuscript. QW, KZ and SQ analyzed data. XF and JG helped to revise the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

Research data can be obtained from corresponding author upon reasonable request.

Ethics approval and consent to participate

The present study was approved by the ethics committee of the Affiliated Suzhou Science & Technology Town Hospital of Nanjing Medical University and consent to

participate from the patient was available.

Consent for publication

All authors approved the final manuscript for publication.

Competing interests

The authors declare that they have no competing interest.

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Tables

Table.1 Characteristics of patients

Patients	Sex/age (years)	Lacation	Size before PLA (mm)	Serum thyroglobulin before PLA(ng/ml)	Active time during PLA (s)	No. of ablation procedures	Complications	Treatment	Follow up (months)
1	F/29	L	6.4×2.9×3.5	0.13	159	1	Pain	Well tolerated	19.5
2	F/42	R	7.8×6.5×4.9	0.17	327	1	Pain	5.0mg dezocin injection	31.1
3	M/36	L	9.1×3.3×6.4	0.09	199	1	-	-	17.6
4	F/54	R	4.8×3.7×3.8	0.25	245	1	-	-	25.4
5	F/37	L	8.7×1.9×6.6	0.16	488	2	-	-	16.3
6	F/31	L	5.2×2.8×3.3	0.11	211	1	Cough and fever	Symptomatic treatment	9.9
7	F/23	R	4.5×3.1×2.8	0.21	349	1	-	-	14.5
8	F/58	L	8.9×6.1×4.2	0.13	187	1	Pain	Well tolerated	29.4
9	M/42	R	7.4×4.2×3.8	0.09	236	1	-	-	21.2
10	F/33	L	3.9×2.7×2.9	0.14	756	2	Serum hormone abnormalities	Self Recovery 1 month later	13.5
11	F/39	R	6.8×4.1×2.4	0.12	293	1	-	-	5.6
12	F/40	L	9.3×7.1×4.6	0.08	385	1	-	-	26.2
13	F/28	R	7.6×3.5×6.8	0.10	416	1	Pain	Well tolerated	15.1
14	M/32	R	8.5×4.1×2.8	0.19	522	2	-	-	23.6
15	F/55	L	9.1×4.4×7.2	0.22	183	1	Unilateral recurrent laryngeal nerve injury	Self Recovery 3 month later	17.8
16	M/56	L	6.7×5.2×3.4	0.17	166	1	-	-	13.4
17	F/37	L	7.7×4.9×5.1	0.11	217	1	Pain	Well tolerated	6.0
18	F/46	L	4.5×3.9×2.7	0.14	208	1	-	-	27.9

Table.2 Maximum diameter and volume change before and after PLA treatment

	Pre-PLA	Post-PLA						
		30 min N=18	1 month N=18	3 months N=18	6 months N=16	12 months N=15	18 months N=8	24 months N=5
Maximum diameter(mm)	7.1±2.3	15.8±3.9*	16.9±4.2*	8.4±3.1	5.2±2.5	3.1±1.2*	1.8±0.9**	1.2±0.5**
Volume(mm^3)	79.5±24.6	739.5±106.8**	754.8±99.7**	96.5±21.8	50.3±26.4	13.7±7.4**	6.5±3.1**	3.2±1.5**

*P<0.05, **P<0.01, as compared with Pre-PLA

Figures

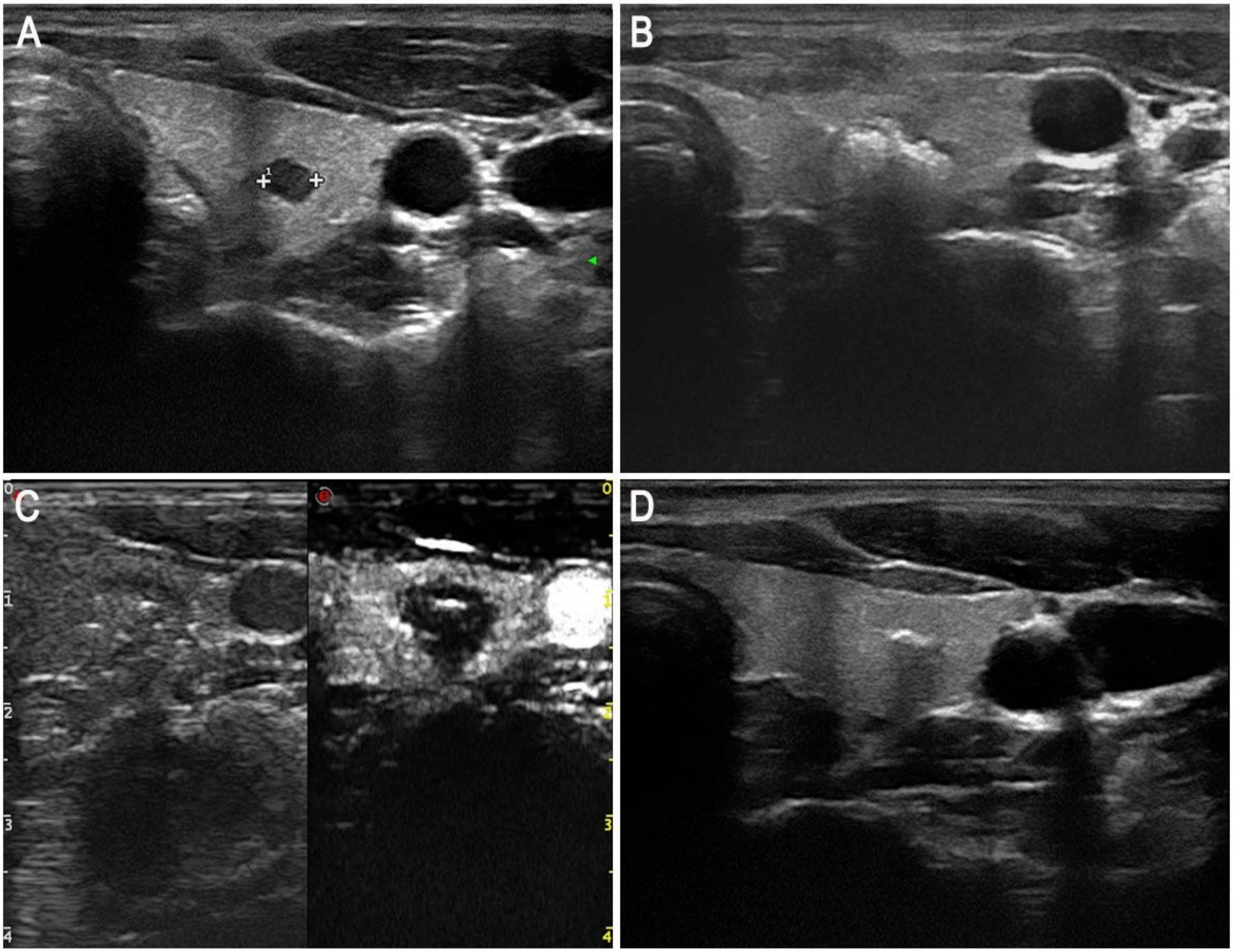

Figure 1

A 31-year-old female with PTMC on the left side of the neck. Preoperative ultrasound showed a hypoechoic nodule with a size of 5.2×2.8×3.3 mm (A). Intraoperative ultrasound showed a vaporized area during ablation (B). CEUS showed a vaporized cavity in the ablation area after operation (C). Six months later, ultrasound showed a scar like tissue with a size of 4.2×1.2×1.7 mm (D).

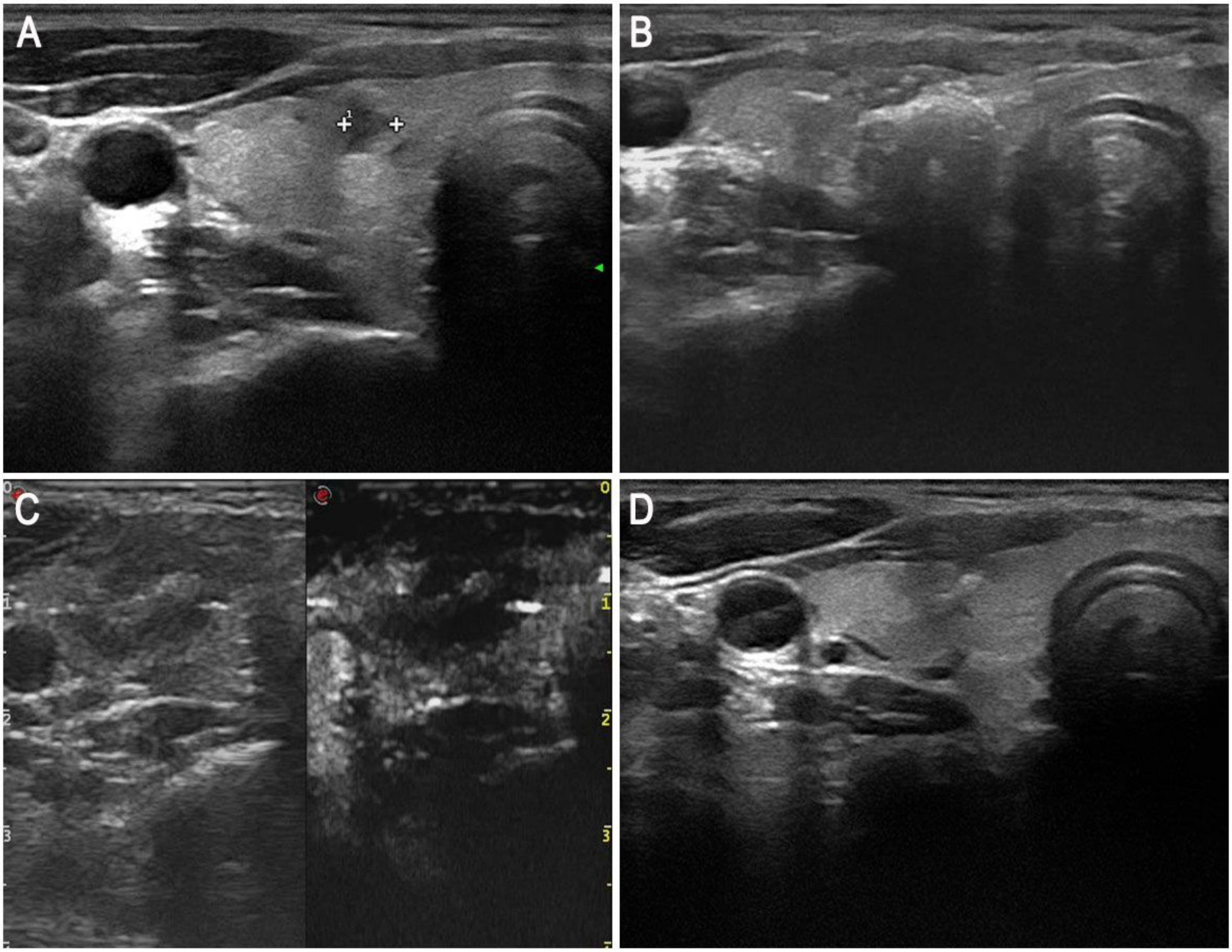

Figure 2

A 23-year-old female with PTMC on the right side of the neck. Preoperative ultrasound showed a hypoechoic nodule with a size of 4.5×3.1×2.8 mm (A). Intraoperative ultrasound showed a vaporized area during ablation (B). CEUS showed a vaporized cavity in the ablation area after operation (C). Six months later, ultrasound showed a scar like tissue with a size of 2.1×0.8×1.1 mm (D).