Percutaneous Laser Ablation of Metastatic Lymph Nodes in the Neck From Papillary Thyroid Carcinoma: Preliminary Results

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Context: Percutaneous laser ablation (PLA) may be useful in treating patients with metachronous metastatic lymph nodes in the neck.

Objective: Our objective was to assess PLA as a treatment of difficult-to-treat metachronous cervical lymph node metastases from papillary thyroid carcinoma.

Design and Setting: We conducted a retrospective analysis of prospectively collected data at a public hospital.

Patients: Fifteen patients with previous resection of papillary thyroid carcinoma with elevated serum levels of thyroglobulin (Tg) or anti-Tg antibodies (TgAbs) and 24 metachronous nodal metastases treated between September 2010 and April 2012 were followed with [^{18}F]fluorodeoxyglucose (^{18}FDG) positron emission tomography (PET)/computed tomography (CT) and contrast-enhanced ultrasound (CEUS).

Intervention: Intervention was PLA.

Outcome Measures: Technique feasibility and technical success were evaluated. Tg/TgAb serum levels and ^{18}FDG-PET/CT, and CEUS appearance were assessed at 6 and 12 months and compared with baseline. Complications were recorded.

Results: PLA was always feasible, and technical success was achieved in all patients. At 6 months, local control was achieved in 11 of 15 patients (73%), with 6 (40%) having serum Tg/TgAb normalized ($P = .017$ vs baseline). Whereas 20 of 24 (83%) nodes were negative at ^{18}FDG-PET/CT and CEUS ($P < .001$ vs baseline), 4 were ^{18}FDG-PET/CT-positive (3 also CEUS-positive). At the 12-month follow-up, local control was achieved in 10 of 14 patients (71.4%). Sixteen of 20 nodes (80%) were negative at ^{18}FDG-PET/CT and CEUS ($P < .001$ vs baseline), 4 were ^{18}FDG-PET/CT-positive (2 also CEUS-positive). Four of 10 (40%) patients had normalization of serum Tg/TgAb ($P = .098$ vs baseline). No major complications occurred.

Conclusions: PLA is potentially feasible, safe, and effective for the treatment of metachronous cervical nodal metastases from papillary thyroid carcinoma. This procedure may reduce or delay a large number of highly invasive repeat neck dissections. (***J Clin Endocrinol Metab* 98: E1203–E1207, 2013**)

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Abbreviations: CEUS, contrast-enhanced US; CT, computed tomography; ^{18}FDG, [^{18}F]fluorodeoxyglucose; PET, positron emission tomography; PLA, percutaneous laser ablation; Tg, thyroglobulin; TgAb, anti-Tg antibody; US, ultrasound.

Papillary thyroid cancer is the most frequent (about 85%) of all thyroid cancers (1, 2). Treatment is based on surgery followed by radioiodine ablation (3, 4).

Cervical nodal recurrence may occur in up to 30% of patients and requires repeated surgery and/or radioiodine ablation, which may be challenging or impossible to perform (3, 5, 6).

Percutaneous laser ablation (PLA) is a recent technique that has been successfully used for percutaneous ablation (7–9). The aim of our work was to assess the feasibility, safety, and effectiveness of percutaneous ultrasound (US)-guided laser ablation for the treatment of metachronous cervical lymph node metastases from papillary thyroid carcinoma with particular attention placed upon contrast-enhanced US (CEUS) and [^{18}F]fluorodeoxyglucose (^{18}FDG) positron emission tomography (PET) findings.

Subjects and Methods

Study population

Institutional review board approval was obtained, and patients' informed consent was waived.

We retrospectively reviewed our prospectively collected database of 19 patients treated with PLA between September 2010 and April 2012. Four patients without at least 6 months of follow-up were excluded. They did not have evidence of disease progression at last follow-up. Hence, 15 patients (8 males and 7 females, age 62 ± 14 years [mean ± SD]; range 32–80 years) were included in our series. A total of 24 metachronous nodal metastases (size range of 0.6–1.6 cm [mean 1.1 ± 0.4 cm]) were treated with PLA. All patients previously underwent surgery and radioiodine ablation and were at high surgical risk and had negative radioiodine scan and uptake of ^{18}FDG-PET/computed tomography (CT) in up to 4 lymph nodes.

Ablation procedure

Procedures were performed by 3 interventional radiologists with more than 10 years experience by using a commercially available US system with an integrated laser source (EchoLaser X4; Esaote, Genoa, Italy) under local anesthesia. A case is shown in Figure 1. Each lymph node was preoperatively evaluated by US and CEUS (Figure 1B). One or two (according to lymph node size and shape) introducer needles were inserted into the lymph node. Subsequently, a 300-μm quartz bare optic fiber with a plane cut tip was introduced and advanced up to the introducer needle tip (Figure 1C). The introducer needle was then withdrawn to expose the fiber by at least 5 mm. The optic fibers were then con-

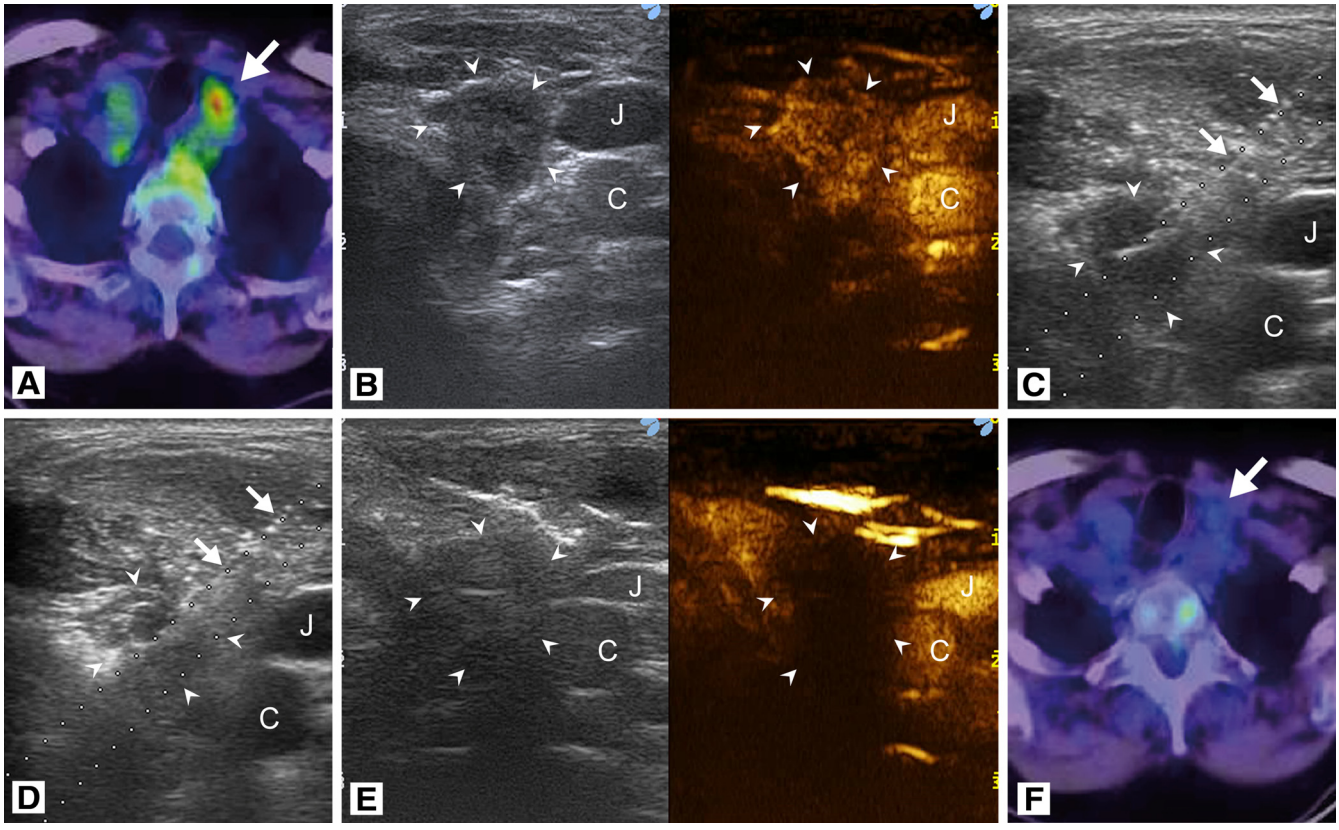

Figure 1. Percutaneous laser ablation of a metachronous cervical lymph node metastasis. Panel A, Preprocedural ^{18}FDG-PET/CT demonstrated high uptake in a lymph node in the neck (arrow) in a patient previously treated with total thyroidectomy and ^{131}I ablation for a papillary thyroid carcinoma. Panel B, CEUS demonstrated an 11-mm lymph node (arrowheads) with enhancement at the same level. Panel C, The lymph node (arrowheads) was treated by a percutaneous laser ablation under US guidance by 1 fiber insertion (arrows indicate needle with laser fiber). Panel D, Ultrasound monitoring of the procedure demonstrated gas formation at the level of the lymph node (arrowheads) during ablation (arrows indicate needle with laser fiber). Panel E, CEUS performed immediately after the ablation demonstrated a complete lack of enhancement at the level of the treated lymph node (arrowheads). Panel F, Follow-up ^{18}FDG-PET/CT demonstrated absence of uptake at the level of the treated lymph node (arrow). Abbreviations: C, carotid artery; J, jugular vein.

nected with the laser source, a continuous-wave Nd-YAG laser operating at 1.064 mm (EchoLaser X4; Esaote).

Each treatment was performed with a fixed-power protocol (3 W power), changing the application time case by case, trying to cover several millimeters more than volume of the nodule. Total energy deployment was maintained between 1200 and 4200 J. A new optic fiber was used when there was concern of charring around the first fiber that would prevent effective repeat treatment. After a few minutes (necessary to obtain the disappearance of gas formed during the ablation), CEUS was performed to assess the lack of enhancement (Figure 1E). In case of incomplete ablation, a subsequent ablation was performed.

Follow-up and endpoints

Technique feasibility was considered as the ability to target the lymph node and perform the ablation. Technical success was defined as complete absence of enhancement at CEUS at the end of every procedure.

All patients were followed at 6 and 12 months with US, CEUS, ^{18}FDG-PET/CT, and serum levels of thyroglobulin (Tg), and anti-Tg antibodies (TgAbs).

Local control was defined as absence of enhancement at CEUS and no uptake at ^{18}F-FDG-PET/CT.

Data analysis

Technique feasibility, technical success, and rate of complications were derived. Results of serologic tests (Tg and TgAb), and imaging findings (CEUS and ^{18}F-FDG-PET/CT) were analyzed at 6 and 12 months and compared with baseline by using Fisher's exact test. $P < .05$ was considered significant. For statistical analyses, GraphPad Prism version 5.0 (GraphPad Software Inc, San Diego, California) was used.

Results

Procedure results

In all cases, it was possible to correctly target the lymph node and to perform the ablation as planned. The procedures were well tolerated in all patients. Technical success was achieved in all cases. In 2 patients after the first ablation, CEUS showed residual enhancement into the treated lymph node, and a second PLA was performed in the same session (13.3% immediate retreatment rate). Results of serological tests in each patient and of imaging tests in each lymph node at 6 and 12 months are reported in Table 1.

The 6-month follow-up

Local control was achieved in 11 of 15 patients (73%). In 6 patients with proven local control, serum levels of Tg/TgAb were normalized ($P = .017$ vs baseline). In 2 of the remaining 5, distant progression was demonstrated, whereas in other patients, the reasons for elevation of serum levels of Tg/TgAb were not readily apparent. All 4 patients in whom local control was not achieved had also persistently elevated serum levels of Tg/TgAb. At imaging tests, 20 of 24 nodes (83%) were found negative at both ^{18}FDG-PET/CT and CEUS ($P < .001$ vs baseline), 3 were positive at both ^{18}FDG-PET/CT and CEUS, and 1 was positive at ^{18}FDG-PET/CT but negative at CEUS. No in-

Table 1. Data Regarding Follow-up of 15 Patients Treated With Percutaneous Laser Ablation of 24 Metastatic Lymph Nodes in the Neck From Papillary Thyroid Carcinoma

		Lymph Node				Baseline		6-Month Follow-up				12-Month Follow-up				
Patient	Age (y), Sex	No.	Size (mm)	Level	Side	Tg (ng/mL)	TgAb (IU/mL)	Tg (ng/mL)	TgAb (IU/mL)	CEUS	PET/CT	Tg (ng/mL)	TgAb (IU/mL)	CEUS	PET/CT	Progression Elsewhere
1	72, F	1	9	II	L	<0.2	<20	<0.2	<20	Neg	Neg	<0.2	<20	Neg	Neg	No
2	72, M	2	14	VI	R	27	<20	2.63	<20	Neg	Neg	70	<20	Neg	Neg	No
3	75, M	3	13	II	R	6.3	<20	<0.2	<20	Neg	Neg	2.4	<20	Neg	Neg	Lung progression
4	48, F	4	7	IV	L	4.4	<20	2.4	<20	Neg	Pos	1.9	<20	Neg	Pos	No
5	59, M	5	15	III	L	1	<20	<0.2	<20	Neg	Neg	1.2	<20	Neg	Neg	No
		6	8	III	L					Neg	Neg			Neg	Neg	No
		7	13	IV	L					Neg	Neg			Neg	Neg	No
6	73, F	8	7	III	L	3.4	<20	0.6	<20	Pos	Pos	0.6	<20	Pos	Pos	No
7	73, F	9	8	VI	L	<0.2	1931	<0.2	2625	Pos	Pos	<0.2	2524	Pos	Pos	No
8	60, M	10	15	III	R	0.5	<20	<0.2	<20	Neg	Neg	<0.2	<20	Neg	Neg	No
9	50, M	11	8	VI	L	<0.2	155	<0.2	88	Neg	Neg	<0.2	43	Neg	Pos	No
		12	8	IV	L					Neg	Neg			Neg	Neg	No
10	65, F	13	6	II	R	0.2	<20	0.6	<20	Neg	Neg	0.8	<20	Neg	Neg	Lymph node
		14	14	II	R					Neg	Neg			Neg	Neg	progression
11	78, F	15	12	III	L	0.3	<20	0.3	<20	Neg	Neg	2.6	<20	Neg	Neg	No
12	80, M	16	6	IV	R	1.8	<20	<0.2	<20	Neg	Neg	<0.2	<20	Neg	Neg	No
		17	9	IV	R					Neg	Neg			Neg	Neg	No
		18	16	V	R					Neg	Neg			Neg	Neg	No
13	32, M	19	15	III	R	13	<20	2.0	<20	Neg	Neg	2.9	<20	Neg	Neg	No
14	43, F	20	7	I	L	17.3	<20	16.6	<20	Neg	Neg	122	<20	ND	ND	Lung and lymph
		21	15	I	L					Neg	Neg					node progression
		22	7	I	L					Pos	Pos					
		23	14	I	R					Neg	Neg					
15	64, M	24	15	III	R	0.7	<20	<0.2	<20	Neg	Neg	<0.2	<20	Neg	Neg	No

Abbreviations: F, female; L, left; M, male; ND, not performed due to diffuse disease progression; Neg, negative; Pos, positive; R, right.

flammatory uptake around the treated lymph nodes was noted.

The 12-month follow-up

A patient with extensive disease progression was excluded from the 12-month follow-up. Local control was achieved in 10 of 14 patients (71.4%). In 4 patients with local control, serum Tg/TgAbs were normalized ($P = .098$ vs baseline). One previously negative patient developed metastatic lung disease. One patient became positive at Tg but did not have an identifiable site of production. All 4 patients in whom local control was not achieved also had elevated serum levels of Tg/TgAbs. One patient with positive serum tests and negative imaging at 6 months became positive at imaging at 12 months. In total, 16 of 20 nodes (80.0%) were found negative at both ^{18}FDG-PET/CT and CEUS ($P < .001$ vs baseline). Two nodes that were positive at ^{18}FDG-PET/CT and CEUS at 6 months remained positive at both imaging tests. One node that was positive at ^{18}FDG-PET/CT and negative at CEUS remained stable, whereas one previously negative at both imaging tests became positive at ^{18}FDG-PET/CT.

Complications

No immediate or late major complications occurred. One patient experienced a transient change in voice tone and a sense of discomfort in the neck after the procedure. No treatments were required, because both discomfort and voice change recovered spontaneously after 1 month.

Discussion

Our initial results show that PLA is feasible, effective, and safe for the treatment of metachronous cervical nodal metastases from papillary thyroid carcinoma and that this technique can potentially reduce the number of radical neck dissections in selected patients.

Several different techniques are now available for percutaneous treatments, such as ethanol injection, radiofrequency, microwaves, cryoablation, and laser ablation (7–13). PLA appears to have some advantages when dealing with neck pathologies. First, a very small needle can be used to reach the target, thus theoretically reducing problems in such a complex region. Moreover, thermal energy is deployed very precisely and in a highly predictable way, and small ablation volumes can be obtained, thus theoretically minimizing risks of burning undesired structures. To our knowledge, only a single brief report on 5 patients treated with PLA of metastatic lymph nodes in the neck from papillary thyroid carcinoma has been previously reported (9).

Judicious laser application in the hands of an experienced interventional oncology team likely led to the fact that there were no complications in our series. In our series, no track seeding occurred despite not activating the needle in pull-back given the short course and surrounding critical structures. Nevertheless, one potential risk of this technique is nerve damage caused by thermal injury. We believe that this risk can be mitigated by using low power and prolonging the time of the procedure to have a better control of the energy deployment.

By using PLA, 80% of lymph nodes in our series demonstrated complete ablation at 12 months follow-up after 1 single ablation session. These results are similar to those reported by Lewis et al (13), for whom 5 of 14 (35.7%) patients treated with percutaneous ethanol injection had initial treatment failure.

There is a wide debate now as to whether it is better to always perform lymph node dissection at the time of thyroidectomy or to perform lymph node dissection only in patients who develop metachronous metastases (14).

In our series, 3 patients developed distant metastases in the follow-up period and would not have benefited from surgical redissection. In these patients, a highly invasive neck redissection was spared. Thus, PLA may be used in a test-of-time approach to avoid the morbidity of a surgical operation in patients who finally will develop other or distant metastases. Moreover, PLA results in less scar formation than a surgical resection, without making subsequent surgery more difficult. If our results are confirmed, we envision a scenario where low-risk patients could be treated with thyroidectomy alone and with PLA in case of development of metachronous lymph node metastases, with the advantage of reducing the number of unnecessary preventive dissections and of minimizing the morbidity of a second operation in patients with metachronous lymph node metastases.

The best methodology for evaluating tumor response after thermal ablation is still debated, and evaluation of response is still not completely validated (15–17). ^{18}FDG-PET has been proven to have a high diagnostic accuracy regarding metachronous lymph node metastases from papillary thyroid carcinoma (18, 19). CEUS utility in percutaneous ablative treatments and in surgery has been reported, particularly for the liver (20). In our series, all patients in which local control was not achieved or who developed disease progression had elevated serum levels of Tg/TgAb, whereas all patients with negative serum levels of Tg/TgAb were found to have local control. Furthermore, at follow-up, all lymph nodes positive at CEUS were also positive at ^{18}FDG-PET/CT, whereas ^{18}FDG-PET/CT was able to detect incompletely ablated lymph nodes that were negative at CEUS. Thus, our experience supports the utility of ^{18}FDG-PET/CT over CEUS. Moreover, ^{18}FDG-PET/CT showed the advantage of identifying distant me-

tastases in 3 patients in our series. Thus, patients may be followed with Tg/TgAb serum levels, using ^{18}FDG-PET/CT when these serologic tests remain or convert to elevated levels. It is, however, worth stressing that CEUS was very helpful in monitoring the immediate result of the procedure (Figure 1E).

Some limitations of our study should be taken into account. First, this study does not provide comparison with repeat surgical management or other treatment alternatives. Second, because this was our initial experience with a novel technique, our results may be affected by a certain grade of inexperience. Moreover, we report only data about a relatively short follow-up period in a small series of patients affected by a slowly growing disease.

In conclusion, PLA likely represents a new option in the treatment of metastatic lymph node in the neck from papillary thyroid carcinoma. Such a technique appears to be safe, effective, and without major complications and may allow to completely treat or to avoid unnecessary surgery in a high number of patients. Although our results should be viewed as preliminary, further investigations are likely warranted to confirm these clinically favorable results.

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