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ORIGINAL ARTICLE

Ultrasound-guided Ethanol Ablation: Where does It fit in the Treatment of Recurrent Metastatic Papillary Thyroid Cancer?

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ABSTRACT

Introduction: Ethanol (ETOH) ablation of metastatic neck nodes has been described as a potentially safe and effective alternative to surgical excision. We sought to describe a subset of these patients well suited for ETOH ablation.

Materials and methods: We report ultrasound-guided ETOH ablation of metastatic papillary thyroid cancer (PTC) at a Tertiary Care Endocrine Surgery Unit over 5 years. A retrospective review of all reoperative lymph node dissections was undertaken. Ethanol injection was used as second-line treatment to operative excision and was standardized with ultrasound guidance and the use of 1 cc/cm^3 of 100% ETOH solution.

Results: Five treatments of ultrasound-guided ETOH ablation were studied. All patients had been previously treated with radioactive iodine (RAI) (mean: 1.25 treatments of 174mCi), however, in three cases with pretreatment I-131 scan, no uptake of radioiodine was seen in the treated disease. In four cases with pretreatment fludeoxyglucose-positron emission tomography (FDG-PET), treated lesions were avid. Median follow-up time for treatment was 28.5 months, with no disease progression in all ablated lesions. Serum thyroglobulin (Tg) values in patients without Tg-antibody were lower after treatment. There were no complications.

Conclusion: Surgeons seeking a less-invasive approach for nodal metastases in the neck can consider ETOH ablation. Small ultrasound detectable lesions in scarred necks (irradiated and/or reoperative) which are radioiodine non-avid and FDG-PET avid may be best suited for this treatment. As demonstrated by a small set of patients in a Tertiary Care Endocrine Surgery Unit, ETOH ablation is safe and effective at controlling progression of targeted local disease.

Keywords: Papillary thyroid cancer, Recurrent thyroid cancer, Surgeon performed ultrasound, Ultrasound-guided ethanol ablation.

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INTRODUCTION

Although papillary thyroid cancer (PTC) portends a very favorable prognosis compared to other cancers, 5 to 20% may develop recurrence in lymph nodes.[1] Patients with recurrent disease are at high risk for further episodes of recurrence and subsequent intervention. While repeat surgical excision is currently the mainstay of therapy, each repeated intervention carries with it increased surgical risk to parathyroid glands or the recurrent laryngeal nerve in the central neck, as well as carotid sheath structures and other major nerves in the lateral neck.

Ultrasound-guided ethanol (ETOH) ablation has been used in the past two decades to treat recurrent thyroid cancer in the cervical nodes. Nearly 200 cases have now been described in the literature demonstrating effectiveness and minimal morbidity.[2-9] What remains unclear is how ETOH injection fits into current endocrine surgical practice and which patients should be selected for treatment.

MATERIALS AND METHODS

Patients

A retrospective chart review was undertaken at a Tertiary Care Endocrine Surgical Unit in the USA. All reoperative neck dissections for recurrent PTC were reviewed and patients having ETOH ablation were selected for further analysis. Clinical information, such as demographics, previous operative history, ETOH ablation, and any morbidity or complications were collected. Pretreatment imaging was also reviewed where available, including radioactive iodine (RAI) scanning (both I-123 and I-131) as well as fludeoxyglucose-positron emission tomography (FDG-PET). Pre- and postintervention thyroglobulin (Tg) and Tg antibodies were reviewed. The protocol was approved by the University of California, San Francisco (UCSF) Committee for Human Research, the university's institutional review board.

Operative Strategy

After general anesthesia was induced, preoperative ultrasound was done either by the surgeon or interventional radiologist specializing in thyroid and neck ultrasound.

The lesions were evaluated for expected proximity to a functioning recurrent laryngeal nerve, and accessibility to needle localization. For percutaneous ETOH ablation, 1 cc/cm^3 or less of 100% ETOH was injected into the center of the suspicious lesion at a sufficient volume to ablate the node in its entirety. The extent of ETOH injection was guided by real-time ultrasound. Care was taken to avoid extravasation of ETOH into the surrounding tissues, especially close to the expected region containing the recurrent laryngeal nerve. Since we prefer surgical excision over ETOH injection, if a node was deemed to be resectable, we injected an equivalent volume 1:5 dilution of methylene blue dye instead of ETOH, which facilitated recognition of the involved nodes during reoperative exploration and surgical resection.

RESULTS

From 2009 to 2014, 149 reoperations for lymph node metastasis in the neck were performed by two surgeons, for all variants of PTC. Operations included 76 repeat central neck dissections (level VI) and 97 repeat lateral neck dissections (within levels I to V). Of these, there were five cases of percutaneous ETOH ablation which represent 3.4% of all reoperative lymph node dissections. Percutaneous ETOH ablation was used in the lateral compartment in four cases (4% of patients treated for recurrent lateral neck nodes), and used in the central neck in two cases (3% of patients treated for recurrent central neck nodes).

Patients undergoing ETOH ablation had an average of three prior neck operations. Mean size of treated lymph nodes was 1.17 cm (0.8–1.6 cm). After treatment, mean decrease in size of lymph node was 0.8 cm (0–1.6 cm) with one lymph node (initially 0.8 cm) completely disappearing. No lymph nodes increased in size after treatment or were subsequently excised after ETOH ablation (Table 1).

Serum thyroglobulin (Tg) decreased after ETOH ablation (when anti-Tg antibodies were absent). Mean pretreatment Tg was 390 ug/L, which fell to 86 ug/L after ablation. All patients had previous RAI treatment, with a mean of 1.25 treatment episodes with a mean dose of 174 mCi; however, all RAI scans prior to ETOH ablation, when negative, were negative. The FDG-PET scans were performed in four of five cases prior to ETOH treatment, all of which showed uptake of FDG within the target neck lesions. There were no posttreatment PET scans. No patients were treated with external beam neck irradiation. Mean follow-up was 35 months, and all patients are currently still alive.

There were no complications of percutaneous ETOH ablation, specifically no reported posttreatment pain, hoarseness, or dysphagia. All patients had same day (<24 hours) discharge. In the surgical reoperative neck dissection group, there were four recurrent laryngeal nerve injuries (2.7%) and one tracheal perforation (0.7%), in addition to usual postoperative pain associated with an incision. No patients had postoperative hypocalcemia.

DISCUSSION

Our experience with ultrasound-guided percutaneous ETOH ablation of metastatic PTC in the neck demonstrates good clinical effectiveness and low morbidity, which echoes the results of previously reported literature.[2-9] One important difference is that our treatment takes place in the operating room after induction of general anesthesia and not under local anesthetic in the clinic setting as others have described. If at all possible we prefer to surgical excision with blue-dye localization to treat recurrent PTC metastasis in the neck. We reserve ETOH ablation as second line, specifically for patients whose risk for excision is high because of multiple prior surgical interventions or in difficult locations, such as low in level IV or very far posterior location. In general, RAI scan non-avid and FDG avid recurrences are considered clinically more aggressive.[10,11] The five interventions of ETOH ablation described here were not good candidates for further RAI treatment, given that none had positive RAI avidity. We consider FDG avidity as a relative indication for resection, and if not possible, ETOH injection ablation.

Table 1: Demographics

				Pretreatment				*Posttreatment*	
Case	*Age*	*Gender*	*Location (level)*	*Size (cm)*	*Tg (ug/L)*	*I^{131} scan*	*FDG-PET*	*Size (cm)*	*Tg (ug/L)*
1	85	F	RL (IV)	1.2	48	Np	Avid	1.0	77
2	62	F	LL (IV)	0.9	1256	Np	Np	0.6	171
3	52	M	RC (VII)	0.8	33.1	Non-avid	Avid	–	11.3
			LL (II)	1.3				0.9	
4	64	M	LC (VI)	1.6	*	Non-avid	Avid	1.5	*
			LL (II)	1.4				1.4	
5	64	M	LC (IV)	1.0	223	Non-avid	Avid	0.9	83.7

F: Female, M: Male, RL/C: Right lateral/central, LL/C: Left lateral/central, NP: Not performed; *Undetected

Operative Field and Ultrasound View

All patients had advanced recurrent disease which had undergone multiple operations in the past. On average, patients selected for ETOH ablation had three previous operative interventions. Patients after multiple operations have scar which increases risks to major structures, such as the recurrent laryngeal nerve and trachea when dissection is attempted. Deeper lesions in the neck require increased dissection, making this situation an agreeable scenario for percutaneous ETOH ablation.[6] A clear intraoperative ultrasound view of the target lesion is imperative for access with a percutaneous approach. Therefore, in addition to preoperative ultrasound localization, a good intraoperative view is necessary to proceed with ETOH injection (Fig. 1). In this example, the operating room setup is seen and the ultrasound image clearly delineates a target lesion just lateral to the jugular vein (Fig. 2, Movie 1). Percutaneous access with a 27 gauge needle can be easily obtained and the tip is seen within the center of the node.

Radioactive Iodine and FDG PET

While all of the patients had FDG avid scans, their RAI scans were negative. Tumors expressing this imaging pattern have been shown by Palmedo et al to represent more dedifferentiated lesions.[12] Schreinemakers et al showed that metastatic lesions in the neck or mediastinum which are PET positive portend a worse prognosis than PET negative lesions. Robins et al echoed this idea and further correlated PET positivity with mortality. Further outcome analysis showed that loco-regional control may be obtained if these lesions are therapeutically managed.[10] Overall, lesions which are both FDG avid and RAI non-avid are more aggressive, lending further support for local palliative control with ETOH ablation when surgical excision is not possible.[10-13]

There are several important limitations to this study. The study group is small; only about one in 30 patients who needed reoperative node dissection underwent ETOH injection. There is obviously a selection bias, since our surgeons prefer resection over ETOH injection. Most of these cases were planned, since the possibility of difficulty for resection was appreciated in the planning of operation. At UCSF, ETOH injection is still considered a second-line alternative rather than primary locoregional treatment. ETOH injection, however, provides the surgeons an alternative in situations where resection is difficult or is associated with higher risks. This patient selection bias, however, is tempered by the process at our Tertiary Care Endocrine Surgery Unit with the use of multidisciplinary thyroid cancer tumor board conference. Within this conference, each complex thyroid cancer patient is presented and consensus for treatment including possible ETOH is reached. Members of the tumor board rounds consist of surgeons, endocrinologists, pathologists, radiologists, nuclear medicine physicians, and radiation oncologists.

In addition, most lymph nodes in our series as well as those described in the literature are under 2 cm. Further, most ETOH ablated lymph nodes are solitary or potentially a small number of adjacent nodes. Both large or numerous lymph nodes would be difficult to manage with ETOH ablation and may be better candidates for surgical excision or other adjuvant therapies. This constraint potentially limits the broad applicability of ETOH ablation in the treatment of metastatic PTC.

Fig. 1: Operating theater setup for ultrasound-guided ETOH ablation or preexcision blue-dye injection

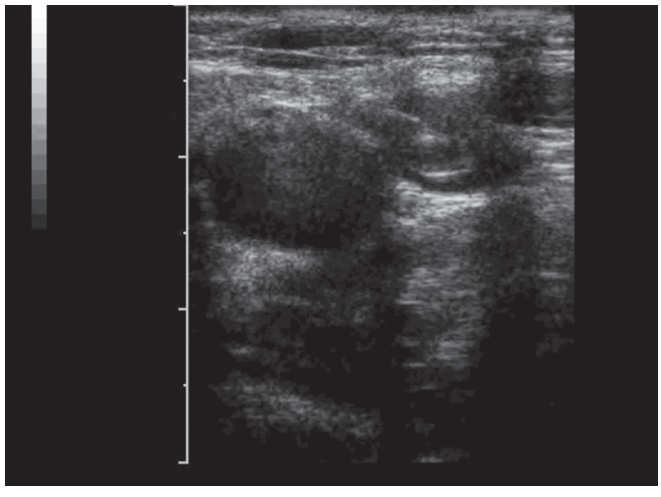

Fig. 2: Ultrasound image depicting image-guided needle insertion into small lymph node lateral to the internal jugular vein. Once the needle tip is seen within the center of the lymph node, ETOH or blue dye is injected

CONCLUSION

Ultrasound-guided ETOH ablation appears to be both effective and safe. It is used as a second-line alternative to surgical resection for regional nodal metastasis for thyroid cancer. In our center we use ETOH injection for those with small volume nodal recurrence in a surgically difficult reoperative field, such as deep nodes in a scarred neck. These patients usually have RAI non-avid and FDG-PET avid lesions. Because we use ETOH ablation technique only in the operating room under anesthesia, its use is limited to fewer than 5% of our patients with recurrent PTC in the neck.

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