—Original Article—

Endosonographic examination of thyroid gland among patients with nonthyroid cancers

Amer A. Alkhatib[1,2], Abdulah A. Mahayni[1], Ghaleb R. Chawki[1], Leon Yoder[1], Fateh A. Elkhatib[3], Mohammad Al-Haddad[2]

[1]Southwestern Regional Medical Center, Cancer Treatment Centers of America, Tulsa, OK, USA, [2]Department of Gastroenterology, Digestive Disease Institute, Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE, [3]Division of Endocrinology, INTEGRIS Southwest Medical Center, OKC, OK, USA

ABSTRACT

Objectives: There is limited endosonographic literature regarding thyroid gland pathology, which is frequently visualized during upper endoscopic ultrasound (EUS). Our objective was to assess the prevalence of benign and malignant thyroid lesions encountered during routine upper EUS within a cancer center setting. **Materials and Methods:** The data were prospectively collected and retrospectively analyzed. All upper EUS procedures performed between October 2012 and July 2014 were reviewed at a large referral cancer center. Data collected included patient demographics, preexisting thyroid conditions, thyroid gland dimensions, the presence or absence of thyroid lesions, and EUS morphology of lesions if present, and interventions performed to characterize thyroid lesions and pathology results when applicable. **Results:** Two hundred and forty-five EUS procedures were reviewed. Of these, 100 cases reported a detailed endosonographic examination of the thyroid gland. Most of the thyroid glands were endosonographically visualized when the tip of the scope was at 18 cm from the incisors. Twelve cases showed thyroid lesions, out of which three previously undiagnosed thyroid cancers were visualized during EUS (two primary papillary thyroid cancers and one anaplastic thyroid cancer). Transesophageal EUS-guided fine needle aspiration of thyroid lesions was feasible when the lesion was in the inferior portion of the thyroid gland, and the tip of the scope was at 18 cm or more from the incisors. **Conclusions:** Routine EUS examination may detect unexpected thyroid lesions including malignant ones. We encourage endosonographers to screen the visualized portions of the thyroid gland during routine withdrawal of the echoendoscope.

Key words: Cancer, endoscopic ultrasound, endoscopic ultrasound-guided fine needle aspiration, fine needle aspiration, thyroid

INTRODUCTION

Upper endoscopic ultrasound (EUS) is frequently performed in patients with various cancers for diagnosis, staging, restaging, and for endosonographic interventions (e.g., celiac plexus neurolysis, placement of fiducial markers, and others). Furthermore, EUS is more commonly used in general gastrointestinal practice to evaluate for pancreatic and biliary diseases.

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Address for correspondence
Dr. Amer A. Alkhatib, Room C 06-233, Digestive Disease Institute, Cleveland Clinic Abu Dhabi, PO Box 112412, Abu Dhabi, UAE.
E-mail: khatibamer@yahoo.com
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Several other organs are visualized by EUS due to proximity to gut wall but are not routinely assessed by endosonographers. During EUS examination, the thyroid gland is frequently noted during withdrawal of the scope. However, there is scant literature about endosonographic findings of the thyroid gland in general and in cancer patients specifically.

We conducted a retrospective study in a cancer center in the USA to describe the endosonographic findings of the thyroid gland. To the best of our knowledge, this study represents the first attempt at describing EUS findings of the thyroid gland. The secondary aim of the study was to assess the prevalence of incidental thyroid cancer diagnosed during routine upper EUS performed in patients with other malignancies.

MATERIALS AND METHODS

Clinical data were prospectively collected over 21 months (October 2012 to June 2014) and retrospectively analyzed in a cancer center after the Institutional Review Board of Cancer Treatment Centers of America approved this study. We reviewed the medical records of all patients who underwent upper EUS in our institution. We excluded patients in whom EUS findings of the thyroid gland were not reported. Collected data included patient age, gender, body mass index, history of previous thyroid disease, and type of preexisting nonthyroid cancer. All patients underwent deep sedation using propofol administered by anesthesiologists. All procedures were performed by two endosonographers; each having performed more than 500 prior examinations. In each case, the thyroid gland was examined with either the radial or linear EUS scope or both. All the procedures were performed under monitored anesthesia care.

The thyroid gland was best visualized during withdrawal of the echoendoscope in the upper esophagus between 16 and 22 cm from the incisors while remaining distal to the cricopharyngeus muscle. The tip of the scope was kept in the straight position, whereas the scope faced anteriorly when linear scope was utilized. All fine needle aspirations (FNAs) were performed using 22-gauge needles when EUS-guided sampling was performed. Furthermore, we noted the endosonographic descriptions of the thyroid gland including the presence of thyroid cysts, solid nodules, size of cyst/nodules, and whether EUS-guided FNA was attempted, and whether conventional transcutaneous thyroid ultrasound (US) or FNA was performed at any point in time. Detailed review of the final cytology reports was performed and reported.

RESULTS

Two hundred and forty-five EUS procedures performed by two different gastroenterologists were reviewed. Of those, there were 100 patients (52 males, median age of 54 years, range 29–84), whose reports included a detailed description of the thyroid gland. In most of the cases, the thyroid gland was endosonographically visualized when the tip of the EUS scope was in the upper third of the esophagus right below the cricopharyngeus, approximately 18 cm from the incisors. Overall, thyroid tissue was noted as distal as 20–22 cm from the incisors and as proximal as 15 cm from the incisors. It should be noted that, in most of the cases, the right lobe of the thyroid gland was more readily visualized than the left lobe.

Table 1 lists the 12 cases in which EUS revealed abnormal findings of the thyroid gland on EUS. Few of these cases required further testing such as conventional thyroid US with and without FNA. In some cases, EUS-FNA was performed, specifically when it was felt that the lesion was not amenable to percutaneous sampling under conventional thyroid US guidance due to its retrosternal location.

FNA was performed using 22-gauge needles (Expect Needles®, Boston Scientific, Natick, MA, USA). One or more passes were made using the fanning technique without suction. Rapid on-site examination of the specimens was available for one case only. For the rest of the cases, the specimens were collected in CytoLyt® solution Hologic (Marlborough, Massachusetts, USA) and then sent to the cytology laboratory for interpretation. Core biopsies were not obtained. Three patients (3%) were found to have unexpected thyroid cancers that were either missed or not found on previous radiographic studies performed before EUS. Two patients were diagnosed with papillary thyroid cancer [Figures 1-3] and one with poorly differentiated thyroid cancer [Figure 4]. Table 1 summarizes the endosonographic description of these tumors. Two of the tumors showed internal vascularity on color flow assessment [Figure 1]. After establishing the diagnosis, the first patient was referred to an oncologist and surgeon. Both opted to follow-up the patient with US (transcutaneous). One year later, thyroid US showed no progression of his tumor. Given

Table 1. Patients with positive endosonographic findings on EUS examination of the Thyroid gland

Age	Gender	Established cancer	Endosonographic findings	Right or left lobe	Presence of internal vascularity	Largest diameter (mm)	Methods of performing FNA	Nature of thyroid lesion
66	Male	Esophageal adenocarcinoma (in remission)	Rounded, hypoechoic, well-defined mass	Right	Yes	17	Endosonographic-guided expect (22-gauge), two passes	Primary papillary thyroid cancer
61	Male	Rectal cancer and gastric GIST	Rounded, hypoechoic with what appeared to be cystic changes. Well defined	Right	Yes	20	Endosonographic-guided expect (22-gauge), two passes	Primary papillary thyroid cancer
60	Female	Carcinoma of unknown origin	Irregular shape, well-defined, hypoechoic	Right	Was not documented	38	Transcutaneous-guided thyroid biopsy 22 gauge FNA (5 passes)	Anaplastic thyroid cancer
63	Male	Esophageal adenocarcinoma	Heterogeneous mass	Right	No	25	Transcutaneous US-guided 22-gauge needle, 2 passes	Benign colloid nodule
78	Male	Rectal cancer	Round well-defined anechoic large cyst in the right thyroid	Right	No	19	FNA was not performed	Cyst
62	Female	Gastric lipoma	Several subcentimeter round hypoechoic and anechoic lesions in both lobes	Both	No	13	Followed with her primary care provider	Unknown
38	Female	Endometrial cancer	Round with mixed echogenicity in the right lobe	Right	No	10	Transcutaneous US-guided 22-gauge needle, 4 passes	colloid nodule with cystic degeneration
50	Female	Papillary thyroid cancer and GIST	Hypoechoic thyroid mass	Right	Yes	26	FNA was not performed. Patient presented for EUS with established diagnosis of papillary thyroid cancer	Papillary thyroid cancer
56	Female	Adenocarcinoma of unknown origin	Ill-defined hypoechoic area	Right	No	13	Patient did not follow-up with the clinic	Patient did not follow-up with the clinic
47	Female	Small cell lung cancer	Anechoic well-defined lesion [Figure 5]	Left	No	12	NA	Cyst
60	Female	Pancreatic adenocarcinoma	Small hypoechoic lesion	Left	No	6	FNA was not performed	NA
53	Female	Gastric cancer	Small hypoechoic lesion	Right	No	3	Patient went to hospice	Patient went to hospice

GIST: Gastrointestinal stromal tumor, FNA: Fine needle aspiration, US: Ultrasound, EUS: Endoscopic ultrasound, NA: Not available

the fact that the patient's original cancer was in remission for 2 years, the patient was offered two options: Surgical resection of the tumor or following up with another thyroid US in 6 months. The patient opted to be followed by thyroid US in 6 months.

The second patient had advanced rectal cancer, gastric gastrointestinal stromal tumor, and papillary thyroid cancer. It was decided to follow the patient with thyroid US in 6 months.

The third patient presented with a cancer of an unknown origin. During upper EUS examination, a large thyroid mass was noted. The patient was sent for transcutaneous US of the thyroid with FNA. The result of the core thyroid biopsy was consistent with anaplastic cancer. The patient opted to pursue hospice care and succumbed to her disease within a month.

During EUS examination, we did not detect any local extension of the tumor to the esophageal wall or cervical nodes in any case. However, in the case of the patient with anaplastic thyroid cancer, mediastinal lymph nodes were noted on the EUS examination but not biopsied.

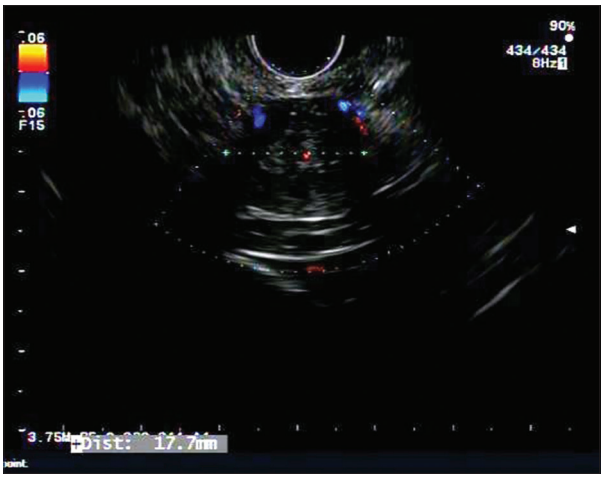

Figure 1. Endosonographic image showing hypoechoic thyroid lesion with intranodule vascularity. Final fine needle aspiration was consistent with primary papillary thyroid carcinoma

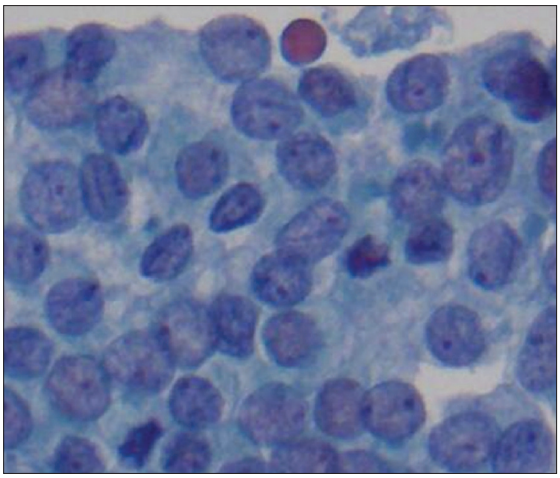

Figure 2. Cytological image (Papanicolaou, ×40) of primary papillary thyroid carcinoma. Nuclear grooving was seen consistent with thyroid papillary carcinoma, the diagnosis was established by endoscopic ultrasound-guided fine needle aspiration

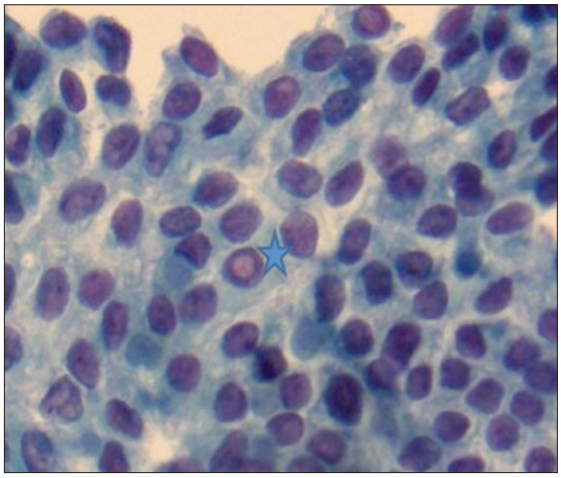

Figure 3. Cytological image (Papanicolaou, ×40) of primary papillary thyroid carcinoma. Intranuclear inclusions (star) was seen consistent with thyroid papillary carcinoma, the diagnosis was established by endoscopic ultrasound-guided fine needle aspiration

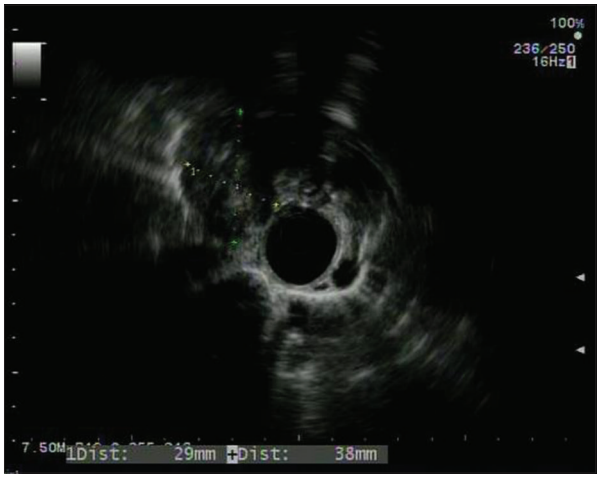

Figure 4. Endosonographic image showing hypoechoic thyroid lesion. Transcutaneous fine needle aspiration was consistent with poorly differentiated thyroid cancer

DISCUSSION

Around 4%–7% of the adults in the United States have a palpable thyroid nodule; however, only 5% of clinically recognized thyroid nodules are malignant. The rest of the nodules represent colloid nodules, cysts, and thyroiditis, accounting for 80% of these nodules. Benign follicular neoplasms are seen in 10%–15% of the cases.[1]

This is the first study that describes endosonographic findings of the thyroid gland during a routine upper EUS. Medical literature about the role of EUS in identifying thyroid lesions is limited. Thyroid lesions found during routine EUS have been reported in case reports.[2] In addition, EUS-guided FNA of thyroid lesions was described in three separate case reports.[2-4] FNA in these case reports detected benign goiter,[3] Hurtle cell neoplasm,[4] and primary papillary thyroid cancer.[2]

In addition, EUS was reported to be more sensitive in detecting esophageal invasion by thyroid cancer, especially in tumors involving lower and middle lobes, than esophagography, esophagoscopy, and MRI.[5,6] Nonetheless, EUS examination of the thyroid gland has its limitations because it cannot visualize the upper lobes of the thyroid gland.[6] From our experience, to achieve a good examination of the upper portions of the thyroid gland, the EUS scope should be stationed in the pharynx or very close to the upper esophageal

Figure 5. Endosonographic image of benign thyroid cyst. Fine needle aspiration was not performed due to benign features and lack of high-risk stigmata

sphincter. This position is unstable and usually induces gag reflex and patient's discomfort. The other way to achieve a better visualization of the superior portion of the thyroid gland is to station the tip of the scope distal to the upper esophageal sphincter and then attempt to deflect the tip of the scope upward. However, this position can also induce patient's discomfort and can be associated with esophageal trauma.

A thyroid nodule is a sonographically distinguishable lesion within the thyroid parenchyma.[7] US can characterize thyroid nodules by their size, echogenicity, composition, the presence or absence of calcifications, a halo, irregular margins, and internal blood flow.[7] The relationship between the size of the nodule and the risk of thyroid cancer is controversial.[7-9] Large retrospective study suggested that the risk of thyroid cancer increases in nonlinear mode in relation to the size of the nodule. However, the papillary cancer risk is unchanged once the nodule size exceeds 2 cm. Nonetheless, the risk of follicular thyroid cancer and other rare thyroid malignancies increases as the nodule size increases even beyond 2 cm.[9]

Beside nodule size, several other US features can help determine if a nodule is malignant including calcifications, hypoechogenicity, irregular margins, the absence of hypoechoic halo around the nodule, predominantly solid composition, and intranodule vascularity.[7] Furthermore, the sensitivities and predictive values of these measures vary significantly among different studies, and none of these measures is both highly sensitive and highly predictive for thyroid cancer. However, combining these measures improve predictions significantly.[7] Assessing multiple ultrasonographic measures can help refine the diagnosis of a nodule as benign or malignant, particularly the measures of solid composition (most sensitive sign), microcalcifications (the sign with highest positive predictive value), and internal vascularity (by Doppler ultrasonography).[7] Nonetheless, it is important to bear in mind that none of the ultrasonographic signs are diagnostic for thyroid cancer.[7] Because many of these measures from US can be similarly be assessed using EUS, this can offer an additional method of diagnosis through FNA.

For the same reason, it is common to pursue cytological diagnosis by performing FNA of thyroid nodules.[8] Due to high prevalence of thyroid nodules, different studies attempted to establish ultrasonographic signs that predict malignant thyroid nodules. One study suggests that US-guided FNA should be performed on all 8–15 mm hypoechoic nodules with irregular margins, intranodular vascular spots, or microcalcifications. If lesions of the thyroid have no high-risk US features, the study suggests that it should be evaluated clinically and sonographically within 6–12 months. The study emphasizes that it places a minimum diameter of 8 mm on FNA to avoid large-scale treatment with thyroidectomy, and to ensure cost-effectiveness.[8]

Guidelines published by the Society of Radiologists in Ultrasound in 2004 and 2006 recommend FNA differentially based on specific lesion criteria. The guidelines strongly recommend FNA for single nodule >1 cm in diameter with microcalcifications, single nodule >1.5 cm in diameter which is almost entirely solid or with coarse calcifications.[7] In addition, the guidelines recommend to consider FNA for a nodule >2 cm which is mixed between cystic and solid or have some solid mural. Furthermore, the guidelines recommend considering FNA for nodules with substantial growth since the previous US examination. On the other hand, the guidelines discourage FNA if the nodule is almost entirely cystic and fits none of the previous criteria (microcalcifications, solid mural component, and substantial growth since the last examination).[7] The guidelines suggest that, when confronted with multiple nodules, one should consider FNA for more than one nodule if the nodules exhibit any of the above characteristics.[7,10] Finally, if a lymph node appears abnormal regardless of the US criteria, a

biopsy of the lymph node and/or the ipsilateral thyroid nodule is strongly recommended.[7]

In our study, unexpected thyroid cancers were detected in 3% of patients who underwent EUS examination of the thyroid gland. A large American autopsy study reported that around 3% of patients with cancers have metastatic disease to the thyroid gland.[11] Nonetheless, we did not detect any metastatic disease in the thyroid gland during EUS examination. This could have been due to the small sample size and the limitations of EUS in visualizing the entire thyroid gland. In addition, the lesions found during the autopsy study might have been microscopic metastases, which EUS cannot detect. Nonetheless, the reported 3% incidence of metastatic lesions seen in the thyroid gland suggests that any suspicious lesion seen in the thyroid gland in patient with known cancer should be evaluated in the case noted during EUS examination.

The main limitation of the study includes its retrospective nature. Furthermore, the cohort of this study comprises patients from a cancer center, and thus the findings may not be generalized to the general population.

We do not suggest or support the use of EUS solely to examine the thyroid gland. However, this study urges endosonographers to examine the thyroid gland while withdrawing the scope. Because thyroid cancer is common with estimated 62,000 new cases to be diagnosed in 2015 in the USA, with a lifetime risk of 1.1%, endosonographers outside cancer centers may detect incidental thyroid cancers.[12]

Furthermore, we do not recommend the routine use of endosonographic-guided FNA of a thyroid lesion. However, FNA of a thyroid lesion may be reasonable option and useful in patients with a retrosternal thyroid mass that is not amenable to the conventional transcutaneous FNA. Our experience with endosonographic-guided FNA of a thyroid lesion is limited. Nonetheless, we noticed that a thyroid lesion visualized in the very proximal esophagus can be difficult and challenging to target using EUS-guided FNA due to patient discomfort and instable scope positioning at this location. Furthermore, the operator may need to deflect the tip of the scope to visualize the superior part of the thyroid gland well. During this process, we discourage applying excessive pressure on the proximal esophagus for two reasons: First to avoid injury to the proximal esophagus and upper esophageal sphincter, and second: The lesions in the superior part of the thyroid gland are usually accessible by conventional transcutaneous US-guided biopsies. From our limited experience, thyroid lesions seen by EUS at 18 cm or more distally from the incisors are technically easier to target using EUS-guided FNA than lesions more proximal to that. Finally, we believe that using deeper sedation (e.g., propofol) is essential to facilitate EUS-guided FNA because of the poor tolerance. Patients may have to FNA performed from the proximal esophagus with moderate sedation.

CONCLUSION

Thyroid examination during upper EUS should be performed in patients with cancers because malignant thyroid lesions can occasionally be visualized during routine upper EUS. FNA of these lesions should be considered transcutaneously, or transesophageally if not amenable to transcutaneous route. Endosonographic signs that raise concerns of a malignant lesion in the thyroid gland include the presence of internal vascularity on color flow assessment and the lesion is more than 1 cm. The literature from the conventional transcutaneous thyroid US lists different sonographic signs that raise concerns of thyroid cancer. While these signs can serve as a guide, further studies are needed to examine if these sonographic signs are applicable to EUS.

Because EUS cannot visualize the entire thyroid glands, EUS should not substitute conventional transcutaneous thyroid US. Nonetheless, EUS of the thyroid gland can be considered in cases where traditional transcutaneous FNA of a thyroid lesion is not feasible such as lesions which have a retrosternal location. Further prospective studies are needed for characterization of the role of EUS in detecting thyroid lesions.

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Conflicts of interest
There are no conflicts of interest.

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