Intratracheal ectopic thyroid tissue: A case report and literature review

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Abstract

We discuss a case of intratracheal ectopic thyroid tissue (ETT) that was retrieved from the files of the Otorhinolaryngic–Head and Neck Pathology Registry at the Armed Forces Institute of Pathology. The patient was a 54-year-old man who had a history of papillary thyroid carcinoma, which had been treated with a subtotal thyroidectomy. During routine follow-up 4 years later, the patient's primary care physician detected an elevated thyroglobulin level. Further referrals and evaluations revealed that the patient had intratracheal ETT. The patient refused to undergo surgical excision and remains without evidence of recurrent carcinoma. In a MEDLINE literature review, we found only 13 other well-documented cases of intratracheal ETT since 1966; in all but two cases, patients had benign disease. Once the possibility of thyroid carcinoma has been eliminated by histologic examination, intratracheal ETT can be managed by complete surgical excision with the prospect of an excellent long-term clinical outcome.

Introduction

Ectopic thyroid tissue (ETT) can be found anywhere along the embryologic "path of descent" of the thyroid gland, and it has been documented in the tracheal lumen. Patients with intratracheal ETT usually have signs of dyspnea or upper airway obstruction, although the nature of the signs and symptoms depends on the size and location of the ectopic nest. Numerous factors are believed to affect the size of ETT, and varying levels of hormone stimulation appear to play a major role. ETT can be either benign or malignant; the most common thyroid malignancy is papillary thyroid carcinoma. Neoplasms of the thyroid gland can invade the tracheal wall and give rise to the development of thyroid tissue in the trachea. This locoregional spread must be distinguished from a malignancy arising in intratracheal ETT.

Only 13 well-documented cases of intratracheal ETT have been previously reported in the English-language literature since 1966 (table).[1-13] In this article, we describe a previously unreported case, and we review what has been published on this rare lesion, with emphasis on the features necessary for its diagnosis.

Case report

We reviewed the files of the Otorhinolaryngic–Head and Neck Pathology Registry at the Armed Forces Institute of Pathology and found a case of intratracheal ETT. For the purposes of this report, information contained in this file was supplemented by a review of the patient's clinical record, operative report, and surgical pathology reports. Additional clinical details and follow-up information were obtained from the treating physicians. Hematoxylin and eosin-stained slides were reviewed to confirm the diagnosis. Our clinical investigation was conducted in accordance and compliance with all statutes, directives, and guidelines contained in the Code of Federal Regulations, Title 45, Part 46, and in Department of Defense Directive 3216.2 relating to human subjects in research.

The case involved a 54-year-old man who had visited his primary care physician for routine medical care. Four years earlier, the patient had been diagnosed with papillary thyroid carcinoma. He was treated with a right lobectomy and isthmusectomy at that time. There was no nodal involvement, and the lesion was classified as a clinical stage I tumor. The left lobe was described as atrophic, and no additional surgery was performed. The

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Originally presented at the 105th annual meeting of the Triological Society; May 12-14, 2002; Boca Raton, Fla.

The opinions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of Defense.

Table. Review of cases of intratracheal ETT reported since 1966

Case report	Age/ sex	Initial symptom	Tumor size	Diagnosis	Initial treatment	Outcome
Myers and Pantangco, 1975[1]	56/F	Dyspnea	3 cm	ETT*	Bronchodilation	Alive; NED*
Rotenberg et al, 1979[2]	47/F	Hemoptysis	3 cm	ETT, PC*	Radiation	Alive; NED
Donegan and Wood, 1985[3]	31/F	Neck swelling, dyspnea	2 cm	ETT	Surgical excision	Alive; NED
Ferlito et al, 1988[4]	77/M	NR*	NR	ETT	NR	Alive; NED
Chanin and Greenberg, 1988[5]	Birth/M	Dyspnea, respiratory distress	0.5 cm	ETT	Hormone suppression	Alive; NED
Osammor et al, 1990[6]	57/M	Hoarseness, dyspnea, hemoptysis	2.5 cm	ETT	Surgical excision	Alive; NED
Ogden and Goldstraw, 1991[7]	43/F	Stridor, dyspnea	2 cm	ETT	Surgical excision	Alive; NED
al-Hajjaj, 1991[8]	30/F	Wheezing, dyspnea on exertion	1 cm	ETT	Bronchodilation	Alive; NED
Soylu et al, 1993[9]	32/F	Dyspnea	NR	ETT	CO_2 laser	Alive; NED
Muysoms et al, 1997[10]	62/F	Dyspnea, cough	1.5 cm	ETT	Surgical excision	Alive; NED
See et al, 1998[11]	33/M	Stridor	NR	ETT	Surgical excision	Alive; NED
Hari et al, 1999[12]	64/M	Stridor	NR	ETT, PC	Radiation	Died of lung metastases
Dossing et al, 1999[13]	27/F	Dyspnea during pregnancy	2 cm	ETT	Surgical excision	Alive; NED
Byrd et al, 2003†	54/M	None	2 cm	ETT	Refused surgery	Alive with residual disease

** ETT = ectopic thyroid tissue; NED = no evidence of disease; PC = papillary carcinoma; NR = not reported.*
† Present case.

patient was placed on thyroid hormone replacement therapy, and he had been monitored with routine laboratory evaluations and radiographic studies. He had not received radioactive iodine (^{131}I) ablation therapy or chemotherapy.

During the most recent follow-up visit with his primary care physician, the patient denied any shortness of breath, dysphagia, odynophagia, or hoarseness, and examination revealed no signs of a palpable neck mass, thyrotoxicosis, or myxedema. However, the patient was considered to be less than compliant with his medication regimen.

Laboratory investigation indicated that the patient's thyroid function was abnormal. His thyroid-stimulating hormone (TSH) level was 24.3 μU/ml (normal: <10), his free thyroxine (T_4) level was 9.4 ng/dl (normal: 0.8 to 2.3), and his triiodothyronine uptake (T_3RU) was 38.6% (nor-

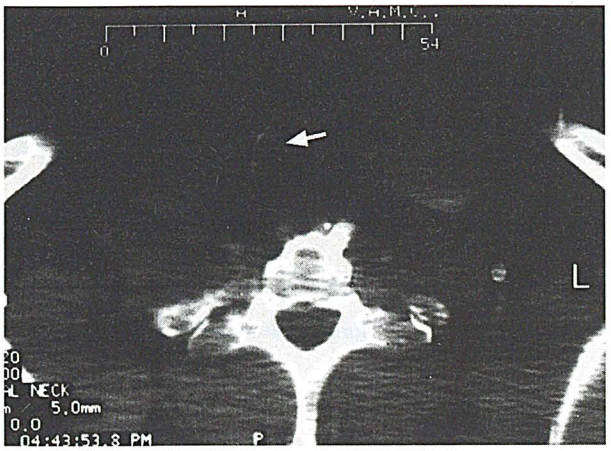

Figure 1. CT of the soft tissues of the neck demonstrates the intratracheal mass (arrow) immediately below the true vocal folds. The lesion measures approximately 2 cm at its widest point.

mal: 25 to 38%). These findings prompted an endocrinology consultation for optimal management of the patient's abnormal thyroid function. The endocrinologist's evaluation revealed that the patient's thyroglobulin level was markedly elevated at 1,360 ng/ml (normal: 3 to 40), which raised the possibility of a thyroid carcinoma.

Magnetic resonance imaging of the neck was obtained to exclude recurrent disease. A luminal density was noted in the trachea, along with a thickening of the lateral pharyngeal wall that involved the pyriform sinuses and epiglottis. Computed tomography (CT) disclosed the presence of a 2-cm soft-tissue mass at the level of the first tracheal ring (figure 1). Scattered lymph nodes in the submental, submandibular, jugular, and spinal accessory chains were seen, but their size did not indicate the presence of pathology.

In light of these radiologic findings, the otolaryngologist elected to proceed with direct laryngoscopy and biopsy of the subglottic mass. At laryngoscopy, a smooth right-anterior submucosal mass was identified approximately 1 cm below the true vocal fold. The mass was biopsied and found to be extremely vascular. Microscopic examination demonstrated a pseudostratified respiratory epithelium overlying a focus of thyroid tissue (figure 2). In order to exclude the possibility of a well-differentiated recurrent carcinoma, an expert pathology consultation was sought. We noted no histologic features of thyroid carcinoma, but we did identify a small focus of ETT in an immediately submucosal location without any tract or attachment to the left lobe of the thyroid gland (figure 2). We determined that the tissue represented a benign focus of intratracheal ETT.

We reviewed the slides of the original lobectomy specimen and compared them with the slides of the most recent tracheal specimen. We determined that the original tumor was actually a medullary thyroid carcinoma rather than a papillary thyroid carcinoma. Our interpretation was confirmed by immunohistochemical studies, which showed that the tumor cells were reactive with chromogranin and calcitonin and negative for thyroglobulin. The elevated TSH level that had prompted the endocrinology work-up was believed to have been the result of the patient's noncompliance with his recommended thyroid hormone replacement regimen.

In light of the revised diagnosis of medullary thyroid carcinoma, the patient continues to be evaluated with additional clinical studies, and further surgery remains an option. His thyroglobulin level remains elevated, which leaves open the possibility that he harbors an additional thyroid neoplasm of follicular epithelial derivation in the other lobe that was not resected during his original surgery. Because medullary thyroid carcinoma does not produce elevated thyroglobulin levels, a recurrence of this malignancy is an unlikely etiology.

Discussion

Background. Intratracheal thyroid disease was first described in 1875 by Ziemssen, who reported the case of a 30-year-old man with a 2-week history of dyspnea and was found to have a subglottic mass.[14,15] In 1888, Heise successfully removed an intratracheal lesion in a 25-year-old man by tracheal fissure and curettage.[16] These two cases acted as catalysts in establishing a pattern for the diagnosis and management of intratracheal thyroid lesions. Intralaryngotracheal thyroid disease remains a rare clinical condition. When it does occur, it is usually accompanied by progressive upper airway obstruction.

Our MEDLINE review of the English-language literature revealed that only 13 well-documented cases of intratracheal ETT have been reported since 1966.[1-13] These lesions were benign in all but two cases, both of which were papillary thyroid carcinomas. There was no gender predilection for intratracheal ETT, and nearly all patients had some evidence of upper respiratory obstruction. At the time of each report, all but one of the 13 patients remained alive without evidence of disease.

Intratracheal ETT accounts for less than 1% of all primary endotracheal tumors that have been identified on surgical pathologic examination.[3,11] Occasionally, nests of endotracheal ETT are asymptomatic (some have been found incidentally at autopsy), but in most cases, the presence of intratracheal ETT is masked by an associated external thyroid goiter. These patients are typically euthyroid, suppressing the development of the intratracheal ETT and allowing them to remain symptom-free referable to the intratracheal lesion. A number of factors—including diet, hormone levels, and previous total thyroidectomy—are believed to affect the size of ETT. When these factors are brought into play, the quiescent thyroid tissue mass begins to enlarge, which leads to symptoms of obstruction.

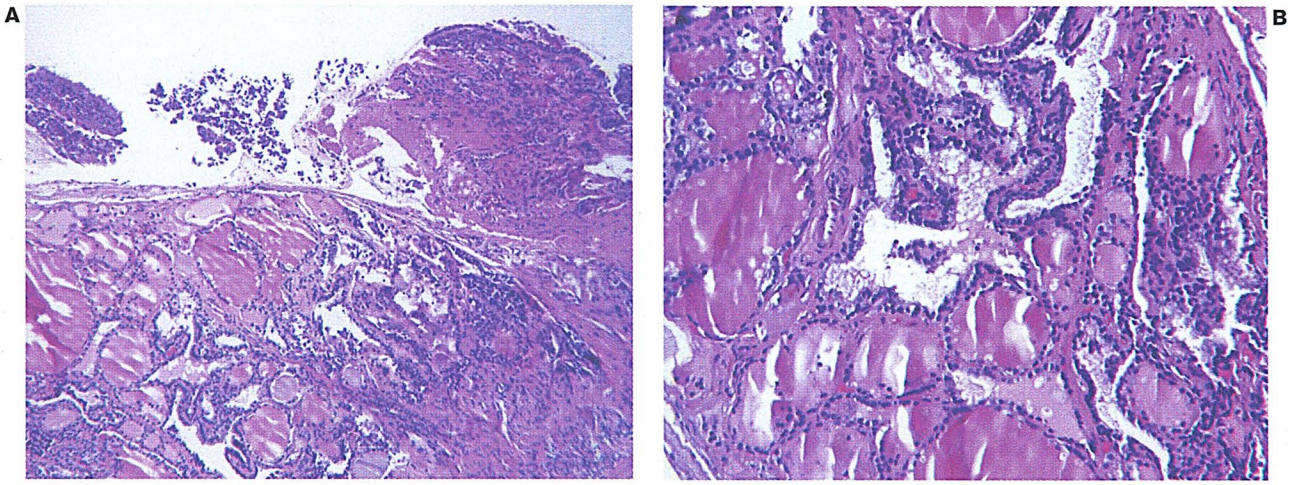

Figure 2. ***A:*** *Low-power view of the tracheal biopsy specimen demonstrates respiratory epithelium overlying benign thyroid tissue (H&E, original magnification × 30).* ***B:*** *High-power view reveals a normal-appearing thyroid follicular epithelium filled with colloid (H&E, original magnification × 300).*

Malignant change in intratracheal ETT has been reported in up to 11% of patients.[15] The most common neoplasm is papillary thyroid carcinoma.[11,12] In one case, the tumor was interpreted as the "tall-cell variant" of papillary carcinoma.[12]

Pathogenesis and embryology. ETT has been reported to occur in a variety of locations along the embryologic path of descent of the thyroid gland—from the base of the tongue all the way to the porta hepatis.[17] The thyroid gland, the first endocrine gland to develop embryologically, arises from an endodermal thickening of the ventral floor of the pharynx as an invagination of the first pharyngeal pouch. This thickening becomes the thyroid diverticulum, which comes to lie at the bifurcation of the aortic trunk. The thyroglossal duct forms concurrently and connects to the base of the tongue at the foramen cecum. Forward growth of the pharynx promotes glandular descent, and the bilobed gland eventually comes to rest anterior to the second and third tracheal rings.[18]

Based on this understanding of the embryology of the thyroid gland, two theories have been proposed to explain the origin of intratracheal ETT. In his 1875 publication, Ziemssen proposed that the later-developing tracheal cartilage splits the thyroid gland, creating a small ectopic nest in the lumen.[14] This "malformation theory" was supported by Falk in his 1936 report of benign intratracheal thyroid tissue in 9 of 21 autopsied neonatal specimens.[19] In 1892, Paltauf proposed that late fetal or postnatal thyroid tissue directly invades the already-formed laryngotracheal cartilage; his proposal led to the coining of the term "ingrowth theory."[20] The case that we have reported does not lend specific insight into either of these two theories, but given a lack of attachment or identification of a tract of tissue to suggest invasion, we favor the malformation theory.

Treatment of intratracheal thyroid disease. A variety of surgical techniques has been employed in the management of intratracheal ETT; there is little place for nonsurgical management.[15] Although an endoscopic approach has been used to treat lesions at the level of the true vocal fold,[15] this condition is optimally treated by combining the creation of a laryngotracheal fissure with a tracheotomy. This combination approach was meticulously documented by Randolph et al, who firmly believed in establishing a distal tracheostomy first, then proceeding to blunt dissection of the thyroid mass, being careful to preserve the overlying surface mucosa that can be later used to cover the operative defect.[21] In addition, it is believed that cartilaginous support of the trachea should be maintained by the use of intratracheal stenting.[3]

Our current management strategy is still based on these time-proven techniques, although surgeons have now incorporated the use of the microscope, loops, and laser techniques to improve surgical resection. With so few cases reported in the literature, it is difficult to assess the value of other therapies. Nevertheless, we would be remiss if we did not mention the use of hormone suppression with ablative therapy, which has resulted in a limited degree of success.[5,9]

In conclusion, although intratracheal ETT is uncommon, it should be included as part of the differential diagnosis of tracheal masses and upper airway obstructions. The presence of an endotracheal lesion should prompt an endoscopic examination and biopsy, as clinically indicated, to determine the nature of the lesion. Careful microscopic examination can document the presence of ETT as well as identify the presence of a thyroid malignancy, whether it be a primary tumor in the ETT or an invasion by direct extension from a thyroid gland primary. When a malignant process has been excluded, hormone suppression and either ablative therapy or surgery should be thoughtfully considered, bearing in mind

that surgery appears to yield the best long-term clinical outcomes.

Acknowledgment

The authors thank Dr. Paul J. Howlett for his contribution of this case.

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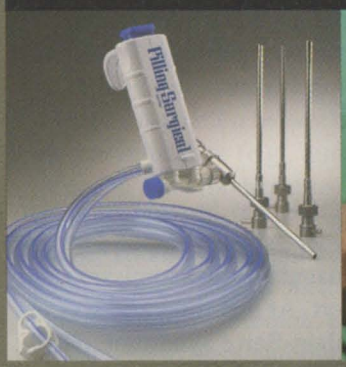

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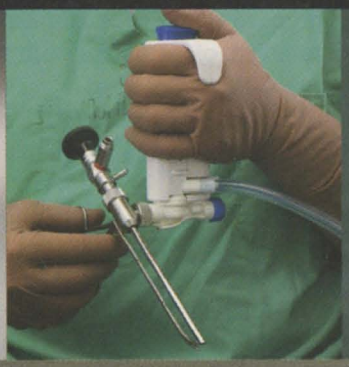

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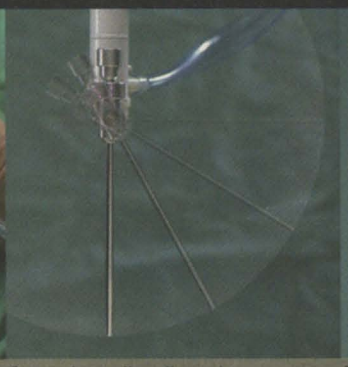

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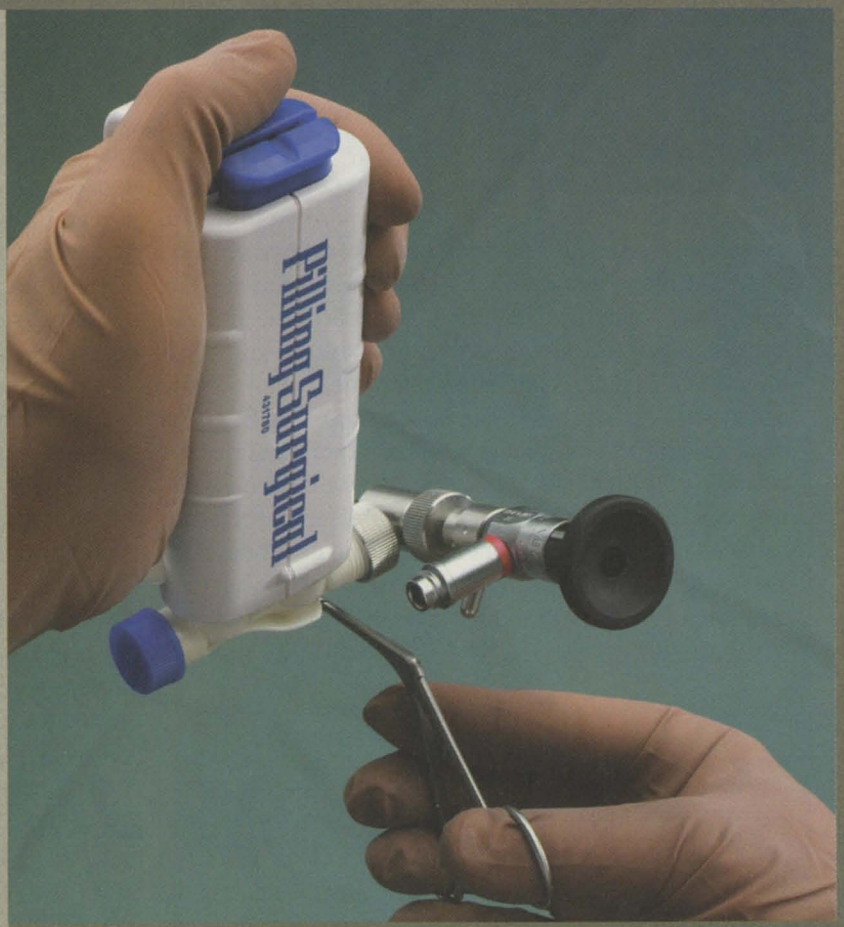

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