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Intralaryngotracheal thyroid – ectopic thyroid or invasive carcinoma?

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Abstract
Intralaryngotracheal thyroid is a rare clinical condition with only about 125 cases described so far in the literature. We present an unusual case of intralaryngotracheal thyroid which had many clinical features of malignancy and yet appeared benign on histology. As in this case, well-differentiated thyroid cancer can present with locally aggressive clinical features and can pose a dilemma in management if treatment decisions are guided solely by histological features.

Key words: Laryngeal neoplasms; Airway obstruction; Laser surgery; Tracheal neoplasms; Thyroid neoplasms; Radiotherapy; Surgery

Introduction

Intralaryngotracheal thyroid is a rare condition, usually presenting with progressive upper airway obstruction. Its rarity often results in delayed recognition, and this can pose challenging diagnostic and management problems.

We recently treated a case of intralaryngotracheal thyroid with unusual clinical and pathological features, and we present this case, together with a review of the current available information in the medical literature on this interesting condition.

Case report

A 33-year-old Caucasian male with mild mental retardation presented to us with slowly progressive stridor over a four-month duration. Clinical evaluation suggested a subglottic swelling, and at a subsequent examination under anaesthesia he was found to have a diffuse left subglottic swelling obliterating approximately 60 per cent of his airway. Histological examination of an endoscopic biopsy from this swelling showed benign looking thyroid tissue beneath normal respiratory endothelium (Figure 1), an appearance compatible with ectopic thyroid tissue. A computed tomography (CT) scan of the neck was reported as showing a tumour in the left thyroid lobe continuous into the larynx and upper trachea (Figure 2). The intralaryngotracheal component of the tumour extended from the level of the cricoid down to the upper 4 cm of the trachea. There were no significantly enlarged lymph nodes, and a CT of the thorax performed at the same time was normal.

Radioiodine thyroid scanning revealed a slight enlargement of the left lobe as compared to the right, but the distribution of the tracer was homogenous in both lobes. The patient developed sudden airway compromise during the period of investigation while he was waiting for a decision on definitive treatment, and required an emergency tracheostomy. The subglottic tumour was resected by laser, and again histological examination showed benign ectopic thyroid tissue with no features of malignancy.

Pre-operative serum thyroglobulin was 576 mg/l (normal range: 5–20 mg/l), free T4 20.6 pm/l (normal range: 9.5–25.0 pm/l), free T3 0.7 pm/l (normal range: 4.2–8.4 pm/l) and TSH was 0.82 mU/l (normal range: 0.4–0.6 mU/l). The patient was returned to theatre a few days later for definitive surgery. At operation, a large left-sided tumour was found adherent to the oesophagus, the trachea, cricoid and left cricothyroid muscle. A total thyroidectomy was carried out and although the tumour was dissected off the larynx and trachea as completely as possible we could not demonstrate any communication between the intraluminal and extraluminal components through the cricothyroid membrane or a tracheal defect. There were no palpable lymph nodes along the internal jugular veins or in the paratracheal gutters. Histological examination of sections from both lobes and the isthmus of the total thyroidectomy specimen showed diffuse involvement of the thyroid by a well-differentiated follicular proliferation, without any cytological atypia, mitoses or vascular invasion. Although the histology showed no evidence of malignancy, the tumour was managed as a well-differentiated follicular carcinoma in light of the clinical picture.

Post-operatively he was treated with a total of 31.4 Gbq of I^{131} in three courses over 18 months, as well as a total of 60 Gy of external beam radiotherapy in 30 fractions over 44 days. He responded with good initial results and his thyroglobulin levels fell to normal (16.6 mg/l) six months after surgery. Eighteen months following surgery, he remains asymptomatic on a daily dose of 80 mg of liothyronine. His latest thyroglobulin measurement is down to 7.6 mg/l and he has no clinical evidence of recurrent tumour.

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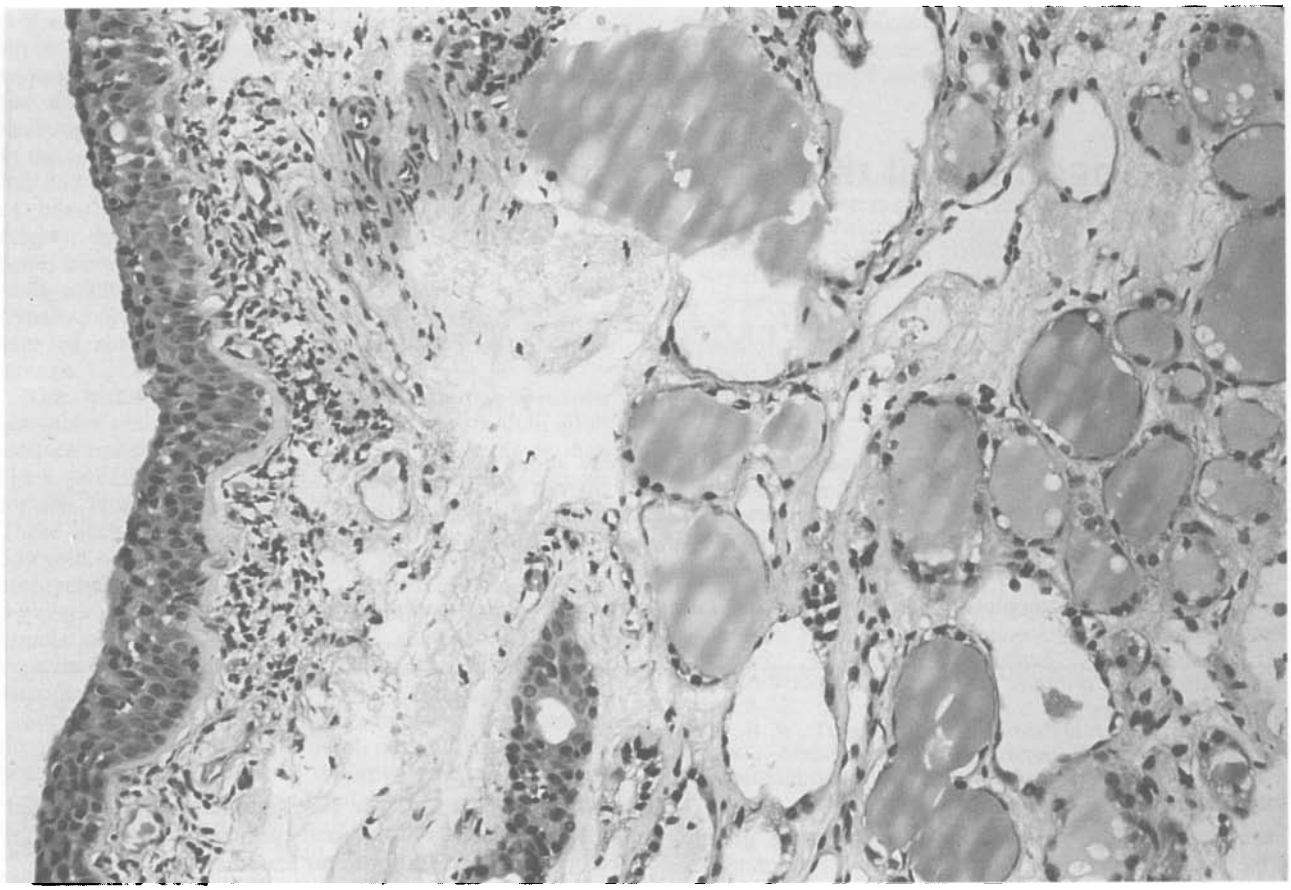

FIG. 1

Histological examination of an endoscopic biopsy from the subglottic swelling showed benign-looking thyroid tissue. The respiratory epithelium can be seen to the left with underlying normal-looking differentiated follicular proliferation. Note the absence of cytological atypia, mitoses or vascular invasion. (H & E; × 40)

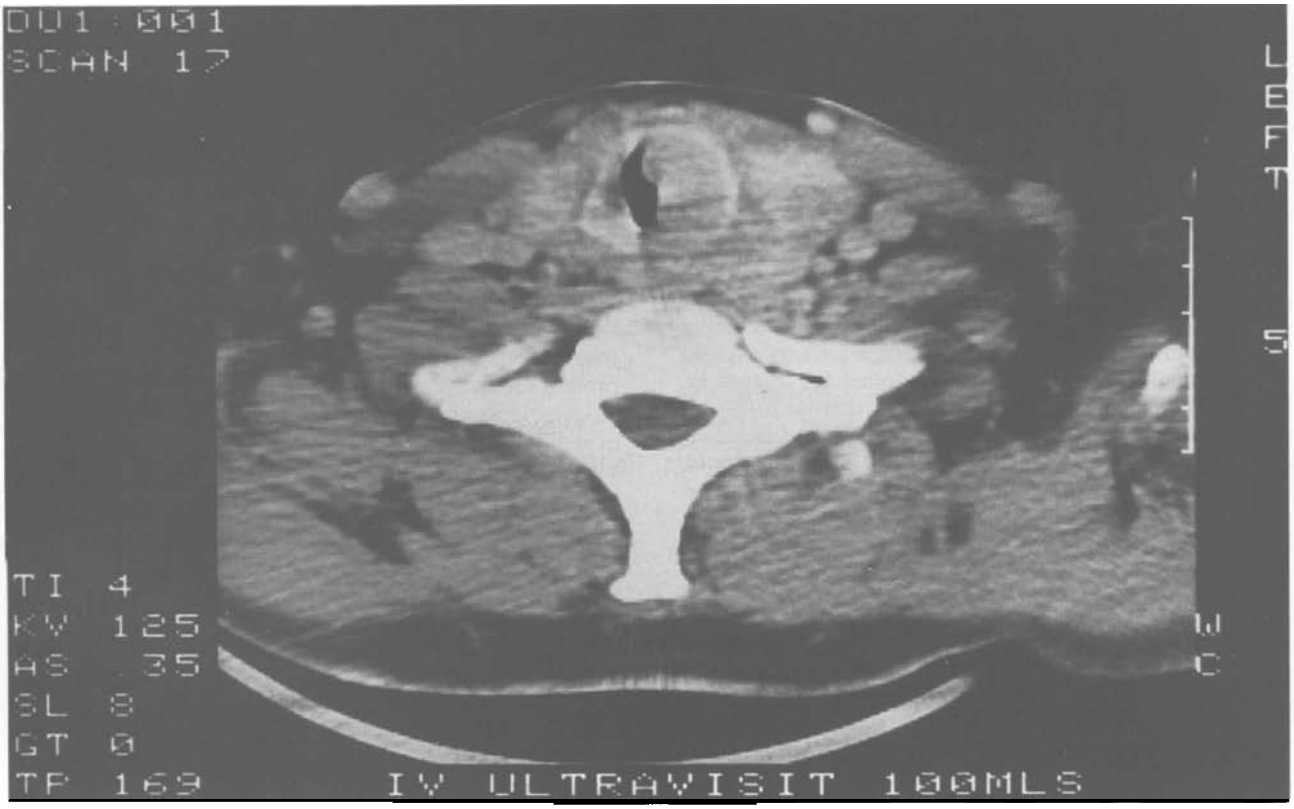

FIG. 2

CT scan showed a tumour in the left thyroid lobe continuous into the larynx and upper end of the trachea.

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Discussion

Although often described in the medical literature under the common name of 'intralaryngotracheal thyroid', thyroid tissue found within the larynx or trachea can be either benign or malignant, and can arise in several different situations: (a) 'true' ectopic intralaryngotracheal thyroid, with no connection with the main thyroid gland (Waggoner, 1958), (b) 'false' aberrant intralaryngotracheal thyroid, connected to the main gland through a defect in the laryngeal or tracheal cartilages (Waggoner, 1958), and (c) intraluminal invasion of the larynx or trachea by frank carcinoma. A fourth, much rarer situation (d) is when there has been a malignant transformation of ectopic intralaryngotracheal thyroid.

Embryology and pathogenesis

The thyroid gland begins its embryological development (Moore and Persaud, 1993) at 24 days after fertilization as the thyroid diverticulum, arising from a median endodermal thickening in the floor of the primitive pharynx. Called the medial thyroid anlage, it then descends, passing ventral to the developing hyoid and laryngeal cartilages, and achieves its definitive position at seven weeks, where it is joined and coalesces with the two lateral thyroid anlages (the ultimobranchial bodies) which are derived from the fourth pharyngeal pouches. The laryngotracheal groove develops at 27 days from the caudal end of the ventral wall of the primitive pharynx, just caudal to the fourth pair of pharyngeal pouches. The laryngeal cartilages themselves are derived from cartilages in the fourth and sixth pairs of branchial arches, developing from mesenchyme which is derived from neural crest cells that surround the original mesoderm in these arches.

There are several locations where thyroid tissue in aberrant sites has been described (Table I). Cases which present as clinical problems are relatively rarer in the medical literature, but the true incidence of ectopic thyroid tissue is difficult to ascertain and is probably much higher.

Lingual and sublingual thyroid are the commonest ectopic sites of actual thyroid tissue, present in 10 per cent of tongues examined at autopsy in one series (Baughmann, 1972). Clinically apparent cases are much rarer, although more are being incidentally discovered since the advent of radioisotope thyroid scanning. The concept of lateral aberrant thyroid has been a matter of controversy since the term was first coined in 1906 (Schrager, 1906). Since the dictum was advanced in 1942 that lateral aberrant thyroid is always metastatic thyroid cancer (King and Pemberton, 1942) there have been several reports challenging this (Myers and Steinberg, 1969; Kozol *et al.*, 1993), and the incidence or actual existence of this entity is still debatable. Ectopic thyroid tissue in other sites is very rare, and intralaryngotracheal thyroid falls within this category.

Intralaryngotracheal thyroid was first described in 1875 (Thoren, 1947) and by 1975 approximately 115 cases had been documented (Myers and Patangco, 1975). Since then, to the best of our knowledge, 10 further cases (Donagen and Wood, 1985; Chanin and Greenberg, 1988; Ferlito *et al.*, 1988; Osammor *et al.*, 1990; Al-Hajjaj, 1991; Ogden and Goldstraw, 1991; Soylu, 1993) have been reported in the medical literature, giving a total of approximately 125 cases (Table II).

TABLE I
CLASSIFICATION OF ECTOPIC THYROID TISSUE

Type	Site
(a) Maldescended	Lingual, sublingual, thyroglossal
(b) Medial aberrant	Intralaryngotracheal, paratracheal, paraoesophageal
(c) Lateral aberrant	Lateral cervical
(d) Distant	Mediastinal, within a Teratoma

TABLE II
REPORTED CASES OF INTRALARYNGOTRACHEAL THYROID

Author and year	Number of cases
Myers and Patangco (1975)	115*
Rotenberg *et al.* (1979)	1
Donegan and Wood (1985)	2
Chanin and Greenberg (1988)	1
Ferlito *et al.* (1988)	1
Osammor *et al.* (1990)	1
Ogden and Goldstraw (1991)	1
Al-Hajjaj (1991)	1
Soylu *et al.* (1993)	1
Present case	1

*Collection of previously reported cases.

The evidence for the existence of congenital ectopic intralaryngotracheal thyroid has been provided in two series (Falk, 1936; Wegelin, 1939) which demonstrated foci of submucous thyroid rests in foetal and newborn tracheas. However the embryological basis for its development has not been firmly established.

There are two theories addressing the embryological basis of intralaryngotracheal thyroid. The 'malformation' theory (Bruns, 1878; Thoren, 1947) proposes that the thyroid gland in the early embryonic period is encroached upon and divided by the later developing laryngeal and tracheal cartilages. The 'ingrowth' theory (Paltauf, 1892; Thoren, 1947) proposes that the thyroid gland may grow into incompletely formed laryngotracheal cartilages in the late foetal or postnatal period. It has been suggested that both theories may be correct (Waggoner, 1958), the former giving rise to 'true' ectopic thyroid separate from the main gland, and the latter resulting in 'false' aberrant thyroid with the intralaryngotracheal component connected to the main gland through a defect in the wall of the larynx or trachea. Certainly there have been examples of both subtypes reported in the literature.

Malignant potential

Malignant thyroid tissue within the larynx or trachea can represent either malignant transformation of ectopic intralaryngotracheal thyroid or intraluminal laryngotracheal invasion by thyroid carcinoma. Due to the rarity of intralaryngotracheal thyroid, its malignant potential cannot be reliably estimated. Only two cases (Falk, 1936; Waggoner, 1958) of malignant transformation of intralaryngotracheal thyroid have been reported, out of a total of about 125 cases, suggesting an incidence of about 1.6 per cent. Although this denominator does not take into account the (potentially vast) number of subclinical cases of intralaryngotracheal thyroid, malignant transformation should be regarded as a potential risk associated with recognized intralaryngotracheal thyroid. Intraluminal invasion by thyroid carcinoma usually presents with a different clinical scenario (Djalilian *et al.*, 1974; Lawson *et al.*, 1977). Clinically these tumours tend to present with voice change and thyroid masses, often associated with previous thyroid operations or neck masses representing lymph node metastases, rather than airway obstruction and stridor.

It is difficult to determine which group our case would fall into. The tumour was obviously invasive at the time of surgery but we could not demonstrate any communication between the intraluminal and extraluminal components through the cricothyroid membrane or a tracheal defect, as

is frequently described in the literature. Although the tumour had no histologically malignant features, it certainly behaved like a malignant tumour with an unequivocally high titre of thyroglobulin which fell to within normal levels after treatment. There have been reports of thyroid tumours with no histological evidence of malignancy that eventually behave in a malignant fashion (Staunton, 1976; Seidlin *et al.*, 1990), and these have been previously termed as 'malignant adenoma' or 'metastasizing goitre'. Considering the clinical evidence, we believe that the present case was a follicular thyroid carcinoma that was so well differentiated as to appear histologically benign.

Management

The management of intralaryngotracheal thyroid is not clearly established. Although there is a report (Moore and Persaud, 1993) of shrinkage of one lesion in an infant using thyroxine suppression, it has not been shown to be effective in adults, and most would agree that treatment should be primarily surgical (Wegelin, 1939; Waggoner, 1958; Myers and Steinberg, 1969; Djalilian *et al.*, 1974; Staunton, 1976; Soylu *et al.*, 1993).

Laryngofissure or tracheofissure with submucous resection is probably the treatment of choice for benign lesions (Wegelin, 1939; Myers and Steinberg, 1969; Bone *et al.*, 1972). The approach for malignant lesions may be aggressive or conservative. An aggressive approach (Falk, 1936) would entail a wide surgical resection including, if necessary, a partial or total laryngectomy, tracheal resection and reconstruction. A more conservative approach (Waggoner, 1958) would involve aggressive surgical debulking, including the intraluminal component either endoscopically or at open surgery via a laryngofissure or tracheofissure, and a total thyroidectomy and lymph node dissection when indicated, but sparing the larynx and trachea and relying on post-operative radiotherapy and radioiodine ablation for differentiated carcinomas. In this case we elected to be conservative because of several factors including the benign appearance on histology and the impact of laryngotracheal resection on a relatively young, mentally retarded patient who may have had difficulty coping with the care of his stoma in addition to the loss of his larynx.

Conclusions

Intralaryngotracheal thyroid can pose challenging diagnostic and management problems, and failure to recognize it can result in delayed treatment. Diagnosis is made at endoscopy and biopsy. Management is often not clear-cut, but should primarily be surgical. While histology is an important factor in choice of treatment of thyroid tumours, management must necessarily take into account the overall clinical picture as well-differentiated thyroid carcinoma can appear entirely benign on histological examination.

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