

The ectopic thyroid gland and the role of nuclear medicine techniques in its diagnosis and management

Abstract

Ectopic thyroid gland (ETG) is a rare entity. It may be located anywhere from the base of the tongue to mediastinum, and seldom in other sites. Most of the patients usually present with midline swelling which can be easily confused with other midline pathology, thereby leading to mismanagement in the form of surgical excision. The diagnosis of this entity requires clinical and imaging examinations for proper management. Radionuclide studies play an important role in the diagnosis and further management of patients with ETG. In the present review we shall discuss various issues about location, embryology, clinical presentation and management including treatment of ETG.

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Introduction

Ectopic thyroid gland (ETG) or ectopic thyroid tissue (ETT) is an uncommon entity with the prevalence rate ranging from approximately 1 per 10^6 – 3×10^6 persons [1]. ETG is defined as thyroid tissue not located in its usual pretracheal region of the lower neck. In most of the cases, the ETG may be found in the midline position between the foramen caecum and the normal site of the thyroid gland. The most common location of ETG is at the base of the tongue, just posterior to the foramen caecum [2]. The other extralingual sites for ETG include sublingual, higher or lower cervical, laryngo-tracheal, mediastinum and even in the abdomen [3]. As in other pathological conditions, the correct diagnosis of ETG remains the key for its proper management. The diagnosis of this entity requires clinical examination and different imaging modalities including radionuclide studies. In the present review, we discuss in detail, the diagnosis, management and treatment of ETG.

Anatomical development and embryogenesis

Thyroid gland is the first endocrine gland to develop during embryogenesis on approximately the 24th day of gestation. It develops from an outgrowth of the pharyngeal endoderm, descends into the neck and reaches its final destination in the neck by the 7th week of gestation [2]. The ETG is seen after failure of the thyroid gland to descend or after incomplete descent of the gland from its origin to its normal position. This anomaly is due to abnormal embryologic development and/or migration of the gland. A somatic mutation of the transcription factor responsible for thyroid migration could explain these findings. Thus, thyroid tissue can be entirely or partially located at the base of the tongue. The spectrum of thyroid dysgenesis (developmental abnormalities) includes: ectopically placed thyroid gland in addition to agenesis or hypoplasia and it is usually associated with congenital hypothyroidism [4, 5]. Congenital malformations, mostly cardiac in nature, have been observed with primary congenital hypothyroidism in association with thyroid dysgenesis [4]. Genetic defects including mutation in the paired box transcription, factor PAX8 and the thyroid transcription factors TTF1 and TTF2, have been implicated in the etiology of thyroid dysgenesis [5].

Sites of location

ETG is defined as thyroid tissue not located antero-laterally between the second and the fourth tracheal cartilage. ETG may be found anywhere along the line of the obliterated thyroglossal duct, usually from the tongue to the diaphragm (Fig. 1). The thyroid gland during its development and descent, lies in anatomical juxtaposition with the heart. The mechanical pull of the descending heart on the thyroid gland may lead to its positional anomalies [6]. Remnants of the thyroglossal duct may persist as isolated nests of functioning thyroid tissue. The majority of ETG are in the cervical midline area extending from lingual, sublingual, subhyoid,

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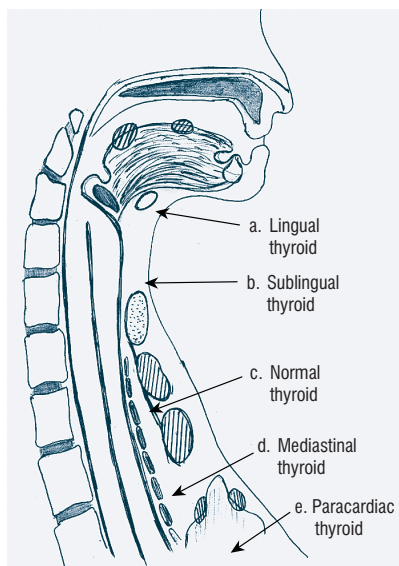


Figure 1. Sketch diagram showing the different positions where ectopic thyroid gland is found.

laryngeal, to the submandibular regions. Lingual ectopic thyroid is the most frequent ETT (90%) [7]. Extralingual thyroid tissue is commonly located in the anterior cervical area along the path of the thyroglossal duct. Benign thyroid follicles in cervical lymph nodes have been demonstrated by many authors [8, 9]. ETG have also been demonstrated in the intratracheal and intrathoracic regions. Intra-laryngotracheal EET constitutes 7% of all intratracheal tumours [10]. ETG have also been demonstrated in other rare sites including submandibular region [11], trachea [12], parotid salivary gland [13], laterally to the carotid arteries and the jugular veins, mediastinum [14], heart [15], lung [16], esophagus [17], duodenum [18], pancreas [19], gall bladder [20], mesentery of the small intestine [21], adrenal gland [22], uterus [23] and iris [24].

ETG along its route of descent is not always symptomatic, thereby leading to under-estimation of its incidence. The actual incidence of ETG is unknown, however post-mortem studies showed that 7%-10% of adults had asymptomatic ETT in the neck [25]. The ETG as a separate structure, may coexist with a normally located thyroid gland or may be the only functioning thyroid tissues [11]. One study showed that there was no normally placed thyroid gland in 70%-75% of the cases reported to have lingual thyroid [3]. So ETG should be considered in the differential diagnosis of a mid cervical mass [26]. Lateral aberrant thyroid tissue in adults can be either metastatic thyroid carcinoma or ETG [27]. Most or all ETG described by others were benign [27].

It is very unusual for two ectopic foci of ETG to be present simultaneously. In a recent review, our group reported 27 cases of dual ETG [28]. The mean age of these patients was 15 years with a range from 4-71 years. In these patients ETT was seen at the lingual in 19 and sublingual sites, in 8 patients. The second ETT was located at the subhyoid area in 15 cases, the suprahyoid in 8, the sublingual in 2, porta hepatis in 1, and in the submandibular area in 1.

Intratracheal ETT can cause airway obstruction with dyspnea and the patient may be misdiagnosed as having bronchial asthma [29]. Similarly, intrathoracic ectopic goiters

have been reported in patients presenting with intrathoracic mass that may be paracardiac or around the aorta [14].

An incidental ETG has been demonstrated in the pancreas in a patient undergoing bilateral truncal vagotomy and pyloroplasty for a duodenal ulcer [19]. A few cases of ectopic lesions have been reported in the abdominal organs including the adrenal glands where in an adrenal mass, normal adrenal tissue and ETG have been found [22].

Intrathoracic ETG has been presented as a mass over the ascending aorta, as a paracardiac mass, a right ventricular mass, a mass at the left ventricular outflow tract or a mediastinal mass. Surgery and histology examination should always be considered in cases of intratracheal ETT, even in elderly patients because of the high risk of tracheal compression.

A few cases of ETG in the abdominal organs (liver, gall bladder pancreas and adrenal glands) and pelvis (uterus and vagina) have also been reported [19, 20, 22, 23]. The presence of ETT below the diaphragm is difficult to explain as the thyroid descends from the tongue to its normal location during its development. The reason for migration of thyroid tissues into the abdomen is poorly understood. The presence of ETT has been confirmed on surgical exploration such as on pyloroplasty or adrenalectomy

Clinical presentation

The ETG is seen at any age, but mostly at adolescence or after pregnancy, due to increased physiological demand of thyroid hormones. ETG is more common in females, with a female to male ratio of 3-4:1. In females, ETG may increase in size during the times of marked endocrine activity such as puberty, pregnancy or menopause, and the majority of patients are diagnosed during this period [7]. There are a few cases of lingual thyroid in the siblings [30, 31].

Usually the chief complaints in patients with ETG are: palpable mass, growth retardation and lump sensation in the throat. The most common clinical feature of the intra-tracheal thyroid tissue is stridor due to progressive upper airways obstruction. Sensorineural hearing loss along with mental retardation has been an associated finding in a few cases where intrauterine infection like toxoplasmosis, might be the etiological factor [32]. Intrathoracic ETG may either be asymptomatic with the tumor reported as an incidental finding on chest X-rays or may have respiratory or gastrointestinal symptoms like cough, dyspnea, dysphonia and hemoptysis, dysphagia or the superior vena cava syndrome. We have reported dual ETG cases, asymptomatic, or having an anterior neck swelling and most of them hypothyroid [28].

Thorough head and neck clinical examination should be done in patients with suspected ETG, including palpation of the neck to identify the presence or absence of the thyroid gland in situ. Ultrasonography and thyroid scan are confirmative. Any history suggestive of altered thyroid function should be elicited. Thyroid hormone production from ETG is usually low, leading to subclinical or to clinical hypothyroidism. Clinical hypothyroidism with ETG may range from 24%-60%. Very rarely hyperthyroidism is seen [21, 33].

Histopathology

Any disease involving normal thyroid gland such as nodular hyperplasia and rarely malignant transformation, can also affect ETG. The incidence of malignancy arising from ETG is similarly low, approximately 1%. Surgically removed lesions submitted for histopathological examination from outside the normal anatomic location of the thyroid gland may establish the diagnosis of ETT. Benign ETT in the parotid gland showed secondary changes in the cyst wall and colloid in the lumen of cyst. The possible origin of the ETT in the parotid salivary gland could be related to embryological evolution, heteroplasia or metaplasia [13]. ETG in the left axilla with histopathology of a benign thyroid gland has also been reported [34].

ETT may undergo malignant transformation [6], although primary thyroid cancer arising from ETG is uncommon. There are reports of primary thyroid cancer in ETT present in the thyroglossal cysts, branchial cleft cyst, thyroglossal duct, lateral cervical lymph nodes, lingual thyroid, and mediastinum [6, 35, 36]. Most tumors in the ectopic locations are papillary carcinomas, a mixed variety of papillary and follicular carcinomas or Hurthle cell carcinomas. Such a malignancy is virtually always diagnosed at pathological examination after surgical excision of the lesion [36].

Diagnosis

The differential diagnosis of any basilingual mass must include ETG apart from: tongue neoplasm, haemartoma, choristoma, thyroglossal duct cyst, epidermoid cyst, enlarged lymph node, lipoma, vascular malformation, malignant conditions and swellings at the base of tongue such as hypertrophic lingual tonsil or mucous retention cyst [37].

Imaging and especially thyroid scintigraphy with ^{99m}Tc , ^{131}I or ^{123}I play an essential role in the evaluation of neck swelling especially at the midline and has high sensitivity (Fig. 2) [38]. It may reveal functioning ETT, not clinically apparent. ETG may mimic a thyroglossal cyst and may be the only functional thyroid tissue. Inappropriate excision in such cases must be avoided. Apart from scintigraphy, ultrasonography is very helpful in demonstrating the ETT. Other imaging modalities like plain X-rays, computed tomography (CT) scans or magnetic resonance imaging (MRI) may also be helpful. Chest X-rays may demonstrate the goiter, tracheal displacement, tracheal compression, calcifications and a soft tissue mass. CT and MRI may determine malignant transformation and plan surgical approach by delineating the size of the gland and its infiltration to the nearby tissues. Detailed clinical and laboratory examination along with imaging and fine needle aspiration cytology, before surgical treatment are essential for the diagnosis and management of ETG.

The role of nuclear medicine techniques. Images of thyroid scintigraphy are acquired either by dynamic mode and/or static mode 20 min after the i.v. injection of 74-111 MBq of ^{99m}Tc pertechnetate which has a comparable molecular size to iodine and is transported via the sodium iodide symporter to the thyroid follicular cells.

Stable iodine ^{127}I is a natural constituent of the thyroid hormones. There are two isotopes of radioiodine: ^{131}I and ^{123}I used for thyroid scintigraphy. ^{123}I has a favorable dosimetry for imaging. However, it is cyclotron produced, therefore more expensive and not commonly available. On the other hand ^{131}I is reactor produced, hence cheaper and commonly available. However, it has poor imaging characteristics and emits beta radiation. Moreover, it has long half-life of 8.02 days as compared to 13 hours of ^{123}I . Therefore, it is not commonly used these days.

Radioactive iodine uptake measurements (RAIU) are usually done with radioactive iodine either ^{123}I or ^{131}I in small doses administered orally and the RAIU from the thyroid gland is measured at different time intervals e.g. 2hr, 4hr, 24hr or 48 hr. ^{131}I RAIU has been used successfully to demonstrate the function of partially implanted large sublingual thyroid in the left iliac fossa, keeping its functional activity up to 105 days after implantation. This large sublingual thyroid had to be partially removed because it caused dysphagia to the patient [39].

In patients with ETG whole body scan (WBS) with ^{131}I is indicated in the postoperative period if malignancy is proved histopathologically. WBS documents any residual normal thyroid tissue and any metastasis, which are avid to radioiodine for further treatment with ^{131}I [34].

Management

Once the diagnosis is established, the ET swellings are not readily excised, as they may be the only functioning thyroid tissue in the body. Early diagnosis is essential for early starting the appropriate treatment since hypothyroidism in neonates or young infants may lead to poor growth, deranged psychoneurological function and poor school learning abilities [40]. The patients are put on thyroid replacement treatment with thyroxine to which they respond well. This treatment achieves a good euthyroid status and decreases the size of the swelling, because it lowers the elevated TSH.

There are several reports in the past where ETG were managed by total excision and its transplantation in a created

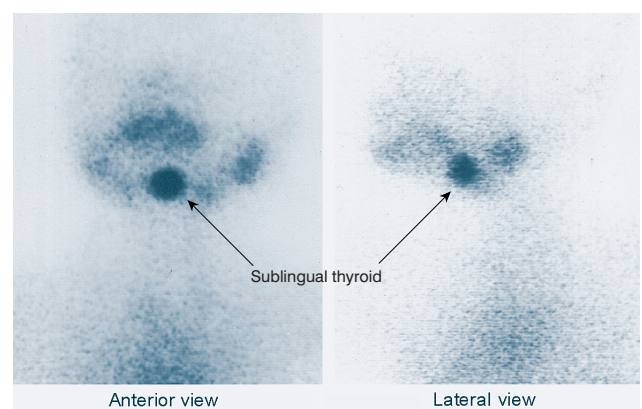


Figure 2. Thyroid scan with ^{99m}Tc -pertechnetate shows a focal area of abnormal radiotracer uptake in the sublingual region (arrow) with no evidence of radiotracer uptake in the normal thyroid bed.

space like in the neck the iliac fossa muscles or the submandibular region [39, 41-43]. The ETG had been dissected along and was auto-transplanted. Post-operative scintigraphy revealed normal uptake in the area of transplanted ETG with normal thyroid function for several weeks [39, 43]. Surgical excision is the mainstay of treatment for these tumors, if they give rise to compressive symptoms or to airways obstruction and dysphagia [39], which do not respond to thyroxine treatment.

Endoscopic CO₂ laser has been used successfully prior to surgery to avoid hemorrhage due to high vascularity of the lingual thyroid and secure free airway pathway [44]. The ectopic tissue must also be excised in case of suspicious or proven malignant disease. Prognosis is the same as for the thyroid gland in situ.

Treatment of the swelling with ¹³¹I may shrink a large ETG but the outcome is not predictable because it may also destroy the thyroid gland if present. It is usually not recommended unless patient refuses surgery and/or hormone replacement treatment fails [6].

In the past, subhyoid ETT was misdiagnosed as thyroglossal cyst and was excised. This induced a permanent hypothyroidism, as in most of these cases this was the only functioning thyroid tissue.

In conclusion, ETG can pose diagnostic and management problems. A thyroid scan should be performed in all cases of midline neck swelling before contemplating any intervention. Although rare, the possibility of ETG should be kept in mind whenever such swellings are encountered in clinical practice.

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