



Review

Morphological, diagnostic and surgical features of ectopic thyroid gland: A review of literature



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ABSTRACT

Ectopic thyroid tissue remains a rare developmental abnormality involving defective or aberrant embryogenesis of the thyroid gland during its passage from the floor of the primitive foregut to its usual final position in pre-tracheal region of the neck. Its specific prevalence accounts about 1 case per 100.000–300.000 persons and one in 4.000–8.000 patients with thyroid disease show this condition. The cause of this defect is not fully known. Despite genetic factors have been associated with thyroid gland morphogenesis and differentiation, just recently some mutation has been associated with human thyroid ectopy. Lingual region in the most common site of thyroid ectopy but ectopic thyroid tissue were found in other head and neck locations.

Nevertheless, aberrant ectopic thyroid tissue has been found in other places distant from the neck region. Ectopic tissue is affected by different pathological changes that occur in the normal eutopic thyroid. Patients may present insidiously or as an emergency. Diagnostic management of thyroid ectopy is performed by radionuclide thyroid imaging, ultrasonography, CT scan, MRI, biopsy and thyroid function tests. Asymptomatic euthyroid patients with ectopic thyroid do not usually require therapy but are kept under observation. For those with symptoms, treatment depends on size of the gland, nature of symptoms, thyroid function status and histological findings. Surgical excision is often required as treatment for this condition.

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1. Introduction

Thyroid gland ectopia is an infrequently encountered clinically observed condition, resulting from a developmental abnormality during the migration of the thyroid anlage from the floor of the primitive foregut to its final position in the neck. It can be found along the way of thyroid descent, in the midline, or laterally in the neck or even in the mediastinum or under the diaphragm or in other different sites [1]. Clinically, the majority of patients with thyroid ectopia are asymptomatic, so that the true incidence is unknown, but obstructive symptoms as well as hypothyroidism have been observed related to ectopic thyroid size, to its

relationships with surrounding organs or to diseases affecting the ectopic thyroid in the same way they involve orthotopic glands. Sometimes, a growing mass can lead to the clinical suspicion of a tumor disease. On the other hand, thyroid ectopy must be distinguished from metastasis of thyroid cancer [2]. Scintigraphy and ultrasonography are the main diagnostic means for evaluating ectopic thyroid tissue, whereas fine needle aspiration could be useful in the presence of a nodular ectopic gland or when the coexistence of an orthotopic thyroid can arise the suspicion of a metastasis from a thyroid cancer [1,2]. The treatment of ectopic thyroid depends on its location and size and on the presence of symptoms or complications. In cases of small and asymptomatic ectopic thyroid, the functioning thyroid should be kept under observation, while patients with suspected bleeding, malignancy and ulceration or recurrent pathology should be treated with radioiodine therapy or surgical removal [1,2]. The aim of this review

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is to highlight current knowledge about the embryology, etiology, molecular pathogenesis, and clinical or surgical management of this condition.

2. Embriology and anatomical sites

The thyroid gland is normally located in the anterior neck region between the 2nd and 5th tracheal rings in humans. It develops on approximately the 24th day of gestation. The thyroid primordium originates as a proliferation of endodermal epithelial cells in the floor of the primitive pharynx at the foramen cecum located in the midline at the junction of the anterior two thirds of the tongue (first branchial arch derivative) and posterior one third (third branchial arch derivative) during the fourth week of the embryonic development. Subsequently, between 5 and 7 weeks of gestation, the gland anlage penetrates the underlying mesoderm and descends, anterior to the pharyngeal gut, as a bilobed diverticulum through the tongue into the neck, passing anterior but can also be posterior to the hyoid bone and thyroid cartilage to reach its final position anterolateral to the superior part of the trachea in the seventh week of embryonic development. During its migration, the thyroid gland is attached to the foramen cecum by a narrow tube, the thyroglossal duct. This duct is normally obliterated and finally disappears. It is substantially clear that two anlagen, one for each lobe, are involved in the morphogenesis of the thyroid gland. These lateral thyroid anlagen should derive from the ultimobranchial body, a descending diverticulum of the fourth pharyngeal pouch. They should become incorporated into the median thyroid anlage to contribute a small proportion of the final thyroid parenchyma. However, the existence of the lateral thyroid anlagen is controversial and it seems unlikely on the grounds of comparative embryology. In mammals it rapidly disappears. In birds it persists and shows a follicular structure similar to the thyroid. It is proposed, if the thyroid follicular cells are thought to derive from the median primordium, a contribution derives from the endoderm of the pharyngeal pouches. Thus, the existence of the lateral thyroid anlage may explain the occurrence of non-midline ectopic thyroid tissue in the neck. In fact, an arrest of migration of one of the lateral thyroid anlagen could cause the failure of fusion with the median anlage. The gland has two diverse cell types, the thyroid follicular cells (TFCs) which produce thyroid hormones and the parafollicular or C cells which produce calcitonin. The cells originate from two different embryological structures: the thyroid anlage and the ultimobranchial bodies which are the sites of origin of the TFCs and C cells, respectively. Ectopic thyroid tissue, the presence of functioning thyroid tissue in a location other than its normal pretracheal location, can be found anywhere along the course of descent of the thyroid gland. According to autopsy studies, the prevalence of ectopic thyroid tissue varies between 7% and 10%. Most cases of ectopic thyroid are diagnosed during the first three decades of life, and they are more common in females. Ectopic thyroid tissue co-existing with a eutopic thyroid may be equal to that without a normally located gland [1–4].

2.1. Lingual and sublingual thyroid

Approximately 90% of ectopic thyroid tissue is found in the base of tongue as lingual thyroid. Lingual thyroid results from complete arrest of descent of the median thyroid anlage. In 75% of patients with lingual thyroid, it is the only thyroid tissue present and the sole source of thyroid hormone production. Seventy percent of cases present with hypothyroidism. Rarely, lingual thyroid can be present along with normal pretracheal thyroid, but only the lingual thyroid is functional. Hyperthyroidism from hyperfunctioning lingual thyroid has also been reported. Most patients with lingual thyroid are asymptomatic; however, some can enlarge sufficiently to cause

symptoms. Common symptoms include cough, pain, dysphagia, dysphonia, dyspnea and hemorrhage. When the mass is too large can present with airway obstruction and stridor in children, while a third of patients have evidence of hypothyroidism. Sleep apnea and respiratory obstruction in adult patients with lingual thyroid have been reported. A common finding on examination is enlargement of the posterior base of the tongue by a firm, midline mass. Hypertrophy of the lingual thyroid occurs as a response to thyroid-stimulating hormone (TSH) stimulation from normal physiologic demands. Thyroid hormone production from lingual thyroid tissue often cannot meet the normal physiologic needs, which can result in enlargement of gland. Some authors recommended that patients with lingual thyroid, even when small, be placed on lifelong thyroxine replacement to prevent subsequent enlargement. Lingual thyroid is typically benign but rarely can harbor malignancy, usually papillary thyroid carcinoma. Despite calcitonin-producing cells are not expected to be present in lingual thyroids; recently C cells were found in lingual ectopic thyroid case. This case demonstrates that ultimobranchial bodies are not the only source of calcitonin-producing cells in humans. Sublingual or pre-laryngeal ectopic thyroid commonly presents as an anterior neck mass above, below or at the level of the hyoid bone. It is usually painless, gradually increasing in size, and may move with swallowing. Characteristically, the mass has smooth margins and is soft in consistency, mobile and non-tender. Differential diagnosis should be performed from many clinical conditions such thyroglossal duct cyst, midline branchial cyst, epidermal cyst, lipoma, lymphangioma, lymphadenopathy, sebaceous cyst, cystic hygroma, dermoid cyst and neoplasms [4–8].

2.2. Tracheal thyroid

Some authors report cases of multinodular goiter arising in thyroid tissue within the trachea. Unlike lingual thyroid, 75% of intratracheal ectopic thyroids are associated with functioning thyroid gland in its normal location. Intratracheal ectopic thyroid commonly present clinical symptoms. Progressive dyspnea, stridor, cough, difficulty swallowing and hemoptysis were described. Differential diagnosis should be made between dyspnea observed in this and asthma. It is might be difficult to differentiate stridor from the wheezing of asthma on physical examination. Intra-tracheal ectopic thyroid is visualized during direct laryngoscopy as a sub-glottic or upper tracheal wall mass covered with normal mucosa [9,10].

2.3. Submandibular thyroid

Submandibular region sometimes showed ectopic thyroid mass. It is hypothesized that aberrant thyroid tissues found in the submandibular and lateral neck regions originate from a defective lateral thyroid component that cannot migrate and fuse with the median thyroid anlage. Subjects affected by this abnormality usually present with a lateral, palpable, mobile, painless mass in the carotid triangle or the submandibular area. Submandibular thyroid tissue is more common in females and is located mainly on the right side of the neck. In most cases, orthotopic thyroid gland usually coexists and the patients are euthyroid. Nevertheless, it may also present as the only functional thyroid tissue. Possible explanations provided for this ectopy are displacement during the course of embryonal development, spread of tissue during surgery on an orthotopic thyroid gland, and metastasis of a highly differentiated papillary thyroid carcinoma [11].

2.4. Lateral cervical region thyroid

Cases of ectopic thyroid detected in the lateral cervical region were regarded as malignant (metastatic) lesions and were termed

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