

A Rarely Ectopic Localization of Thyroid Gland Due to an Embryological Defect: Lingual Thyroid

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Introduction

The thyroid gland is largest and a bilobate endocrine gland located in the anterior neck region adjacent to the larynx and trachea. Ectopic thyroid is a presence of thyroid tissue at sites other than its normal cervical location [1].

Ectopic thyroid is a rare embryological aberration which can occur in any moment of the migration of the thyroid resulting in lingual (at tongue base), sublingual (below the tongue), prelaryngeal (in front of the larynx), and substernal (in the mediastinum) ectopy [2]. It is commonly found in the base of the tongue, just behind the foramen cecum, and is subject to the same diseases as the thyroid gland itself. The thyroid gland located at the base of the tongue is called lingual thyroid [3]. Lingual thyroid is the most frequent ectopic location of the thyroid gland, although its prevalence varies between 1:100000 and 1:300000, it occurs more frequently in females, with a female to male ratio of 4:1. The true incidence is probably underestimated due to asymptomatic lingual thyroids. Some Authors reported having found ectopic lingual tissue in % 10 of 200 consecutive necropsies. In the literature, approximately 400 cases of symptomatic patients have been reported [2].

In 1869, Hickman reported the first case of ectopic thyroid tumour of the base of the tongue, pressing down the epiglottis on the larynx and causing death by suffocation sixteen hours after birth [4]. The other localizations in the head and neck region or distant from head and neck region may be occur. Ectopic thyroid tissue may be found in trachea^[5], submandibular salivary gland^[6], lateral cervical region^[7] axilla^[8], palatine tonsils^[9], carotid bifurcation^[10], iris of the eye^[11] and pituitary gland^[12], in the head and neck region. It may be found in the heart^[13], ascending aorta^[14], thymus^[15], oesophagus^[16], duodenum^[17], gallbladder^[18], stomach bed^[19], pancreas^[20], mesentery of the small intestine^[21], porta hepatis^[22], adrenal gland^[23], ovary^[24], fallopian tube^[25], uteus^[26] or vagina^[27], far from the head and neck region [28].

Embryological Development

To understand the formation of ectopic thyroid tissue, we have to look more into the embryological development process and its molecular mechanisms. The thyroid gland is the first endocrine gland to develop in the embryo. Its development begins about 24 days after fertilization in the floor of the primitive pharynx. The thyroid gland appears as an epithelial proliferation in the floor of the pharynx between the tuberculum impar and the copula. Subsequently the thyroid descends in front of the pharyngeal gut as a bilobed diverticulum and it descends to meet the lateral ultimo-branchial bodies; the fusion of these elements leads to the formation of the functional and mature thyroid gland by the third foetal month.

During this migration, the thyroid remains connected to the tongue by a narrow canal, the thyroglossal duct, which disappears at the sixth or eighth week. With further development, the thyroid gland descends in front of the hyoid bone and the laryngeal cartilages. It reaches its final position in front of the trachea in the seventh week. By then it has acquired a small median isthmus and two lateral lobes. The gland has two diverse cell types, the thyroid follicular cells (TFCs) which produce thyroid hormones and parafollicular (C cells) cells which produce calcitonin. These cells group originate from two different embryological structures. The thyroid anlage and the ultimobranchial bodies are the origine of the TFCs and C cells respectively. The thyroid begins to function at approximately the end of the third month, at which time the first follicles containing colloid become visible week. The proximal segment of the thyroglossal duct regresses between the 5th and 10th weeks of development, leaving a permanent pit at the dorsum of the tongue, known as the foramen cecum [3].

The pathogenesis of the lingual thyroid is not clear but it has been postulated that maternal antithyroid antibodies would hinder the descent of the gland during embryogenesis. Several transcription factors are involved in the molecular control of embryological development. Genetic researches has shown that the gene transcription factors TITF-1 (Nkx2-1), Foxe-1 (TITF-2) and PAX-8 are essential for the thyroid morphogenesis and differentiation. Mutation in these genes may be involved in abnormal migration of the thyroid. Animal studies have shown that Foxe-1 is required for thyroid migration and that mice homozygous for Foxe-1 mutations show a sublingual thyroid. The identification of PAX-8 gene regulatory element is believed to represent the first step in the investigation of upstream regulatory mechanisms that control PAX-8 transcription during thyroid differentiation. Studies in animals also showed a possible link between development of major cervical arteries and relocation of the thyroid gland. Variability in the architecture of cervical vessels and branching of carotid arteries from the aortic arch might influence thyroid morphogenesis [28].

Symptoms are related to the growth of the thyroid tissue, causing dysphagia, dysphonia with stomatolalia, bleeding, dyspnoea, nasal twang and hemoptysis [2, 29]. Lingual thyroid can cause foreign body sensation in tongue or sensation of choking. Large blood vessels present on the surface of lingual thyroid predispose it for ulceration [30]. The enlarged lingual thyroid has been described as a cause of difficult intubation during induction of anaesthesia, especially for bleeding. Lingual thyroid is commonly detected during periods of increased demand for thyroid hormones, e.g puberty and pregnancy. This probably occurs when demands for thyroid hormones increase, causing the increase in circulating TSH levels with growth of the ectopic thyroid tissue.

Symptoms of lingual thyroid increase during pregnancy and puberty. Dossing et al reported a case about recurrent pregnancy-related upper airway obstruction caused by intratracheal ectopic thyroid tissue [31]. About 33-62% of all patients with ectopic thyroid showed hypothyroidism with increased levels of TSH. In case of hypothyroidism, thyroid hormone substitution therapy should be started. Hyperthyroidism arising from ectopic thyroid tissue is less common than hypothyroidism. However, an ectopic thyroid gland with histological features of Graves' disease has been found in different locations like the base of the tongue, mediastinum, submandibular region, lateral neck and the mesentery of the small intestine. Thyrotoxicosis arising from a recurrent ectopic mediastinal thyroid was reported in the literature [32].

All diseases capable of affecting the normal thyroid can affect the ectopic thyroid like adenoma, hyperplasia, inflammation, and malignancy. Malignant transformation can occur in ectopic thyroid tissues in different locations. Primary papillary, follicular, mixed follicular and papillary, hurthle cell tumor and medullary carcinomas have been reported in the literature. Frequency of carcinoma in lingual thyroid is estimated to be approximately one in 100 cases with a female to male ratio ranging from 3:1 to 8:1 [33-36]. Sturniolo et al and Stokes et al reported clinical cases about the "differentiated thyroid carcinoma in lingual thyroid" [37,38].

Except from lingual thyroid, some ectopic thyroid tissues rarely localized in the kidney or adjacent to the left atrium are reported in the literature [39,40]. Porqueddu et al. is reported a case of a female patient with a tumor located in the right ventricular outflow tract, and histopathological examination of this biopsy material revealed intracardiac ectopic thyroid [41]. Ectopic thyroid tissue can be found in the ovaries is known as "Struma ovarii" and is considered a thyroid tissue teratoma or can be found uterus [24,26]. Existence of ectopic thyroid glands at two different locations is very rare. Only 27 cases of such dual ectopia have been reported in English literature [28].

Clinically, lingual thyroid presents as a mass at the base of the tongue, pink and firm. The diagnosis is mainly based on clinical and imaging examinations. Palpation of the neck is essential in order to check for the presence or absence of the thyroid gland in its normal position. Thyroid function tests should also be performed, but this examination may often be normal. Radionuclide thyroid imaging employing technetium- 99m pertechnetate, iodine-131 or iodine-123 is useful in the evaluation for ectopic thyroid. Thyroid tissue takes up the radioisotope and this helps in localizing the ectopic thyroid and at the same time in determining the presence of a eutopic thyroid gland. Additionally neck US, CT and magnetic resonance imaging (MRI) may help in defining the extension and location of the ectopic thyroid gland. Thyroid scan can also reveal whether there are other sites of thyroid tissue; in approximately 75% of patients the ectopic tissue is the only functioning thyroid tissue in the body [28]. Most ectopic thyroids are asymptomatic and no therapy is necessary. In case of upper airway obstruction symptoms surgical treatment is applied. Differential diagnosis includes lymphangioma, minor salivary gland tumours, midline branchial cysts, thyroglossal duct cysts, epidermal and sebaceous cysts, angioma, adenoma, fibroma and lipoma.

Result /Conclusion

Ectopic lingual thyroid is a rare congenital anomaly. No treatment is required in patients who have no symptom. Treatment could be conservative with substitutive hormone treatment in patients with mild symptoms, while surgery is recommended in cases with airway obstruction. Evaluation of thyroid function is recommended before and after surgery due to the risk of post-operative hypothyroidism. In patients who have hypothyroidism, thyroid hormone substitution is needed. If the ectopic thyroid has only thyroid lesion, then lifelong thyroid hormone therapy is required.

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