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SHORT REVIEW

Thyroid cancer in lingual thyroid and thyroglossal duct cyst

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KEYWORDS

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Differentiated thyroid cancer

Abstract Ectopy is the most common embryogenetic defect of the thyroid gland, representing between 48 and 61% of all thyroid dysgeneses. Persistence of thyroid tissue in the context of a thyroglossal duct remnant and lingual thyroid tissue are the most common defects. Although most cases of ectopic thyroid are asymptomatic, any disease affecting the thyroid may potentially involve the ectopic tissue, including malignancies. The prevalence of differentiated thyroid carcinoma in lingual thyroid and thyroglossal duct cyst is around 1% of patients affected with the above thyroid ectopies. We here review the current literature concerning primary thyroid carcinomas originating from thyroid tissue on thyroglossal duct cysts and lingual thyroid.

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PALABRAS CLAVE

Defectos embrionarios del tiroides;
Quiste tirogloso;
Tiroides lingual;
Tiroides ectópico;
Cáncer diferenciado de tiroides

Cáncer de tiroides en tiroides lingual y quiste del conducto tirogloso

Resumen La ectopia es el defecto embriogénico más frecuente de la glándula tiroides, responsable de entre el 48 y el 61% de todas las disgenesias tiroideas. La persistencia de tejido tiroideo en el contexto de un resto de conducto tirogloso y el tejido tiroideo lingual son los defectos más comunes. Aunque la mayoría de los casos de tiroides ectópico son asintomáticos, cualquier proceso que afecte al tiroides puede afectar potencialmente al tejido ectópico, incluidos los tumores malignos. La prevalencia de carcinoma tiroideo diferenciado en tiroides lingual y quiste del conducto tirogloso es de alrededor del 1% en los pacientes con las ectopias tiroideas antes citadas. Revisamos aquí la bibliografía actual sobre los carcinomas tiroideos primarios originados a partir de tejido tiroideo de quistes del conducto tirogloso y tiroides lingual.

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Introduction

Thyroid embryogenesis begins by about day 24, from a median endodermal thickening forming the *thyroid diverticulum*. This primordial structure migrates from the floor of the primitive pharynx and by week 7 of embryonic development it reaches its definitive location in front of the trachea. A failure of the thyroid anlage to descend throughout the normal pathway results in abnormalities in thyroid organogenesis, including an incomplete (thyroid hypoplasia) or absent (thyroid agenesis) development of the thyroid gland, or in an aberrant location of the gland along the midline, from the base of the tongue to the mediastinum (thyroid ectopy). All these conditions, overall covering 80–85% of the cases of congenital hypothyroidism, are usually indicated as “thyroid dysgenesis” (TD).¹

Molecular studies suggest that the co-expression of the transcription factors TITF1/NKX2-1, FOXE1, PAX8, and HHEX in the thyroid anlage is essential for regular organogenesis. In particular, mice homozygous for *Foxe1* mutations show sublingual thyroid,² an evidence that indicates that this transcription factor is required for thyroid migration. However, to date no mutation in the above-mentioned transcription factors has been found in patients with ectopic thyroid.

Among ectopic thyroid locations, the most common is the tongue, which accounts for 90% of reported cases. Less frequently, ectopic thyroid tissue may be found in the submandibular area, larynx, trachea, esophagus, mediastinum, diaphragm, and heart.³ In addition, a failure of obliteration of the mid portion of the thyroglossal duct may result in the persistence of epithelial tissue along the path of the descent of the thyroid gland. This embryological remnant may remain clinically quiescent, or presents itself as a cyst (thyroglossal duct cyst, TGDC) located in most cases between the hyoid bone and the thyroid cartilage.

Although most cases of ectopic thyroid are asymptomatic, any disease affecting the thyroid may potentially involve the ectopic tissue, including malignancies.^{4–7} We here review current literature concerning primary thyroid carcinomas originating from thyroglossal duct cysts and lingual thyroid, which are the most common ectopic thyroid malignancies.

Data acquisition

We used the keywords “lingual thyroid” and “thyroglossal duct cyst”, both separately and in conjunction with the terms “thyroid cancer” and “ectopic thyroid cancer” to search MEDLINE for clinical case series and/or case reports and review articles published between 1990 and December 2015, and focused on thyroid cancer originating from the above thyroid ectopies. After exclusion of articles with no abstract available and those in languages other than English, 70 articles were selected and analyzed. For the purposes of this brief review, only case series and review articles were quoted.

Thyroglossal duct cyst carcinoma (TGDC)

TGDC is usually referred to as the most common congenital neck mass.⁷ The development of a carcinoma on a TGDC is rather unusual, with a reported prevalence ranging from

0.7 to 1% of patients with TGDC.^{7–9} However, the estimated prevalence of TGDC in surgical series, likely comprising patients with suspicious clinical and/or imaging features, is as high as 13–14%.^{10,11}

Since Brentano first described one case in 1911,¹² only about 250 cases of TGDC have been reported in the literature.⁸ TGDC originate from both thyroid and squamous cells.¹⁰ Papillary thyroid cancer (PTC) is the most common histological type (80%), followed by the follicular variant of PTC (8%), by squamous cell carcinoma (6%), and by follicular thyroid carcinoma (FTC), Hürthle cell, C-cell and anaplastic carcinoma in the remaining 6%.^{9,13} TGDC has been reported to occur as an isolated lesion, with no coexisting malignancies within the orthotopic thyroid tissue.^{14,15} However, the simultaneous occurrence of a TGDC and a thyroid carcinoma has been reported in 11–62% of all cases of TGDC,^{9,16,17} likely suggesting the lesion to be either a multifocal thyroid neoplasia, or a metastasis of a primary thyroid carcinoma that has spread through the thyroglossal duct. Alternatively, it has been suggested that the cancer originated in the thyroglossal duct cyst may represent the primary tumor, being the thyroid gland a secondary localization.^{17,18}

The majority of TGDCs are located in small cysts and capsular invasion is sometimes reported. Lymph node metastases are found in between 7% and 15% of cases and distant metastases are uncommon.^{18,19} Diagnosis is usually post-operative, due to the fact that many clinical features are common to both malignant and benign lesions.²⁰ Fine needle aspiration cytology can facilitate preoperative diagnosis and should therefore be routinely prescribed for all adult patients with a clinical diagnosis of TGDC.⁹

There is generally unanimous agreement that the surgical treatment of TGDC should employ the Sistrunk technique, which involves excision of the cyst, the central portion of the body of the hyoid bone, and a core of tissue around the thyroglossal tract extending up to the foramen caecum.²¹ Conversely, the need of performing thyroidectomy in the management of TGDCs is debated.¹⁶ In agreement with some authors,^{9,15,17,19} we believe that thyroidectomy should be performed on all TGDC patients. Although this opinion is in apparent conflict with current 2015 ATA guidelines,²² we personally believe that it might be considered for at least two reasons. First, these neoplasias may be metastases of occult thyroid carcinomas, and therefore thyroidectomy would form the basis of a definitive treatment. Second, thyroidectomy allows optimal staging, radiometabolic therapy, if required, and long-term follow-up with thyroglobulin assays.^{7,10,17,23}

Radiometabolic treatment in such patients should be performed in those classified as high risk (being of advanced age, having metastatic or invasive tumors, or histological features indicating a poor prognosis, or a coexisting thyroid carcinoma).^{18,22} The prognosis for differentiated thyroid cancer (DTC) originating from TGDC is as good as that reported for primary DTC in orthotopic glands, with distant metastatic disease occurring in less than 2% of cases.¹⁸

Lingual thyroid cancer (LTC)

Lingual thyroid (LT) is a rare condition, with an estimated prevalence ranging between 1:100,000 and 1:300,000.

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