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Thyroglossal duct carcinoma: report of a case

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Summary. *Aim:* Thyroglossal duct carcinoma (TDCa) is a rare malignant tumor arising within a thyroglossal duct remnant (TDR) or a thyroglossal duct cyst (TDC). Controversies exist regarding its origin: whether it represents a metastatic lesion of a primary thyroid cancer or a "de novo" origin. *Patients and methods:* Man with a visible and palpable subhyoid mass. Preoperative ultrasound scan and US-guided fine-needle aspiration cytology revealed suspicious papillary carcinoma in the TDC and thyroid nodules. Surgery consisted in removal of the hyoid bone and total thyroidectomy. *Results:* Histopathologic examination revealed papillary TDCa and a focus of papillary var. follicular microcarcinoma in the thyroid gland. *Conclusions:* Ultrasound scan with fine-needle aspiration cytology is beneficial in the preoperative diagnosis of carcinoma in TDC. Surgery is an adequate treatment for TDCa and the prognosis for TDCa is excellent. Adjuvant radioactive iodine and post-operative L-thiroxine suppressive therapy are appropriate in these cases. Our experience confirms the controversies about the origin of TDCa.

Key words: thyroglossal duct cyst, thyroglossal duct papillary carcinoma, fine-needle aspiration cytology, Sistrunk's operation, thyroidectomy

Introduction

Thyroglossal duct carcinoma (TDCa) is a malignant tumor arising within a thyroglossal duct remnant (TDR) or a thyroglossal duct cyst (TDC). It is an extremely rare condition as approximately 250 cases have been published in the literature since the first description by Brentano in 1911 (1-3). However, the synchronous occurrence of TDCa and carcinoma in the thyroid gland is rarer (4).

Case report

A 20 year-old man, a moderate smoker with a past medical-surgical history of total adenoidectomy at the age of 5 years and ablation of spinal osteoid osteoma (t12) in adolescence, came to our notice a palpable swelling appeared in the middle region of his neck, without any other symptoms. An ultrasound examination of the neck showed a normal thyroid in dimension and structure, together with a a c. 5 mm diameter nodule in the right lobe and two other nodules (about 6 and 5 mm) in the left one, while other small groups, of about 2 mm, were noticeable on the left side of the isthmus; in the sub-hyoid region there was a hypo-anechoic nodular lesion (23 mm about) with internal vascular flow, suggesting a complex cyst. The patient underwent endocrinological counseling. Another ultrasound examination of the thyroid and CT of the neck confirmed the diagnosis of a complex cyst of the thyroglossal duct. An ultrasound scan showed an ex-

pansive lesion on the midline of the neck (maximum diameter of about 3 cm) with a non-homogeneous structure due to the presence of fluid and solid areas with several calcifications and internal vascular flow; CT neck showed an expansive lesion of about 3.5 x 2.6 cm, semi-fluid, with a central solid component in the median region, below the hyoid bone. Some reactive lymph-nodes (maximum diameter of 1.3 cm) were found bilaterally in the laterocervical and submandibular areas and in the right supraclavicular area.

The patient accordingly performed routine blood investigations and thyroid function tests that showed the following results: FT3=3.29 pg/ml (range 2.2-4.2); FT4=1.27 ng/dl (range 0.9-1.7); TSH=0.999 mUI/L (range 0.3-3.6); Thyroglobulin-Ab=< 5.00 UI/ml (range 5-100); Thyroglobulin=4.93 ng/ml (range 0.2-70); TPO-Ab=7.92 UI/ml (range 1-16); Procalcitonin (PCT)=<0.1 ng/ml (range 0-100).

Subsequently an Ultrasound-guided Fine Needle Aspiration Cytology (FNAC) was performed. The latter showed a negative result for nodules located on the lower and middle third of the left thyroid lobe -TIR 2-; whereas we found a suspicious nodule, due to the presence of several thyrocytes with enlarged nuclei gathered in papillary clusters, on the lesion on the midline of the sub-hyoid region -TIR 4 -, by Italian consensus SIAPEC-IAP published in 2008.

The patient performed all preoperative investigations (x-ray examination, ecg, routine blood tests, preanesthetic assessment and ENT consultation as in all patients that we will submit to total thyroidectomy).

By Kocher incision, the patient underwent removal of the sub-hyoid lesion and hyoid bone itself, followed by total thyroidectomy at the same time. On the first day after surgery, postoperative routine blood tests were performed: serum calcium level and CBC (normal values). The patient was discharged on the third day after surgery in good general condition, with antibiotic and L-thiroxine suppressive therapy (levothyroxine sodium). Histopathological examination revealed an intracystic classic papillary carcinoma, infiltrating the TDC thick wall on the subhyoid lesion. Chronic inflammation and ectopic thyroid tissue remnant were found inside the TDC wall. Margins, bone fragments and skeletal muscle were free from tumor. Besides it showed us an incidental not capsulated papillary variant follicular microcarcinoma on the right thyroid lobe (diameter 1 mm) that did not exceed the thyroid capsule and adenomatous hyperplastic nodule with an oxiphilic metaplasia on the left thyroid lobe . The patient was put on adjuvant radioactive iodine like all our post-total thyroidectomy patients with a final diagnosis of carcinoma, to keep the thyroid-stimulating hormone (TSH) levels between 0.2 and 0.5 mU/l. In follow-up the patient performed annual measurement of serum thyroglobulin and twice-yearly ultrasound scan of the neck. Currently the patient is in a good state of health.

Discussion and conclusions

The thyroid gland is one of the earliest endocrine glands to develop in the human embryo (5). It is first identifiable in embryos with about twenty mesodermal segments as a median thickening of the endoderm in the floor of the pharynx between the first and second pharyngeal pouches. This structure is later invaginated to form a median diverticulum and grows towards the head as a tubular duct, which divides into double cellular plates anterior to the trachea from which the thyroid gland develops (6). The connection of the median diverticulum with the pharynx is called the thyroglossal duct, and it usually disappears during the 6th and 7th week of fetal life; if the remnant of the thyroglossal duct fails to involute, it can persist as a cyst, duct or ectopic thyroid tissue. Thyroglossal duct cyst, the commonest non-odontogenic cyst, presents as a neck mass at any point along the tract, and accounts for more than 75% of childhood midline neck masses. It is rare in the adult population (7%) (7, 8). TDC clinically presents as a soft, firm, fluctuant and generally movable swelling in the midline of the neck. It occurs along the thyroglossal tract: thyrohyoidal (61%), suprahyoidal (24%), suprasternal (13%) and intra-lingual regions (2%) (8). Thyroglossal duct carcinoma is a malignant tumor, which arises within the thyroglossal duct remnant. It is an uncommon development, accounting only for about 0.7% to 1.5% of all thyroglossal duct cysts (9, 10). Approximately 250 cases of TDCa have been published in the literature, mainly as single case reports or small case series, since its first description

by Brentano in 1911 (1-3). Synchronous occurrence of TDCa and thyroid carcinoma is even rarer. TDCa arises more often in females (female:male=1,5:1), and the mean age of patients is 39.2 (range 6-81); about 79% patients are from 20 to 60 years old (9, 11). TDCa are either of thyroid cell or squamous cell origin. The most common histopathological diagnosis is carcinoma originating from thyroid cells, which accounts for roughly 85% of these tumors (6). Squamous cell carcinoma is the second most frequently reported cancer and accounts for 7% of cases, being more aggressive and with worse prognosis. Mixed thyroid and squamous cell carcinoma is described as an extremely rare condition (12). Medullary carcinoma has not been reported because of the absence of parafollicular C cell in TDC. Papillary carcinoma is the most common histologic subtype followed by mixed papillary var. follicular carcinoma. The other subtypes include Hurtle cell, follicular and anaplastic carcinoma (8, 9, 13). Neck node metastases are found in 7% to 15% of patients, but distant metastases are very rare (14). The clinical presentation of TDCa is often similar to that of TDC. Usually, anterior midline neck mass is the chief complaint. Uncommonly, voice change and draining cutaneous sinuses may bring the patient to medical attention. Malignancy should be suspected if the cyst is hard, fixed, irregular or associated with significant neck nodes (13, 15). The exact origin of TDCa in a TDC is still debated as to whether it represents a metastatic lesion from an occult primary thyroid carcinoma versus its "de novo" origin (3, 8, 14, 15).

Some authors believe that it arises "de novo" from an island of normal thyroid tissue found in TDC. This theory is supported by the fact that thyroid follicles are known to exist in a TDC and could potentially undergo malignant transformation, and by the fact that ectopic thyroid nests have been identified histologically in as many as 62% of the surgical specimens of TDC and that carcinoma in a TDC is found without evidence of thyroid malignancy (16). Furthermore, the persistent absence of medullary carcinoma occurring in a TDC in keeping with its embryology, strongly favors the "de novo" theory (8, 15). Moreover, synchronous occurrence of papillary carcinoma in a TDC and the thyroid gland can be explained as representative of multifocal tumor. Others suggest that it is probably metastasis from a thyroid carcinoma through a patent thyroglossal duct (17). They argue that in most of the cases reported, the thyroid gland had not been examined microscopically (6). However, Weiss and Orlish showed that only 11.4% of the microscopically examined thyroid glands in the patients with TDCa had foci of carcinoma (13). Joseph set down strict criteria for the diagnosis of a primary TDCa (18). These included the finding of a thyroglossal remnant that can be distinguished from a lymph node metastasis by the epithelial lining and the thyroid nests within the cyst wall in a patient with a clinically normal thyroid gland. Widstrom also described diagnostic criteria (19). (1) Carcinoma should be in the wall of the TDR; (2) TDCa must be differentiated from a cystic lymph node metastasis by histological demonstration of a squamous or columnar epithelial lining and normal thyroid follicles in the wall of the TDR; (3) there should be no malignancy in the thyroid gland or any other possible primary site (8). These two authors both emphasized that there should be no malignancy in the thyroid gland. This definition is highly debated as 11-45% of all TDCa cases have a synchronous thyroid carcinoma (8, 20). Possible explanations for the finding of synchronous lesions include multi-focal thyroid carcinoma, or metastatic spread through the TDR (9). The diagnosis of a carcinoma in a TDC is usually incidental with no additional clues to suspect this preoperatively at the initial clinical presentation (8).

Preoperative ultrasonography, ultrasound-guided fine needle aspiration cytology (US-FNAC) and CT imaging of the neck are useful to enhance the accuracy of preoperative diagnosis (15). The US finding of a solid mass, especially with micro-calcifications, irregular margin and thick wall, is strongly suggestive of malignancy (15, 21). CT imaging of the neck is rarely indicated preoperatively unless there is a high clinical/FNAC suspicion of malignancy (8, 15). At CT, carcinomas have either a dense or enhancing mural nodule, calcification within the cyst, or both (22). Furthermore these tests helped to reveal thyroid gland abnormalities and suspicious nodes. US-FNAC is a relatively simple, safe, well-tolerated, rapid, inexpensive procedure with minimal risk complications and provides a valuable test for preoperative planning, even though it is more reliable in diagnosing solid tumors than cyst-

ic lesions. Chen *et al.* (23) stated that FNAC is the most reliable method of detecting a malignant process in midline neck masses before surgery. For some authors FNAC should be considered in all patients except children (9, 24). Others consider that FNAC is not cost-effective due to the rarity of this malignancy and remains an inappropriate tool for routine use in children (8, 9, 15). Further, the diagnostic accuracy of FNAC is not high. Sensitivity rates of 56% to 62% and a positive predictive value of 69% have been reported (25). The false-negative diagnosis by FNAC is mostly due to hypocellularity that results from dilution from the cystic contents (26). Ultrasound assistance during FNAC may enhance precision of cytological sampling if mural masses are present in the cyst, and thus may significantly reduce the false-negative diagnostic rate (21). In Miccoli's report, routine FNA had extremely high sensitivity (100%) and specificity (100%) (16). But, in Yang's report the diagnostic accuracy was only 53%, and false-negative rate was 47% (26). Ogawa *et al.* have suggested we use three-dimensional computed tomography to provide an accurate preoperative diagnosis of TDCa in a TDC (27). Surgical treatment of these carcinoma is controversial. There is uniform agreement that the minimum treatment for a TDCa is Sistrunk's procedure consisting of excision of the cyst with the central portion of the body of hyoid bone and a core of tissue around the thyroglossal tract extending up to the foramen caecum (5). Simple excision of the cyst itself is inadequate, as it provides significantly poorer survival than Sistrunk's procedure (28). There is considerable controversy regarding the role of thyroidectomy in the management of a TDCa. Some authors agree that surgical treatment of the thyroid is indicated for any suspicious lesions found in the thyroid gland during preoperative screening or intraoperative exploration, cyst wall invasion and large TDCa lesions (8, 9, 29). It is believed by some authors that these tumors are metastases from occult thyroid cancers, and hence they advocate total thyroidectomy (TT) as part of the definitive treatment (29). Another reason for advocating TT is the occurrence of concomitant cancers in the thyroid gland in adult patients with TDCa. It is also argued that the complications of TT in skilled hands are low. Twenty-five percent of TT done as part of treatment for TDCa showed synchronous well-differentiated cancer (28). Other authors argue that TT is not needed due to the low incidence of microscopic foci found in "normal" thyroid tissue (30) and the high incidence (as high as 35%) of occult "incidental" thyroid carcinoma in autopsy studies. In our patient we performed excision of the TDC and hyoid bone followed by TT at the same time. In our experience TT is not recommended in micronodular thyroid but in (controllare il senso: 'while' non ha senso) euthyroid, in the absence of other risk factors. In this case we worked in this way relying on FNAC and considering the literature from which we know that there may be a synchronous thyroid carcinoma in patients with TDCa and moreover that the latter may be a metastasis from occult thyroid cancers. In our experience we have also noticed a high incidence of incidental carcinoma of the thyroid in benign nodular disease. These cancers have proved to be microcarcinoma (< 1 cm diameter) in several patients, but we found an invasion of the thyroid capsule in many of them. Recently, the concept of stratification by risk has been suggested. Plaza *et al.* (8) recommended more aggressive treatment including total thyroidectomy and radioactive iodine therapy for patients deemed to be at high risk. They defined high risk characteristics as being older than 45 years, having a history of radiation exposure, a tumor in the thyroid on radiological evaluation, having clinical or radiological nodes, a tumor more than 1.5 cm in diameter, cyst wall invasion or positive margins on histopathologic examination (8).

Additional factors that guide risk assessment include gender and tumor characteristics such as histological grade/type, tumor focality and lymphovascular invasion. In our case, the patient was submitted to adjuvant radioactive iodine and post-operative L-thiroxine suppressive therapy, as in our all post-total thyroidectomy patients with a final diagnosis of carcinoma, to keep the thyroid stimulating hormone (TSH) levels between 0.2 and 0.5 mU/l. In our experience, annual measurement of serum thyroglobulin and twice yearly ultrasound scan of the neck are recommended in the follow-up for these patients. The overall prognosis for papillary TDCa arising in a TDC is excellent with reported 10-year survival rates of 95.6% and a long-term metastatic rate of <2% (28).

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