# Surgical approach for nodular neck lesions mimicking primitive thyroid neoplasms Report of three cases



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### Surgical approach for nodular neck lesions mimicking primitive thyroid neoplasm. Report of three cases

AIM: The finding of a neck nodular lesion provides strong suspicion of primary thyroid malignancy. Direct extension into the thyroid parenchyma of carcinomas arising from pharynx, larynx, trachea or esophagus, nervous structures has been also observed in the minority of cases. The intent of our study is to present and discuss rare conditions presenting asymptomatic neck masses, with particular emphasis on pre-operative characteristics and diagnostic criteria.

MATERIAL OF STUDY: In our retrospective analysis, we present three cases of nodular neck lesions that have mimicked primitive thyroid pathologies at the first diagnosis. Results: A 53-mm nodular mass in the right thyroid lobe was observed in one patient. The definitive diagnosis was

RESULTS: A 53-mm nodular mass in the right thyroid lobe was observed in one patient. The definitive diagnosis was Castleman's disease. The second case presented a 20-mm hypocchoic lesion in the contest of a multinodular goiter. The pre-operative suspect was thyroid carcinoma with hypophynode metastases but the definitive histology documented an 'ancient schwannoma'. A further patient presented bilateral supra-clavear and cervical hypophynodes in a multinodular goiter, initially interpreted as thyroid carcinoma with loco-regional spread. After a total thyroidectomy and cervical hypophynodes and a multinodular goiter, initially goiter without atypical cellularity. The patient is considered to have an occult tumor, probably arising from the breast, and she was scheduled in an oncological program.

CONCLUSIONS: Nodular neck lesions are frequently misdiagnosed as primitive thyroid nodules in the common clinical practice. In these rare conditions, surgical exploration is advocated to reach the definitive diagnosis, to indicate the most appropriate treatment and to avoid unnecessary thyroidectomy.

KEY WORDS: Ancient Schwannoma, Castleman's disease, Nodular neck lesion, Thyroid nodule

## Introduction

Solid neck lesions can be easily interpreted as thyroid nodules or lymphnode metastases in the common clin-

ical practice <sup>1</sup>. In the minority of cases, these lesions can originate from extra-glandular structures such as nerves, vessels, cervical fascia, trachea and esophagus <sup>2-5</sup>. Ultrasonography, computed tomography, and fine needle aspiration biopsy (FNAB) represent the armamentarium that might help the clinicians to reach preoperative diagnosis and to define the more appropriate treatment. FNAB has a considerable role in thyroid-nodule diagnosis. Before its routine use, the diagnosis of malignancy could be reach in 14% of observed cases <sup>6</sup>. Only after its introduction, the incidence of malignancy increased about 50% of cases <sup>7</sup>. We report our experience concerning nodular neck lesions initially interpreted as prim-

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itive thyroid diseases. Our limited experience confirms that solid masses of the neck can be easily misdiagnosed as primitive thyroid pathologies, and that surgical resection is advocated to confirm the histological origin and to avoid unnecessary thyroidectomy.

#### Case Report

#### CASE 1

In a 70-years-old woman, a 53-mm vascularized and calcific nodule in the right antero-lateral region of the neck was diagnosed. This lesion, documented by ultrasonography laterally to right thyroid lobe, has an extension in the mediastinum with cervical vessel dislocation and tracheal displacement (Fig.1).

FNAB documented a population of leukocytes but not atypical cells, and the lesion was interpreted as



Fig.1: Ultrasonography shows the vascularized and calcific nodule in the right antero-lateral region of the neck (Clinical case of 70-year-old woman; Case 1).

ipertrophic lymphnode. The mass was followed by ultrasonography, because the patient initially refused surgical excision. During the clinical follow-up, the lesion did not show size variation at the magnetic resonance of the neck. Finally, the patient underwent surgery for severe dyspnea as the result of tracheal displacement. With a right-lateral cervical approach, the cervical-mediastinal mass was removed, and thyroidectomy was avoided. The extemporaneous histology suggests the diagnosis of lymphoma. Only after immunohistochemical analysis with positive staining for CD3, CD20, CD10, CD30, CD138, Bcl-2 (Fig. 2), Bcl-6, MIB-1, FVIII and CD31, the diagnosis of Castelman's disease was confirmed. The postoperative period was uneventful and the patient was scheduled in a clinical follow-up.

#### CASE 2

A 20-mm hypocchoic nodule of the left latero-cervical region was diagnosed in a 31-years-old woman affected by multinodular goiter. This lesion showed the characteristics of a metastatic lymphnode at the ultrasonography, probably as the result of a lymphatic regional spread coming from a primitive thyroid tumor. FNAB was non-diagnostic for cancer cells.

Additional ultrasonography performed four months later documented a significant increase in lesion size, around 30 mm in diameter. The patient underwent surgical excision (Fig. 3). At the extemporaneous histology, the nodule showed the aspects of a benign mesenchymal tumor. For this reason, the thyroid gland was not removed. Finally, the definitive histology diagnosed an ancient schwannoma. In the post-operative period the patient developed the signs of Bernard-Horner syndrome. The patient is currently under pharmacological treatment with sympaticomimetics and eyewashes.



Fig. 2: Immunostaining for Bcl-2. Positive staining was documented in the perifollicular areas, but not in the germinal centers (Clinical case of 70-year-old woman; Case 1).



Fig. 3: Nodular lesion located in the left latero-cervical region. (Clinical case of 31-year-old woman; Case 2).

#### CASE 3

Multiple bilateral supraclavear and cervical lymphnodes were diagnosed in a 52-years-old woman with a past history of euthyroid multinodular goiter associated with autoimmune chronic thyroiditis (Fig. 4).

Ultrasonography revealed bilateral cervical adenopathies ranged from 2 to 22 mm in diameter and an hypoechoic nodule with fine calcifications in contiguity with the inferior pole of right thyroid lobe. A thyroid nodule of 23x15 mm in diameter was documented in the left lobe. The patient underwent FNAB. The right thyroid node aspiration was non-diagnostic for cancer cells. The cytology coming from cervical lymphnode diagnosed an undifferentiated/anaplastic carcinoma that was negative for the expression of thyroid markers, including thyroid transcription factor-1 (TTF-1) and thyroglobulin,



Fig.1: Ultrasonography shows the vascularized and calcific nodule in the right antero-lateral region of the neck (Clinical case of 70-year-old woman; Case 1).



Fig. 5: Immunostaining of HER2/neu protein (HercepTest; Dako A/S, GloStrup, Denmark) suggests the diagnosis of a primitive tumor of the breast. Original magnification, x20 (Clinical case of 52-year-old woman; Case 3).

The immunostaining showed positivity for cytokeratins (CKAE1/AE3).

Any radiological evidence of other primitive tumor was detected. The patient underwent mammography and ultrasonography of the breast. A small, round, hypo-anechoic lesion in the left inferior quadrant was finally documented. Serological carbohydrate antigen (CA 19-9) and carcinoembryonic antigen (CEA) markers were negative. The patient underwent combined neck and thorax computer tomography scan, which confirmed lymphadenopathies in the right supraclavear fossa, and in the bilateral latero-cervical space, submandibular and nuchal regions. Finally, the patient underwent total thyroidectomy and right latero-cervical lymphadenectomy. The extemporaneous histology underlined the suspect of malignant poorly differentiated oncocytoma, and for this reason total thyroidectomy with right latero-cervical lymphadenectomy was finally indicated. Definitive histopathology confirmed the diagnosis of follicular chronic thyroiditis with lymphnode metastases coming by poorly differentiated carci-noma. The morphological and molecular pattern excluded the thyroid origin of the tumor. The tissue up-regulation of HER2 protein suggested the hypothesis of a primitive breast tumor (Fig. 5). Magnetic resonance of the breast did not show evidences of malignancy. Finally, a whole-body positron emission tomography was performed, but no areas with increased metabolic activity were observed in the body. The patient underwent chemotherapy with epirubicin and cyclophosphamide scheme and radiotherapy of the right latero-cervical and supraclavear regions.

Currently the patient is considered to be the carrier of an occult tumor, probably of breast origin, and she is scheduled in an oncological follow-up program.

## Discussion and Comments

In the majority of cases, the finding of a neck mass provides strong suspicion of primary thyroid pathologies <sup>1</sup>. Cases of direct extension into the thyroid parenchyma of carcinomas from pharynx, larynx, trachea or esophagus, have been documented, even if most of these lesions originate from nervous and glandular structures <sup>2-5</sup>.

Sira et al. have reported 29 cases of neck masses that were removed as branchial cysts. Of these, 23 (79.3%) confirmed the diagnosis, and the remaining included two thyroid papillary carcinomas (6.9%) and four benign lesions (laryngocele, neurilemmoma, parotid gland cyst) and cystoadenoma (13.6%) <sup>8</sup>. They also have reported 47 solitary neck masses that were diagnosed as metastatic cancer, where three lesions were clinically mistaken as branchial cysts (6.4%), and subsequently diagnosed as squamous cell carcinomas <sup>8</sup>. FNAB represents a diagnostic tool in association with radiological imaging coming from ultrasonography, computed tomography scan, and magnetic resonance exam. In our first case, the definitive diagnosis was Castleman's disease, an uncommon primary lymphoproliferative disorder originally described in 1954 by Castleman and Towne. This can occur at any age, although it is more common in adults 9. It usually develops as a solitary mass in the mediastinum (60%), neck (14%), retroperitoneum (11%) or axilla (4%) 10. There are two histopathological subgroups of Castleman's disease: the hyaline vascular type (80%-90% of cases) and the plasma cellular type. The first of these is characterized by a hypervascular hyalinized stroma, wherein there are small lymphoreticular follicles. The plasma cellular type of Castleman's disease is rare but more aggressive, and it is characterized by mature plasma cellular clusters among lymph follicles 9. The 3-year disease-free survival rate for patients with unicentric hyaline vascular disease (49.5% of cases) is 92.5%, versus 45.7% for those with multicentric plasma cell disease (20.2% of cases), and 78.0% for those with any other combination (22.6% of cases). HIV positivity is frequently associated with multicentric plasma cell disease with a 3-year disease-free survival rate of 27.8%<sup>11</sup>. After systematic literature research, around 416 cases of Castleman's disease have been identified [11]. The neck is an uncommon site for Castleman's disease and limited clinical cases have been reported 9. The correct diagnosis is always a challenge due to the aspecific clinical symptoms 12-14.

In our second case, definitive histology diagnosed an 'ancient schwannoma'. Schwannoma is a benign, encapsulated nerve sheath cell neoplasm with degenerative histological features, such as nuclear pleomorphism, xanthomatous changes and vascular hyalinization.

Schwannomas may arise from any peripheral nerve, although the cervical is uncommon. In the past, these tumors were considered malignant <sup>15,16</sup>. These tumors can often mimic thyroid nodules or atypical lymph nodes <sup>17</sup>. Schwannomas of cervical sympathetic chain can be asymptomatic or can initially present as neck masses. Dysphagia, lower cranial nerve paralyses, conductive hearing loss, trismus and Horner's syndrome represent the more frequent clinical expression. FNAB and radiological imaging have a low sensibility to reach pre-operative diagnosis. An extemporaneous histology is always recommended to plan a correct surgical removal <sup>16,17</sup>. The most common complication after surgical excision of schwannomas is Horner's syndrome, which is generally permanent <sup>16</sup>. The efficacy of surgical excision strongly depends on the surgeon experience, the dimensions of the lesion and the relationship of surrounding structures <sup>18</sup>.

The third case that we have reported was initially interpreted as primitive thyroid disease with lymphnode metastases. The patient was affected by a multinodular goiter and chronic thyroiditis. Chronic inflammation of the thyroid may represent a risk factor for thyroid carcinoma<sup>19</sup>. In this condition, thyroidectomy with laterocervical lymphadenectomy was finally indicated. The

definitive histology documented a poorly differentiated carcinoma with loco-regional lymphnode metastases arising from a primitive breast tumor. Currently the patient is considered to be the carrier of an occult tumor, due to the negativity of all radiological examinations. She underwent chemotherapy with epirubicin and cyclophosphamide for a suspected tumor of the breast.

Nodular neck lesions can frequently be misdiagnosed as thyroid pathologies. An accurate radiological evaluation in association with FNAB represents the current tools to study these uncommon conditions. Unfortunately only a minority of cases may reach a definitive preoperative diagnosis.

## Conclusions

Castleman's disease, ancient schwannoma of the neck and cervical lymphnode metastases can mimic primitive thyroid pathologies. They represent uncommon clinical conditions nearly exclusively described in medical literature. Even if the reported incidence is very low, they have to be suspected in presence of nodular neck lesions developed in the anatomic region of thyroid gland. Results coming from radiological evaluation and cytological exam should be carefully interpreted to avoid unnecessary thyroidectomy. The operative exploration with tissue biopsy and the surgeon' experience are advocated to reach the definitive diagnosed and to define the more appropriate treatment of care.

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#### Riassunto

OBIETTIVO: Le lesioni solide del collo sono spesso interpretate come patologie primitive della tiroide. Il coinvolgimento tiroideo da parte di tumori della faringe, laringe, trachea o esofago, e delle strutture nervose è stato osservato in una minoranza dei casi. Lo scopo del lavoro è quello di presentare e discutere condizioni cliniche riferibili a lesioni asintomatiche del collo, con particolare enfasi ai criteri diagnostici e alle caratteristiche di presentazione.

MATERIALE E METODO: Nella nostra analisi retrospettiva, presentiamo tre pazienti con lesioni solide del collo che alla valutazione pre-operatoria sono state inquadrate come patologie primitive della tiroide.

RISULTATI: În un caso abbiamo osservato un massa di 53 mm localizzata nel lobo tiroideo destro. La diagnosi defi-

nitiva è stata "malattia di Castelmann". Il secondo caso presentava una lesione di 20 mm nel contesto di un gozzo multinodulare. Il sospetto clinico preoperatorio era quello di un carcinoma tiroideo con metastasi linfonodali, tuttavia la diagnosi istologica definitiva deponeva per "ancient schwannoma". Un altro caso presentava Îinfonodi atipici sopra-claveari e cervicali bilaterali e un gozzo multinodulare, inizialmente interpretato come carcinoma della tiroide con diffusione loco-regionale. Dopo aver eseguito una tiroidectomia totale e una linfoadenectomia cervicale, la diagnosi istologica definitiva documentava la presenza di un carcinoma indifferenziato nel contesto di gozzo multinodulare senza atipie cellulari. La paziente è stata considerata essere portatrice di tumore occulto, di probabile origine mammaria, ed è stata inserita in un programma oncologico.

CONCLUSIONI: Le lesioni solide del collo sono frequentemente interpretate come noduli primitivi della tiroide nella comune pratica clinica. In queste rare condizioni, l'esplorazione chirurgica è indicate al fine di raggiungere la diagnosi istologica definitiva, al fine di programmare il trattamento di cura più corretto e per evitare thiroidectomie non necessarie.

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