APMB - Atti della Accademia Peloritana dei Pericolanti
Classe di Scienze Medico Biologiche
Vol. 106(2) 2018

ISSN 1828-6550

DOI: 10.6092 / 1828-6550 / APMB.106.2.2018.A9

Clinical Case Seminar A9(1-5)

Sporadic Micromedullary Thyroid Carcinoma and Hashimoto's Thyroiditis: a case report and review of the literature

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Abstract

The incidence of Thyroid Cancer (TC) is increasing worldwide during the last decades. A link between TC and inflammation is well documented. A frequent association between Papillary Thyroid Carcinoma (PTC) and Hashimoto's Thyroiditis (HT) is known, but the coexistence of HT and Medullary Thyroid Carcinoma (MTC) is rare. We present a rare case of HT and Medullary Thyroid microCarcinoma (microMTC)

KeyWords: Thyroid Carcinoma, Medullary Thyroid Carcinoma, Hashimoto's Thyroiditis, Calcitonin
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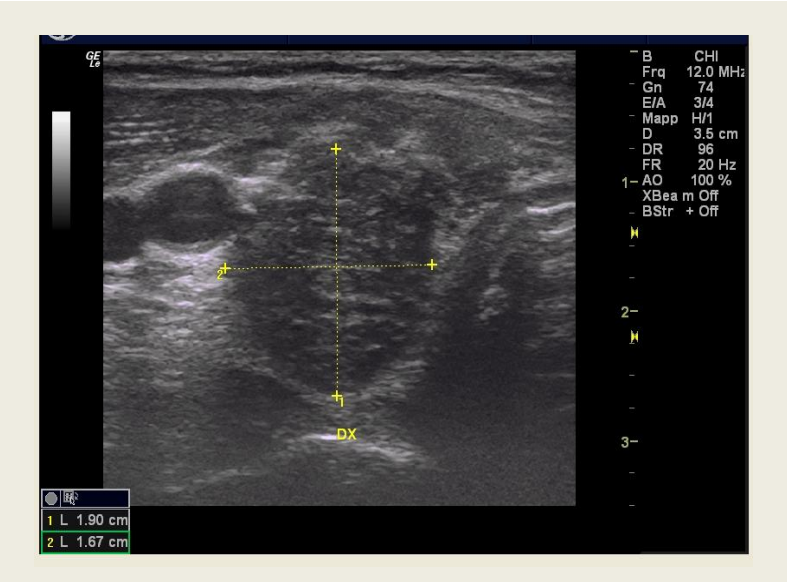
Case Report

A 49-year-old woman presented Hashimoto's thyroiditis from the age of 30 without thyroid nodule. In the last year (Fig.1) she developed a thyroid hypoechoic nodule of 1.90 cm in diameter and fine needle aspiration (FNA) was indicated for the high ultrasound risk, EU-Tirads 5 **(Fig.1)**.

Fig. 1 Thyroid nodule marked hypoecoic, taller-than-wide; High risk, EU-TIRADS 5



ISSN 1828-6550
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Before FNA thyroid function and calcitonin (CT) dosage was performed and CT levels in a year rose from 17.4 to 57 pg/ml (Tab. 1). For the possibility of high levels of CT in HT a Calcium (Ca) test was perfomed to discovered a C-cell hyperplasia (CCH) or MTC (Tab.2). The stimulated Calcitonin (sCT) highlighted a MCT. About this, Ca sCT above 184 pg/ml in females and above 1620 pg/ml in males had the highest accuracy to distinguish normal, CCH cases or patients with MTC (2). The patient underwent total thyroidectomy with a histology of MTC of 0.9 cm without thyroid capsule exceeding and nodes involvement, with immunohistochemical CT pos. Cromogranins A pos, Neuron-Specific Enolase pos. and thyroglobulin neg, synapthoysin negative; (pT1a). The search for the RET proto oncogene was negative as well as urinary catecholamine and parathormone levels were normal. The CT post-operative was <2 pg/ml. The final diagnosis was Sporadic Micromedullary Thyroid Carcinoma and Hashimoto's Thyroiditis and the patient was included in the follow up to MTC.

Table 1. Alterations in the concentration of Calcitonin (serumCtn) other than in the Medullary Thyroid Carcinoma and C-cell hyperplasia.

Reduced	**Increased**
Heterophilic antibodies	Chronic renal failure
The ''hook effect''	Primary hyperparathyroidism (PHPT)
Adrenalin	Autoimmune thyroiditis
	Small cell and large cell lung cancers*
	Prostate cancer*
	Various enteric and pulmonary neuroendocrine tumors*
	Heterophilic antibodies
	Proton pump inhibitors
	Glucocorticoids
	Beta blockers
	Glucagon

*The serumCtn levels in patients with the various nonthyroid malignancies do not increase in response to calcium or pentagastrin stimulation

Table 2. calcium stimulation tes

Calcium test (25mg/kg at 10ml/min)	**Calcitonin pg/ml**	**CEA ng/ml**
0	**54**	**0.5**
2 min	**896**	**-**
5 min	**585**	**-**
15 min	**316**	**-**

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Discussion

Hashimoto's Thyroiditis (HT) is the most common inflammatory thyroid disease and the typical cause of hypothyroidism. A link between Thyroid Cancer (TC) and inflammation is well documented.

A good correlation is documented between HT and Papillary Thyroid Cancer (PTC) and between HT and Thyroid Linfoma (TL). Resende de Paiva et al. in a recent review of 36 records (n=64,628 subjects) confirms this data and found no association between HT and follicular thyroid cancer (FTC), medullary thyroid cancer (MTC) or anaplastic thyroid cancer (ATC). The prognosis of these subtypes of TC associated to HT is more favorable (3).

The association between HT and MTC is very rare with few reported cases, while a Jordanian study suggest that there might be an association between Hashimoto's thyroiditis and medullary thyroid carcinoma, and 20% of the histological diagnosis of MTC are associated with HT only in female patients who undergo total thyroidectomy (4).

Medullary thyroid microcarcinomas (microMTC) are medullary thyroid carcinomas (MTC) that measure 1 cm in size for which there is a paucity of data about clinical behavior over time.

In the United States approximately 20% of MTCs are <1 cm, and incidence has increased over time (5).

It was observed an increased incidence of MTC in recent years, like the increasing incidence of differentiated thyroid cancer, and PTC in particular.

MicroMTCs are rare but important clinical entities that are increasing in incidence, and it is suggested that they have a higher than expected rate of lymph node involvement. Almost 1 in 4 patients with microMTC had a regional or distant disease stage (5-7))

On the other hand the outcome of the disease was more favourable with a decreasing tumour size. Only two patients with a tumour size of 0.3–0.4 cm had distant metastases during follow-up, and central and lateral compartment lymph node metastases are present respectively in 14% of patients with T1 tumors and in 86% of patients with T4 tumors. Ten-year survival rates for patients with stages I, II, III, and IV MTC are 100%, 93%, 71%, and 21%, respectively (7)

Calcitonin (CT) is a highly specific and sensitive marker of this tumor and can be used for the diagnosis and follow-up of both familial and sporadic forms. Depending on the assay, 56%–88% of normal subjects have serum basalCT levels (bCT) below the functional sensitivity, while 3%–10% have bCT levels greater than 10 pg/mL. Current reference ranges for serum bCT are higher in men compared with women, almost certainly due to the larger C-cell mass in men (8). For the diagnosis of MTC, bCT values >100 have been proposed as absolute CT thresholds mandating total thyroidectomy (9).

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Serum bCT levels were measured under basal conditions, and when basal values were more than or equal to 20 and less than 100 pg/ml, testing was repeated after calcium stimulation. Furthermore, Ca stimulatedCT above 184 pg/ml in females and above 1620 pg/ml in males had the highest accuracy to distinguish normal and CCH cases from patients with MTC (2,10)

Like the great majority of microPTC is a cancer not aggressive with active surveillance advice without surgery, can we consider the microMCT in the same way? or is microMTC only one stage from C-cell hyperplasia (CCH) to MTC, without its own characteristic of indolent tumor?

In the presence of germline mutation in the RET proto-oncogene, all C-cell proliferations are neoplastic and may range from the preinvasive CCH to MTC. Indeed, Pelizzo et al reported microMTC in 100% of prophylactic thyroidectomies performed on patients with codon 634 mutation. Furthermore, the low prevalence of the M918T mutation in microcarcinomas may represent a different entity such as carcinoma in situ (11,12).

The sporadic microMTC appears to have a better prognosis than hereditary microMTC. Extrathyroidal extension, size of the microcarcinoma, and the patient's age appear to be independently associated with risk of metastasis.

Conflicts of Interest: There is no potential conflict of interest, and the authors have nothing to disclose. This work was not supported by any grant.

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ISSN 1828-6550

DOI: 10.6092 / 1828-6550 / APMB.106.2.2018.A9

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Communicated and received June 26, 2018, revised August 18, 2018, published on line December 18, 2018