

# Cervical Lymph Node Involvement by Medullary Carcinoma of Unknown Origin; a Rare Presentation

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**M**edullary thyroid carcinoma (MTC), comprising 5-10% of all cancers, is a rare malignancy which frequently spreads to cervical lymph nodes. Occurring in both the sporadic and familial forms, the latter accounts for 20-25% of cases, while the former is considered the most frequent type. We report a case of metastatic MTC presented with cervical lymphadenopathy in a patient without evidences of MTC in thyroid gland.

**Key Words:** Glomus tumor, Neoplasms, Lymph adenopathy, Medullary thyroid carcinoma

**Received:** 25.02.2010      **Accepted:** 21.06.2010

## Introduction

Medullary thyroid carcinoma (MTC) is a rare slow-growing malignant neuroendocrine tumor which frequently spreads to cervical lymph nodes<sup>1,2</sup>. It comprises 5-10% of all thyroid cancers and may occur in sporadic or familial forms. Familial MTC accounts for 20-25% of cases and is associated with multiple endocrine neoplasia (MEN) type IIa or MENIIb. Yet, the sporadic form is considered to be the most frequent type<sup>2,3</sup>.

MTC differs in its embryological origin; it derives from the parafollicular cells of the

ultimobranchial body of the neural crest; these cells are concentrated superolaterally in the thyroid lobes, where MTC usually develops<sup>4</sup>. Considered part of the amine precursor uptake and decarboxilation system of the thyroid, MTC secretes calcitonin and other hormonal peptides<sup>3</sup>. Its biochemical marker, calcitonin, is called a unique feature of tumor<sup>2</sup>.

Patients with MTC often (15 to 20%) present with a neck mass that may be associated with palpable cervical lymphadenopathy. Regional lymph nodes are commonly involved at presentation or at recurrence. Local pain or aching is common in patients with these tumors, and local invasion may produce symptoms of dysphagia, dyspnea, or dysphonia<sup>4</sup>.

Although surgery is the treatment of choice, only approximately 50% of patients can be cured by total thyroidectomy and central neck dissection<sup>2</sup>.

## Case report

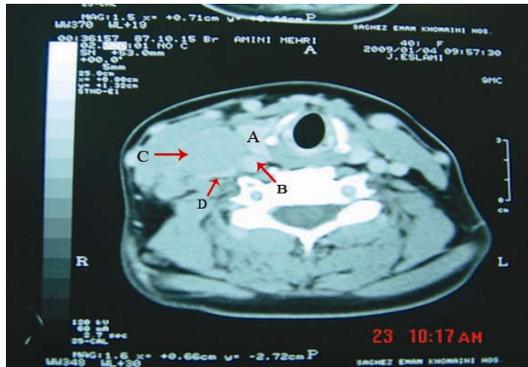
A 34-year-old woman with a left cervical mass was admitted to the surgical ward of Shohada Hospital, Tehran, in January 2009. The mass, which was in the upper left lateral neck had gradually enlarged during the last year and had remained asymptomatic until 2 months prior to presentation, when a dull pain developed in the region. She had no

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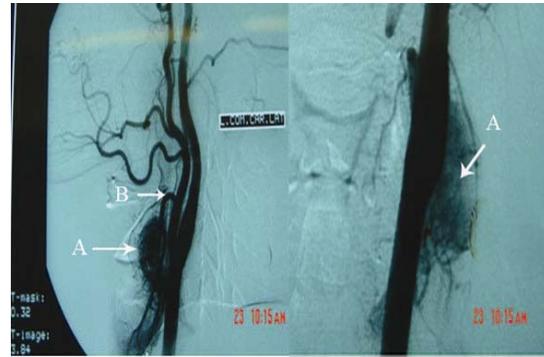
history of headaches, malaise, night sweats, or weight loss, nor any apparent family history of endocrine disorders. The patient did not have any history of previous external radiation therapy. Her past medical history was significant for a diagnosis of hyperthyroidism with high total T4 and T3, which was later attributed to oral contraceptive pill consumption. On physical examination, all vital signs including blood pressure were normal. A rough nodule, about 3 cm in size, was palpated on the left side of the neck. Physical examination revealed a slightly large and nodular thyroid. No other neck or supraclavicular lymphadenopathy was detected.

The mass was confirmed on computed tomography (CT) scan and angiography, which showed an ovoid hypervascular mass, anterior and lateral to the carotid bulb with blush, superior thyroidal artery suggesting glomus vagal tumor (Figures 1 and 2).



**Fig.1. Patient's computed tomography scan of neck. Multi hypodense lesions (A) lateral to carotid sheath (B). Neck mass (C) compressing the jugular vein (D)**

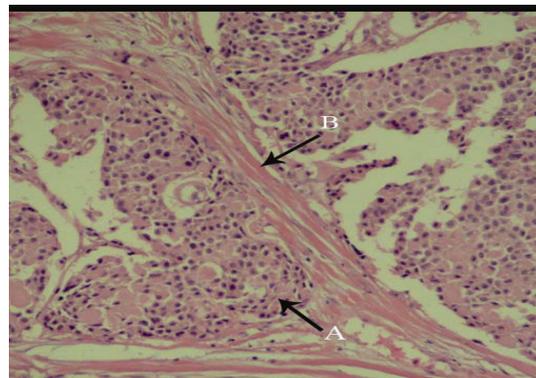
Her serum levels of calcium, thyroid stimulating hormone (TSH) and free thyroxin were normal, while calcitonin was measured at 108 ng/dL, higher than the upper normal limit of 70 for women. Due to the fact that the thyroid gland showed normal size and texture on physical examination, preoperative ultrasonography or fine needle aspiration (FNA) were not performed



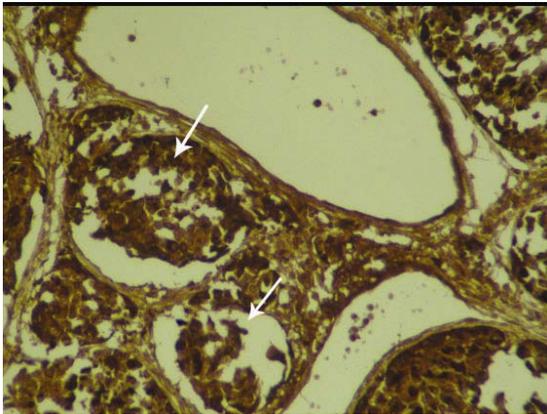
**Fig. 2. Patient's posterior anterior and lateral left common carotid selective DSA. Prominent ovoid blush (A) in seems in territory of superior thyroidal artery (B)**

The mass was resected through an anterior SCM approach. A 3cm nodule was found anterior to the internal jugular vein with some small veins relating the nodule to the internal jugular vein. The pathology report was compatible with MTC infiltrating a lymph node.

For confirmation of diagnoses, immunohistochemical examinations for calcitonin, synaptophysin, thyroglobulin and p53 were performed (Figures 3 and 4).



**Fig 3. Patient's Congo red staining of neck mass. Medullary carcinoma is composed of polygonal cells which form a solid nest (A) and trabecula with amyloid deposits in the stroma (B)**



**Fig 4. Diffuse strong cytoplasmic immunostaini for calcitonin**

Her thyroid was considered the primary suspect and the radionucleotide scan showed a cold nodule in the left lobe. One month later she underwent total thyroidectomy with modified radical lymph node dissection.

Macroscopically, the right and left thyroid lobes both measured  $3 \times 3 \times 2$  cm. Despite the preparation of ten slides from the specimen, each 3 to 4 mm in diameter, microscopic examination of the thyroid showed no evidence of medullary carcinoma.

Radical neck dissection showed only reactive inflammation and fibro connective tissue. CT scan of thorax and abdomen and pelvis with intra venous and oral contrast were also normal, ruling out other possible origins for the malignancy.

The patient was discharged, without complications, on the third postoperative day with a calcitonin level of 65 ng/dl. She was followed up for two years without any clinical complications. Biannual measurement of calcitonin levels also remained within normal limits.

## Discussion

MTC is a rare and aggressive type of thyroid cancer with several distinctive features that distinguish its management from papillary thyroid carcinoma (PTC). Ever since MTC was first recognized as a distinct tumor in 1959, it became clear that, in comparison

with PTC, it is more difficult to cure and has higher rates of recurrence and mortality<sup>5</sup>. In addition, in contrast with PTC, there is no known effective systemic therapy for MTC<sup>3</sup>. The diagnosis of MTC is established by history, physical examination, raised levels of serum calcitonin or carcinoembryonic antigen (CEA) levels, and FNA cytology of the thyroid mass. Paying attention to family history is important because approximately 25% of patients with MTC have familial disease<sup>4,6,7</sup>.

Usually Patients with a sporadic medullary carcinoma have either of two manifestations: a palpable mass for which a diagnosis can be made with FNA or the finding of an elevated basal calcitonin level or the finding of an elevated basal calcitonin level in the absence of the thyroid gland<sup>6,7</sup>. The presence of amyloid is a diagnostic finding, but immunohistochemistry for calcitonin is more commonly used as a diagnostic tumor marker. These tumors also stain positively for CEA and calcitonin gene related peptide (CGRP)<sup>4,6,7</sup>.

Because of the high incidence of multicentricity, total thyroidectomy is the treatment of choice for patients with MTC. I<sup>131</sup> therapy is not usually effective. The central compartment nodes are frequently involved early in the disease process, so that a bilateral central neck node dissection should be routinely performed. In patients with palpable cervical nodes or involved central neck nodes, ipsilateral or bilateral, modified radical neck dissection is recommended. Similarly, patients with tumors larger than 1.5 cm should undergo ipsilateral prophylactic modified radical neck dissection, because over 60% of these patients have nodal metastases. Approximately 30% of these patients will also have contralateral nodal metastases<sup>4</sup>.

This case is unique as the presentation is not by a thyroid mass but with a metastatic lymphadenopathy. Also, even after thyroidectomy no known site of primary tumor was found. Moreover since the presence of C-

cells was proven through immunohistochemistry, the breast is ruled out as a possible primary source. Furthermore, CT scan evaluation of the abdomen failed to show any mass in the ovaries which could have been deemed responsible.

As mentioned above the patient was followed up for two years with physical examination and biannual measurement of calcitonin levels. She remained free of complications and/or disease flare-up during this time.

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