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Metastatic Medullary Thyroid Carcinoma without Evident Thyroid Nodules: A Rare Presentation

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Abstract **Case Report**

Introduction: Uncommon thyroid and neuroendocrine tumor; medullary thyroid carcinoma (MTC) is a rare, aggressive malignancy, with a 10-year survival rate of roughly 50%. Clinical presentation of MTC differs from sporadic to familial variety, but frequently it is showcased as a painless thyroid nodule. Metastatic medullar carcinoma without nodules is scanty, adding to the unpredictable behaviors of this entity. ***Case Presentation***: Thus; the report of this rare presentation in 57-year-old patient with cervical metastatic lymphadenopathy, and a normal sized thyroid and no distant metastases, to which the patient underwent a chemo/ radiotherapy because the encompassment of the vascular axis. ***Conclusion***: Metastasis medullary thyroid carcinoma with normal-size thyroid is somehow unheard of in the literature, as this rare aggressive tumor is usually diagnostic at a stage where the thyroid nodule is accompanied with lymph node metastases.
Keywords: Medullary Thyroid Carcinoma, Metastasis, Lymph Nodes, Non-Nodular Thyroid.

INTRODUCTION

Emerging from parafollicular or C cells, medullary thyroid carcinoma (MTC) is a rather rare aggressive tumor, accounting for up to 3% to 5% of all thyroid malignancies, especially characterized by the production of calcitonin; certified as its tumor marker [1-2]. Sporadic or familial in 75% and 25% respectively, the latter being either syndromic (MEN2B, MEN2A, multiple endocrine neoplasia type 2B, 2A) and non-syndromic (Familial MTC) types [1- 4]. True, the most common presentation of MTC is that of painless nodule, nevertheless in 50% of cases, lymph node metastases take place at the time of diagnosis [1- 3]. That being said, we report a very rare, unique occurrence of MTC; it is that of metastasis medullary thyroid carcinoma with normal-size thyroid in 57 years-old male patient, admitted for right lateral-cervical lymphadenopathy of which the biopsy confirmed metastatic location of MTC and of which the radiological investigation revealing a lack of nodules in a normal sized thyroid and no distant metastases.

CASE REPORT

A 57-year-old male patient, with no pathological history, in particular, no neoplasia or family history of thyroid or other endocrine debases, was admitted to the ENT department for a right lateral-cervical painless mass evolving for 3 years, gradually increasing in volume, without compressive or dysthyroidism signs, as well as no flush syndrome nor diarrhea with no decline in his general condition.

Examination found a hard, right, lateral-cervical mass of 10 cm, painless, restricted in mobility, with normal skin and no inflammatory signs, extended from just under the parotid region to the supraclavicular region and up to the spinal region Figure (1). Neither peripheral facial nerve palsy nor clinical abnormalities in the thyroid gland were found. Ophthalmologic and cutaneous as well as the oral cavity and base of the tongue, along with the rest of the examination were within the normal. Due to the localization, nasofibroscopy was performed revealing a regular surface bulge in the nasopharynx, with a normal larynx.

Ultrasound showed hypoechoic right spinal and jugulocarotidien chain adenopathy with anarchic vascularization measuring 25*13 mm for the largest with an anodular thyroid gland of normal size Figure (2).

CT scan showcased hypodense right cervical jugulo-carotid and spinal (Ib, II, III, IV, V) and para and retropharyngeal lymphadenopathies which are enhanced evenly by the contrast necrosis with a thyroid gland

always of normal size and homogeneous Figure (3).

For a better characterization of the mass, our patient benefited from a cervical MRI which showed a cast of right para and retro-pharyngeal and jugulo-carotid (I, II, III, IV, V) and spinal adenopathy forming a 16 cm long mass isointense T1, heterogeneous hyperintense T2 and in hyperintense diffusion. This mass comes into contact and bulges at the right side wall of the nasopharynx, and fills the ipsilateral infratemporal fossa and both the retro and pre-styloid spaces, encompassing the right internal carotid which remains permeable. The mass also represses and deforms the right side wall of the oropharynx and extends along the jugulo-carotid package, with repression of the internal jugular vein, which is collapsed but remains permeable with a normal size and morphology thyroid Figure (4).

The anatomopathological examination of the sample taken from the nasopharynx was inflammatory without signs of malignancy. A lymph node biopsy was carried out, objectifying a localization of a tumoral proliferation with round cells with amyloid stroma organized in diffuse layers with an outline of acinar structures. The tumor cells are medium to large and have a hyperchromic nucleus with abundant and eosinophilic cytoplasm. immunohistochemical complement was in favor of lymph node metastasis of medullary thyroid carcinoma with a positive expression of antibodies anti-Calcitonin, Pan-cytokeratin, Chromogranin, Synaptophysin, TTF1, CD20, CD3, and 10% expression of antibody anti Ki67.

Blood work revealed a calcitonin serum level 58,500 ng/l, a negative parathyroid hormone at 9.2 pg/ml, calcium serum level, and urinary excretion of metanephrines within the norms; which concord with the diagnosis of sporadic medullary thyroid carcinoma.

The assessment of the tumor extension was indeed negative; thoraco-abdominal-pelvien CT images were clean of any further metastases of the MTC.

In light of all these findings, the patient was deemed inoperative, and therefore, was sent to the oncological and radiotherapy departments; where he received 3 courses of chemotherapy (cisplatin - Adriamycin), and is scheduled to receive 70GY spread over 40 sessions on the thyroid compartment.

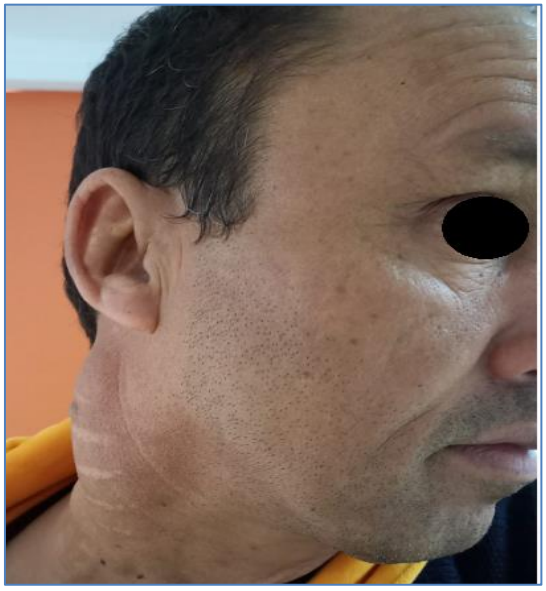

Figure 1: clinical image of the cervical mass.

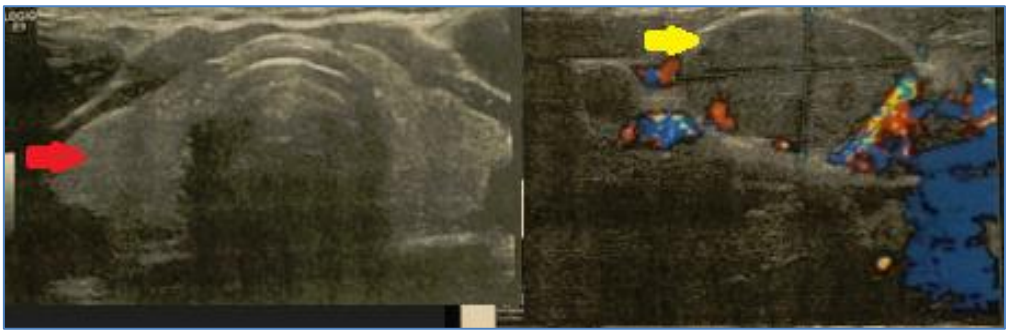

Figure 2: ultrasound images of the lymphadenopathies (yellow arrow) with normal size thyroid (red arrow)

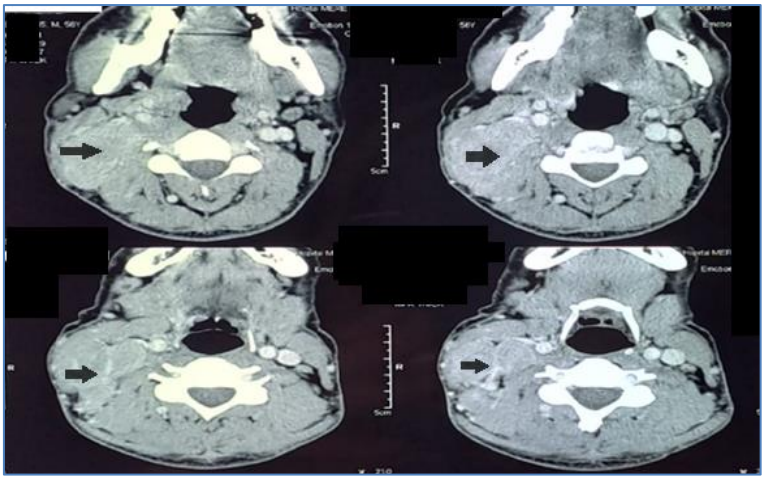

Figure 3: CT scan imaging presenting right magmas lymadenopathies (black arrow) pushing back the vascular axis which remains permeable

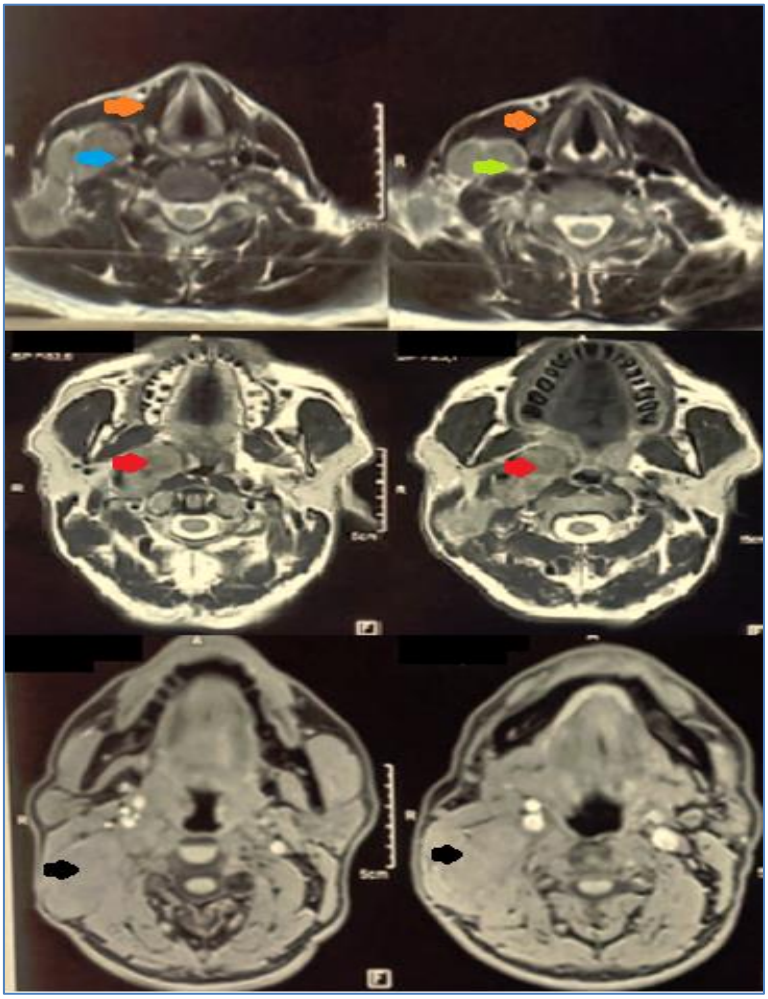

Figure 4: different MRI sequences showcasing isointense T1, heterogenous hyperintense T2 para and right retro-pharyngeal (red arrow) and jugulo-carotid (I, II, III, IV, V) (black arrow) and spinal adenopathies with repression of the internal jugular vein (blue arrow) and filling of the homolateral infratemporal fossa, retro and pre-styloid spaces and encompassing the right internal carotid (green arrow), with a normal size and morphology thyroid (orange arrow).

DISCUSSION

MTC is uncommon thyroid and neuroendocrine tumor, deriving from C cells, which originate from the neural crest, which manufacture and secret calcitonin used as an effective MTC tumor marker [1- 3]. Though its incidence remains unknown, it is estimated up to 3% to 5% of all thyroid malignancies and present in approximately 0.4% to 1.4% of thyroid nodules [1]. MTC is known for its wide age range of occurrence with

a peak in the 4th and 5th decades for sporadic forms but earlier age in hereditary ones and no predilection of sex or ethnicity [4].

The activation of the RET proto-oncogene is incriminated in the pathogenesis of MTC; its mutation may be inherited as germline mutations or sporadically in somatic mutations detected in 50% (20-80%) of patients [5]. Clinical presentation of MTC differs from sporadic to familial forms; in the first, the lesions are usually unilateral, and unicentric; whilst in the latter are bilateral and multicentric [4]. In sporadic forms, the common presentation includes thyroid nodules [1] and the presence of cervical lymph node metastasis with normal size thyroid is very rare, first described by Das *et al.*, [3] presenting a 48 years male, with a huge swelling of the left side of the neck from the parotid region to supraclavicular one with the normal-sized thyroid gland.

Family history or the presence of other disorders; endocrine or non-endocrine ones; such as pheochromocytoma, cutaneous neuromas and megacolon, and so on; may lead to suspicion of the hereditary variety of MTC [1- 4]. Note that up to 35% of the cases presenting palpable nodules have already cervical metastases and during follow-up up to 20-40% of patients will present distant metastases [4- 5]. Biologically speaking, MTC‘s behavior is unpredictable and varies from indolent to rapidly progressive. Clinical symptoms such as flushing or diarrhea are usually found in advanced MTC, whereas the secretion of multiple peptides (histaminase, vasoactive intestinal peptide serotonin…) [4- 6].

Given the morphological diverseness and the resemblances of other primary tumors of the thyroid, calcitonin manifestation is requisite for the pathohistological diagnosis of MTC. Typically, MTC tumor cells are polygonal to round with amphophilic cytoplasm and medium-sized nucleus, and those cells are spread in solid sheets separated by highly vascular stroma, hyalinised collagen, and amyloid [3- 6]. Fine needle aspiration smears show classically isolated, oval to round, large polygonal or spindled cells, but often fail to make a proper diagnosis [1- 7]. Calcitonin is a valuable specific and sensitive tumor marker used for diagnosis, extension, treatment, prediction of reoccurrence, and prognostic; as its serum level is directly correlated with the tumor mass [3- 4].

MTC curative, standard treatment consists of total thyroidectomy associated with central lymph node neck dissection that may be extended to unilateral or bilateral cervical lymph node dissection depending on imaging, calcitonin serum level, and peroperative findings [4]. External beam radiotherapy has its place facing residual tumor or relapse, local/ locoregional and/or extranodal extension, but no benefit with adjuvant radiotherapy in completely resected disease has been proven, and palliative radiotherapy is mainly used in painful bone metastases with or without pathologic fractures [8- 9]. Unfortunately, there is no effective therapy for advanced inoperable and/or distant metastases disease [10], there are narrow response rates, and the data with chemotherapy [4]. However, there is a promising future due to the development of molecular targeted therapies, especially vandetanib or cabozantinibas they are approved, but needing more clinical trials [1- 11].

CONCLUSION

MTC is a rare but aggressive, unpredictable tumor, with an unfavorable prognosis. Metastatic medullar carcinoma without any present nodules in the thyroid gland is extremely rare but not implausible; as the most common presentation is that of an asymptomatic thyroid nodule.

REFERENCES

1. V. David., R, Elisei. (2019). “Management of Medullary Thyroid Cancer“.*Endocrinol Metab Clin North Am. 48*(1), 285-301.
2. Siqueira, D., Rocha, A. P., Puñales, M. K., & Maia, A. L. (2009). Identification of occult metastases of medullary thyroid carcinoma by calcitonin measurement in washout fluid from fine needle aspiration of cervical lymph node. *Arquivos Brasileiros de Endocrinologia & Metabologia*, *53*, 479-481.
3. Das, S. K., Varshney, H., Saha, M. L., Sen, S., Maity, A. B., & Paul, R. (2013). An unusual presentation of medullary thyroid carcinoma. *Indian Journal of Otolaryngology and Head & Neck Surgery*, *65*, 195-198. DOI 10.1007/s12070-013-0624-z.
4. Dabelić, N., Jukić, T., & Fröbe, A. (2020). Medullary thyroid cancer–feature review and update on systemic treatment. *Acta Clinica Croatica*, *59*(Supplement 1), 50-58.
5. de Groot, J. W. B., Links, T. P., Plukker, J. T., Lips, C. J., & Hofstra, R. M. (2006). RET as a diagnostic and therapeutic target in sporadic and hereditary endocrine tumors. *Endocrine reviews*, *27*(5), 535-560.
6. de Lima, M. A., Dias Medeiros, J., Rodrigues da Cunha, L., de Cássia Caldas Pessôa, R., Silveira Tavares, F., de Fátima Borges, M., & Marinho, E. O. (2001). Cytological aspects of melanotic variant of medullary thyroid carcinoma. *Diagnostic cytopathology*, *24*(3), 206-208.
7. Trimboli, P., Treglia, G., Guidobaldi, L., Romanelli, F., Nigri, G., Valabrega, S., ... & Giovanella, L. (2015). Detection rate of FNA cytology in medullary thyroid carcinoma: a meta-analysis. *Clinical Endocrinology*, *82*(2), 280-285. doi: 10.1111/cen.12563.
8. Brierley, J., & Sherman, E. (2012, July). The role of external beam radiation and targeted therapy in thyroid cancer. In *Seminars in radiation*

oncology (Vol. 22, No. 3, pp. 254-262). WB Saunders.

9. Call, J. A., Caudill, J. S., McIver, B., & Foote, R. L. (2013). A role for radiotherapy in the management of advanced medullary thyroid carcinoma: the mayo clinic experience. *Rare tumors*, *5*(3), 128-131.
10. Hadoux, J., Pacini, F., Tuttle, R. M., & Schlumberger, M. (2016). Management of advanced medullary thyroid cancer. *The lancet Diabetes & endocrinology*, *4*(1), 64-71.
11. Schlumberger, M., Bastholt, L., Dralle, H., Jarzab, B., Pacini, F., & Smit, J. W. A. (2012). 2012 European thyroid association guidelines for metastatic medullary thyroid cancer. *European thyroid journal*, *1*(1), 5-14. doi: 10.1159/000336977