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Original Research Paper

Pathology

MEDULLARY CARCINOMA THYROID WITH FOLLICULAR VARIANT – AN INTERESTING CASE

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ABSTRACT We report here a case of 17 yr old male presenting with nodules in both lobe of thyroid along with presence of bilateral cervical lymphadenopathy. The aspiration cytology from the nodule and the lymph node was reported as mixed medullary and follicular carcinoma. Lymph node was received for histopathology which came out to be positive for medullary carcinoma and a total thyroidectomy was performed. The pathology report revealed medullary carcinoma with follicular variant. Immunohistochemical analysis was negative for thyroglobulin and positive for calcitonin. A few patients with this variant have been reported in the literature, mainly diagnosed by immunohistochemical features of the tumor. In light of the limited information we have obtained from the literature, it is reasonable to emphasize that these cases should be distinguished from the mixed medullary-follicular thyroid carcinomas and medullary carcinomas with entrapped follicles. Immunohistochemical examination with calcitonin and thyroglobulin is also essential.

KEYWORDS : Medullary, Follicular Variant, Congo Red, Calcitonin

INTRODUCTION:

Medullary thyroid carcinoma (MTC) is a neuroendocrine tumor that originates from parafollicular or c-cells of the thyroid gland. [1] MTC accounts for <10% of all thyroid carcinomas. It can be either sporadic in 70% of cases or familial in 30% of cases in which there is a germline mutation of RET proto- oncogene. A characteristic feature of this tumor is the production of calcitonin. [2,3] In 2002 Cakir M etal reported a case of medullary carcinoma thyroid with follicular variant in a 48 year female[4]. In 1983 Williams and Harach reported 3 cases of medullary thyroid carcinoma with tubular and follicular variant, which on immunohistochemistry were calcitonin positive and thyroglobulin negative.[5] Medullary thyroid carcinoma with follicular variant is a very rare tumor. Very few cases have been reported in the literature[4,5].

Here, we report a unusual case of thyroid malignancy in which fine needle aspiration showed mixed medullary and follicular carcinoma thyroid with metastasis to lymph node and histopathological report revealed medullary carcinoma with follicular variant.

Case:

A 17 year old male presented with diffuse enlargement of thyroid with largest nodule in the right side of thyroid. He was also having bilateral lymphadenopathy. There were no other physical abnormalities seen. Thyroid function tests were normal. FNAC was done from thyroid swelling and right cervical lymph node (Figure 1 and 2 respectively). Aspiration smears were highly cellular showing plasmacytoid cells mainly dispersed singly and in few clusters of variable sizes. The cells showed anisonucleosis , had eccentric nuclei with coarse chromatin and abundant amphophilic cytoplasm. Few binucleated , multinucleated cells were also seen. Small clumps of amyloid-like amorphous material were seen in the background. Formation of microfollicular pattern was also seen. Calcitonin test was performed for the patient which showed very high value 1900units. Report of FNAC from both thyroid and lymph node was given as mixed medullary and follicular carcinoma (MMFC). Total thyroidectomy with lymphadenectomy was then performed.

Gross:

Total thyroidectomy specimen was received , right lobe and left lobe measures 3.5x2.5x.2.5cm and 1.8x1.5x1cm respectively. Cut surface of right lobe showed grey white ill defined hard nodules, largest measuring 1.7x1.5x1.5cm. foci of neoplastic tissue was also seen in the left lobe. Isthmus was unremarkable grossly. Metastatic deposits were seen in 16 of the 20 lymph nodes with 12 lymph nodes also showing extracapsular extension.

Microscopic Findings:

Several cut sections were stained with hematoxylin and eosin. Solid nests of plasmacytoid cells with mitotic activity were seen along with few areas showing follicular differentiation (Figure 3 and 4) . Histochemically, congo red staining confirmed the presence of amyloid deposition showing apple green birefringence (figure 6) in polarizing microscope. Immunohistochemistry staining was positive for calcitonin (figure 5) and negative for thyroglobulin. Report on histopathology was given as medullary carcinoma thyroid with follicular variant with metastasis to lymph node.

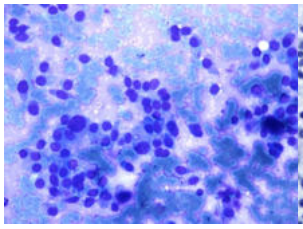

Figure 1

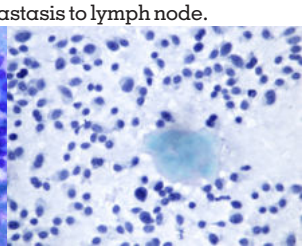

Figure 2

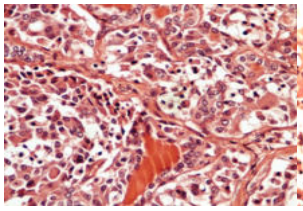

Figure 3

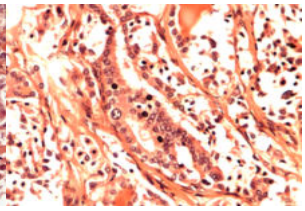

Figure 4

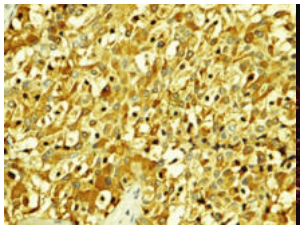

Figure 5

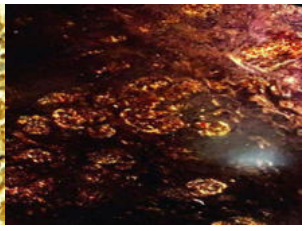

Figure 6

DISCUSSION :

MTC accounts for 5% to 10% of all thyroid malignancies. It originates from the parafollicular or c-cells of the thyroid gland. Tumoral cells typically produce calcitonin. In this unusual thyroid tumor, the predominant histological component of medullary carcinoma with amyloid stroma merged with areas of follicular character, both at the primary site and in cervical node metastases.

There are various hypothesis proposed to explain the occurrence of both the components in the thyroid carcinoma. Volante et al[6] in 1999 pointed out that MTCs may exhibit entrapped, well-preserved residual follicles. It is conceivable that some unknown trophic factors keep the entrapped follicles alive and might even stimulate them to proliferate, and conversely that some follicles might secrete substances preventing them from being destroyed by the MTC. Such a "symbiosis" of neoplastic C-cells and follicular cells might lead to a combined growth of follicular and C-cell structures and result in the mixed tumor pattern of the majority of MMFCs. The microenvironment provided by the MTC might result in hyperplastic and adenomatous follicular foci, which eventually may become neoplastic through the acquisition of molecular defects . Such a scenario could explain the spectrum of follicular patterns and the occasional neoplastic foci in MTCs .

Very few cases in the literature have been reported on medullary carcinoma with follicular variant [4] and this entity must be differentiated from mixed medullary and follicular thyroid carcinoma (MMFC) and medullary carcinoma with entrapped follicles. Calcitonin and thyroglobulin staining is helpful in differentiation as calcitonin is positive and thyroglobulin show negative staining in MTC with follicular variant while both show positive staining in other two entities.

In 2002 Cakir etal reported this entity in a 48 year old female presenting with a solitary nodule in the left lobe of the thyroid.[5]

Sambade etal in 1988 demonstrated that follicular and papillary structures can be a prominent feature of some MCTs reinforcing therefore the major role of immunocytochemistry in the differential diagnosis of thyroid carcinomas.[7]

A precise diagnosis of this uncommon variety of thyroid carcinoma is fundamental for both adequate treatment of the patient and genetic screening for excluding MEN2 syndromes and Familial Medullary Thyroid Carcinomas. Treatment is mainly driven by the medullary component and early diagnosis is essential . In the absence of any efficient conservative treatment, surgery with preservation of laryngeal nerves, including, the tumor and areas of lymphatic drainage (levels II to VII), is the first-choice strategy. Probably because of the major part of the tumor being of medullary origin, there is no evidence regarding the efficacy of adjuvant radioiodine treatment.

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