Case Report

Medullary Thyroid Carcinoma with Melanin Production – A Case Report

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Abstract

Melanin production in medullary thyroid carcinomas are rare. The present report illustrates one such case in a 70 years female. On histo-pathological examination the tumor was extensively pigmented. Amyloid was conspicuously abundant. Confirmation of diagnosis was done by demonstrating positivity for calcitonin and HMB-45 on tissue sections, suggesting a multidirectional differentiation from a common neoplastic source as the tumor cells produce numerous hormonal and non-hormonal products including mucin, peptides and amines.

Introduction

The origin of medullary thyroid carcinoma (MTC) from the parafollicular C cells belonging to the neuroendocrine sysem endows it with the capacity to produce a variety of substances and is highlighted.

Case Report

A 70 years' female presented with a neck mass of 2 months duration which was rapidly enlarging since last 3 weeks. Clinically she was euthyroid and normotensive with no suggestive past history. Family history was not contributory. Physical examination reveled a 8×6 cm, firm, non-tender mass in the neck region. Clinically, no palpable lymphnodes were felt. No clinical evidence of Cushing syndrome, subcutaneous nodules or mucosal neuromas were noted. Routine blood counts, including the liver, thyroid and renal function tests were within normal limits. Ultrasonography showed a 4.2x2.8 cm hyper dense lesion in the right lobe with lymph adenopathy. FNAC was suggestive of anaplastic carcinoma.

A sub-total thyroidectomy specimen including the right lobe measuring 5x5x4cm, the isthmus and the left lobe 2x2x1.5cm was submitted for histopathological examination. The cut section showed an unencapsulated tumour measuring 5x4x3.5cm confined to the right lobe of thyroid.The cut surface was brown black with areas of haemorrhage and necrosis. The surrounding thyroid parenchyma was compressed with the absence of satellite nodules. Five lymph nodes were noted with grey white cut surface.

Formalin fixed, multiple, paraffin sections of 5 micron thickness were stained with haematoxylin and eosin (H&E). Most of the tumor was heavily pigmented with coarse, dense, intra-cytoplasmic, brown granules obscuring the cellular details (**Fig. 1**). The non-pigmented portion of the tumour was composed of sheets of polygonal to oval cells with finely granular amphophilic cytoplasm, vesicular nuclei and small prominent nucleoli. A mitotic rate of 0-1 / hpf was noted. The pigment granules precipitated silver in the Fontana-Masson stain. Iron stain was negative. Amyloid having reactivity for Congo-red were noted. Multiple sections from the lymphnodes showed features of metastatic tumor deposits. No C-cell hyperplasia was noted.

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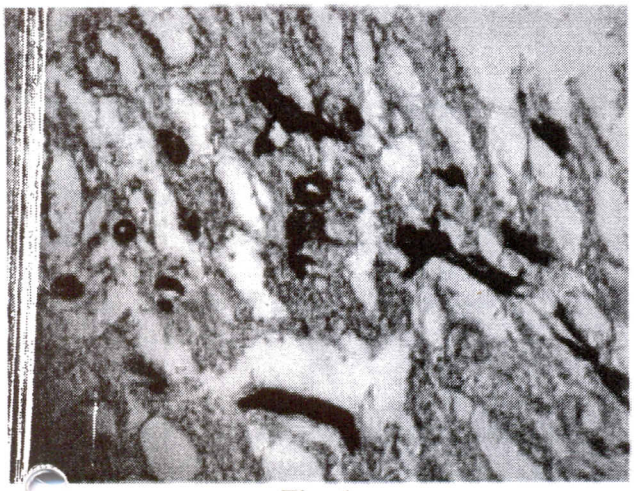

Fig. 1
Microphotograph showing pigmented tumoural cells (H&E x 400).

Subsequently a diagnosis of melanin producing medullary carcinoma of thyroid (MTC)was suggested with lymphnode metastasis and later confirmed by diffuse immunopositivity for calcitonin and HMB-45 (**Fig. 2a / 2b**).

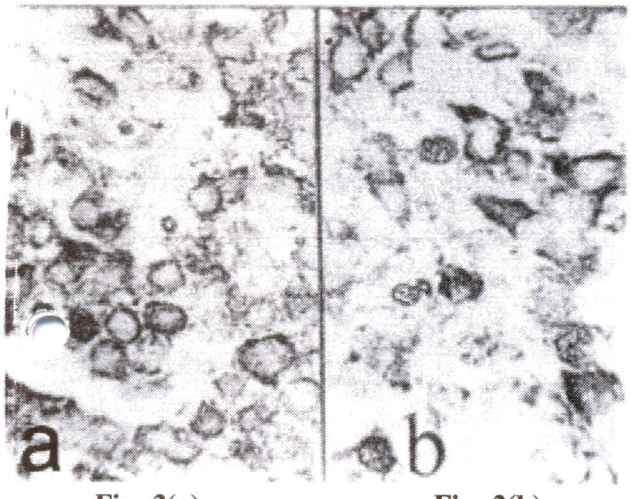

Fig. 2(a)
Photomicrograph showing diffuse intracytoplasmic positivity to Calcitonin (Avidin-Biotin peroxidase x 520)

Fig. 2(b)
Photomicrograph showing diffuse intracytoplasmic positivity to HMB-45 (Avidin-Biotin peroxidase x 520).

The post-operative period was uneventful. Estimation of serum calcium, phosphorous and calcitonin done on the sixth postoperative day were normal. Unfortunately, pre-operative estimation of serum calcitonin was missed. Further, investigations including electron-microscopy and mutational analysis for ret-oncogene could not be done .

The patient was referred to higher center for further follow-up and treatment.

Discussion

Thyroid medullary carcinoma as recognized as a distinct type of thyroid carcinoma by Hazard in 1959[1]. Melanin producing medullary carcinoma was first described by Marcus et al in 1982[2]. Review of literature suggest that till date nine cases have been reported including two cases from India[3,4]. Amongst these cases, the patient age ranged from 20 to 72 years with equal male to female ratio.

All the reported cases described a varied histomorphological features with Marcus *et al*[2] reporting a case having scanty melanin production which was localized to dendritic cells which did not have neurosecretory granules whereas Ikeda *et al*[5] described a paraganglioma like picture and the pigment was localized to the sustentacular cells and Kimura *et al*[6] mentioned a case with pigmented tumor cells having glandular differentiation.

Prognostic factors of medullary carcinoma include whether the tumor is sporadic or familial, the age of the patient, and the tumor size and stage[1]. Pathologic factors include amount of amyloid present, nuclear pleomorphism, necrosis, small cell cytology, nodal metastases, vascular invasion, extra thyroidal spread, and aneuploidy[1]. No single histological criteria can be used to distinguish between the familial variant of MTC from the sporadic variant . Usually,the familial variant of MTC may show multifocality and are associated with C cell hyperplasia[3]. The histological features of a tumor are linked to its clinical behavior, with the more slowly growing tumors, as in our case, showing regular polygonal cells with abundant granular cytoplasm often with abundant stromal amyloid, few mitoses, and a well-delimited, rounded tumor whereas the more rapidly growing tumors show spindle cells, little or no amyloid, frequent mitoses, and wide infiltration of the gland, often including vascular infiltration[3]. The calcitonin content of tumor cells broadly correlates with the degree of differentiation.

Metastatic melanoma has to be excluded before considering melanin producing MTC as the primary diagnosis as melanoma is considered to be the most

common metastatic tumor in the thyroid[7]. Routine H&E stain have limited value in differentiating melanoma from melanin producing MTC. IHC and ultrastuctural examination are essential in diagnosing MTC and differentiating it from melanoma[4]. Features favouring MTC are organoid pattern, moderate to abundant eosinophilic cytoplasm, pleomorphism and the presence of amyloid. Although melanoma can show such features but the presence of amyloid favours the possibility of MTC[7].

The exact histogenesis of the melanin producing MTC is unknown. Several theories exist which include polyclonal evolution of common neoplastic precursor cell, able to produce both melanin and calcitonin, by evolution of a precursor cell of the neural crest, having melanocytic and C-cell characteristics within a single cell, or by a mixed phenotypic expression in an oncogenic setting[8].

The prognostic and therapeutic significance of melanin producing MTC is not exactly known mainly due to rarity of the cases. Of the nine cases reported so far, follow up has been mentioned in five cases only[4]. Of these, two patients developed systemic metastases in the follow up and one had lymph node metastasis at the time of presentation[4]. We report, an additional case of melanin producing MTC with lymph node metastases at presentation. Whether or not the production of melanin in the tumor and the degree of pleomorphism will influence the biological behaviour remains to be seen.

Hence, more such cases need to be documented to avoid surgical diagnostic pitfalls and also for exact categorization and prognostication of melanin producing MTC.

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