



Case Report

Medullary thyroid carcinoma a relatively uncommon entity: A case report

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ABSTRACT

Introduction: Medullary thyroid carcinoma is an uncommon primary thyroid tumour (5-10% of all thyroid malignancies) arising from parafollicular cells or C-cells. Most tumours are sporadic (75-80%) and familial syndrome multiple endocrine neoplasia; MEN-2A, MEN-2B and familial MTC in 20 to 25% cases.

Case Report: We report a case of primary medullary thyroid carcinoma in a 30 years old male patient presented with complaint of midline neck swelling. On fine needle aspiration cytology diagnosis of medullary carcinoma was suggested with a differential of SETTLE (spindle epithelial tumor with thymus like differentiation). The swelling was excised and send for histopathological examination which revealed polygonal to plump spindle shaped tumor cells, arranged in lobules separated by fibrous septa, having abundant eosinophilic granular cytoplasm with round to oval nuclei, finely stippled nuclear chromatin and indistinct nucleoli and diagnosed as primary medullary thyroid carcinoma, confirmed on immunohistochemistry.

Conclusion: MTC is the first human malignancy known to be associated with tumour marker and hormone calcitonin. Immunohistochemistry has definite role in confirmation of diagnosis.

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1. Introduction

Medullary thyroid carcinoma (MTC) is a relatively rare entity, firstly described by Hazard in 1959, arising from parafollicular or C-cell, accounting for nearly 3% to 12% of all thyroid malignancy.^{1,2} It can infiltrate surrounding thyroid structures and metastasize to regional lymph nodes like cervical, mediastinal and to distant organs, like lung, liver, and skeletal muscle as compared to other thyroid malignancy. In all type of MTC the average survival varied from 61% to 75% for 10 years.³ The majority of MTCs are sporadic, while heritable incidence includes 25% to 30% of cases, which is associated with multiple endocrine neoplasia (MEN) 2A, MEN 2B, or with the familial medullary thyroid carcinoma syndrome.^{1,4} Genetic forms of MTC often present as multifocal disease is caused by autosomal dominant mutations of the RET proto-oncogene

with incomplete penetrance with few cases being reported to have new spontaneous mutations of the gene. As serum calcitonin is a sensitive and specific marker for MTC, routine screening of serum calcitonin levels and RET proto-oncogene mutation should be done in the affected patient and the family members, so that the inherited forms of MTC can be detected at an early stage.⁵ Histologically, MTC has no follicle development as the tumor derives from parafollicular C cells and characterized by nests of round, ovoid, polygonal, or plasmacytoid cell. Unusual histological variants of MTC have been described like spindle cell, giant cell, clear cell, melanotic, squamous and angiosarcoma-like variants, however a rarer variant showing a paraganglioma (PG)-like pattern was recognized.⁶

2. Case Report

A 30 year old male visited to outpatient department with chief complaint of midline neck swelling. On local physical

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examination the swelling was firm, mobile and non-tender, moved on deglutition, with no history of trauma. CBC, LFT and KFT were within normal limit. Thyroid Profile including thyroglobulin, TSH, FT3 and FT4 were in the normal range whereas calcitonin level was found to be 54.8 pg/ml (Normal range <10pg/ml). The patient was sent to cytopathology lab for fine needle aspiration cytology from OPD. On fine needle aspiration cytology (done outside), diagnosis of medullary carcinoma was suggested with a differential of SETTLE (spindle epithelial tumor with thymus like differentiation). Hemi-thyroidectomy was done and specimen send to the department of Pathology for histopathological examination. On gross, a globular thyroid specimen was measuring 4.0x3.5x3.0 cm. Cut surface shows haemorrhagic areas [Figure 1]. Microscopically, multiple sections examined revealed tumor cells, arranged in lobules separated by fibrous septa. Cells were polygonal to plump spindle shaped having abundant eosinophilic granular cytoplasm with round to oval nuclei, finely stippled nuclear chromatin and indistinct nucleoli [Figure 2], and amyloid stain was found positive [Figure 3]. The diagnosis of medullary thyroid carcinoma was made histologically which was confirmed by immunohistochemistry. On immunohistochemical examination, the tumour was found to be positive for calcitonin, chromogranin and synaptophysin [Figures 4, 5 and 6].



Fig. 1: Cut surface showing greyish-white tumor area with adjacent normal thyroid gland.

3. Discussion

Hazard et al described histological findings of medullary carcinoma of thyroid in 1959.² Medullary thyroid carcinoma, a neuroendocrine tumor, arises from parafollicular C cells, neural crest in origin. MTC can be a sporadic disease that is typically unilateral and corresponds to approximately 75% of all cases presents in the fourth

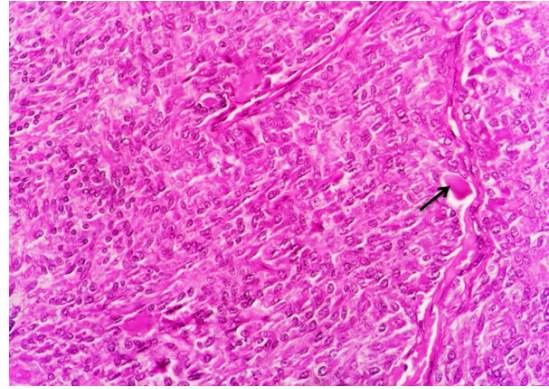


Fig. 2: Cells are polygonal to plump spindle shaped having abundant eosinophilic granular cytoplasm with round to oval nuclei, finely stippled nuclear chromatin and indistinct nucleoli along with focal eosinophilic deposits (Black Arrow) [H&E, 400X].

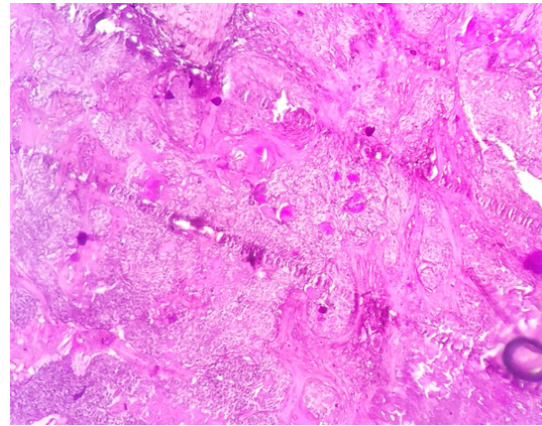


Fig. 3: Showing amyloid deposits (Methyl violet stain, 100X)

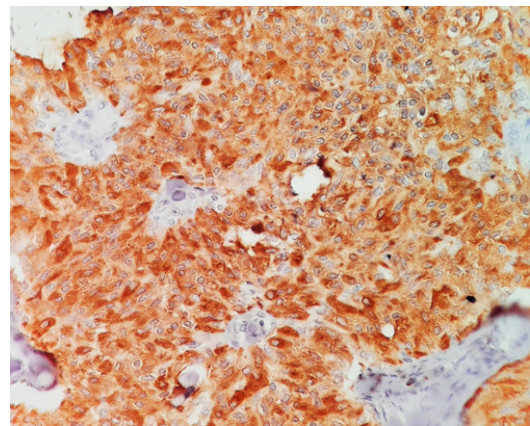


Fig. 4: Showing cytoplasmic granular positivity for calcitonin [IHC, 400X].

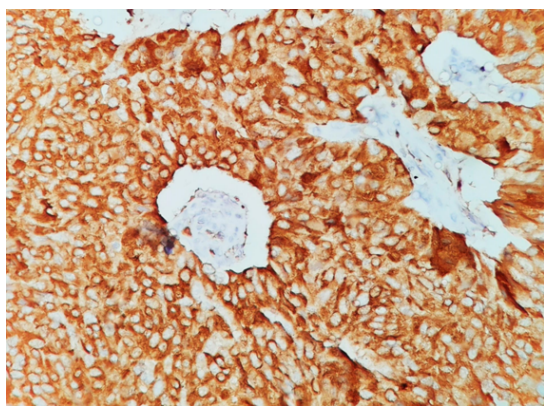


Fig. 5: Showing cytoplasmic granular positivity for Chromogranin [IHC, 400X].

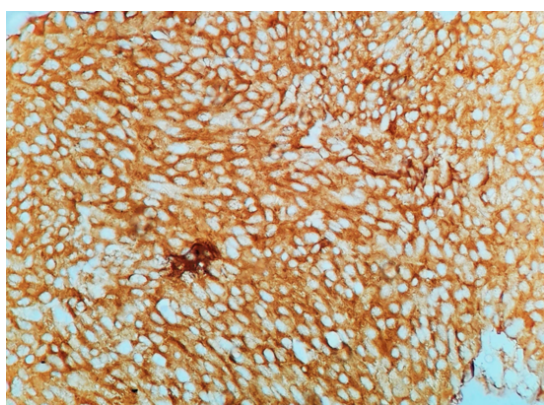


Fig. 6: Showing cytoplasmic granular positivity for Synaptophysin [IHC, 400X].

decade of life. It can also be transmitted genetically (25% of all cases) in an autosomal dominant inheritance pattern. RET proto-oncogene encode the trans-membrane receptor of tyrosine kinase family and exhibits germ-line mutation in patients with MEN 2A and MEN2B, and somatic mutation 50% of sporadic cases.⁷ MTC can be misdiagnosed as a follicular neoplasm, a sarcoma, or a plasmacytoma owing to its variable cytological presentation on fine needle aspiration cytology; hence the accuracy of FNAC has been variably reported in the literature.^{6,7} Measuring calcitonin in the aspirate specimen is a more accurate diagnostic method.⁸ MTC secretes calcitonin and CEA which is in direct proportion to the C cell mass. A thyroid nodule showing benign features on ultrasound, yet harboring MTC, elevated serum calcitonin can help to identify such nodules. Baseline calcitonin levels of 60–100 pg/mL are highly suggestive of MTC; however the clinical importance of lower concentrations of calcitonin is unclear.⁹ The surgical pathological diagnosis of MTC made by its characteristic morphology, demonstrating the solid and nesting growth pattern of tumour cells with moderate amount of granular eosinophilic cytoplasm and centrally to eccentric place

nucleus with finely stippled chromatin and indistinct nucleoli. Some tumour form conspicuous amyloid that is highly characteristic.¹⁰ However, unusual histological variants of MTC have been described like spindle cell, giant cell, clear cell, melanotic, squamous and angiosarcoma-like variants can misdiagnose; such as pseudo papillary variants mimic papillary thyroid carcinoma, tumour cells infiltrate around follicles and proteinaceous material can mimic follicles resembling follicular neoplasms, oncocytic variants as Hürthle cell carcinoma, plasmacytoid variants as plasmacytoma, spindle-cell and giant-cell variants as sarcomas or anaplastic carcinomas, and rare but aggressive small-cell types resemble lymphomas. In such condition the diagnosis should be confirmed with immunostain for chromogranin, calcitonin, synaptophysin and CEA. The significant role Ki-67 expression is not clear in MTC while used in other neuroendocrine tumours.¹¹

4. Conclusion

Apart from the classic plasmacytoid cell pattern, the neoplastic cells may resemble spindle cells or small cells with scant cytoplasm and nuclear moulding. MTC is the first human malignancy known to be associated with tumour marker and hormone calcitonin. Despite a high rate of metastasis to lymph node, 5yrs & 10yrs survival rates of MTC are 78-91% and 61-75% respectively.

5. Conflicts of Interest

All contributing authors declare no conflicts of interest.

6. Source of Funding

None.

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