

## Cytomorphologic Features of Medullary Carcinoma Thyroid

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**Abstract:** Medullary thyroid carcinoma (MTC) is a rare calcitonin producing neuroendocrine tumour which arises from the parafollicular or C cells of the gland. The cytological diagnosis of MTC is often difficult due to varied cytological features, however it is associated with specific diagnostic markers. We report here a case of MTC. The diagnosis was made on fine-needle aspiration cytology (FNAC) and confirmed by histopathology, immunohistochemistry and special stain.

**Keywords:** Thyroid, Medullary carcinoma, Calcitonin, Amyloid.

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### INTRODUCTION

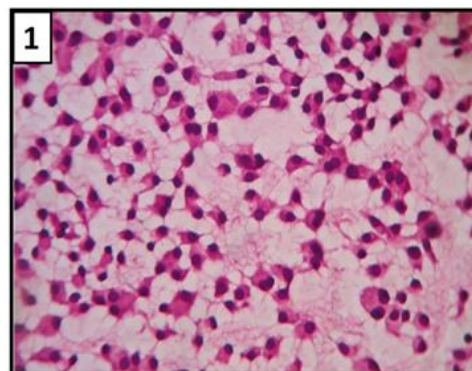
Medullary carcinoma is an uncommon tumour of the parafollicular C- cells. It accounts for less than 10% of thyroid carcinomas. Sporadic MTC account for 70% of cases and inherited MTC constitute the rest. Familial MTC is inherited autosomal dominantly either alone or as part of multiple endocrine neoplasia (MEN) type 2A or 2B and has been associated with germline gain-of-function mutations of the RET proto-oncogene [1, 2].

### CASE REPORT

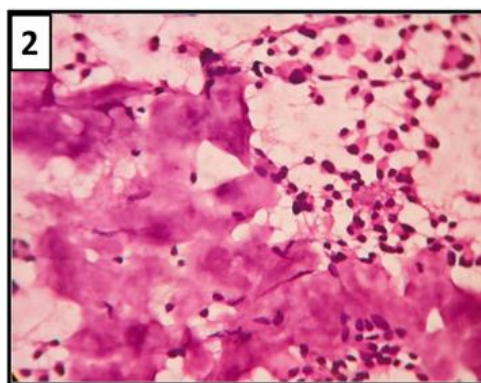
A 35 year old male patient presented with a progressively increasing midline neck (thyroid) swelling since 3 months. Physical examination revealed a solitary swelling in the right lobe of thyroid which was oval, firm to hard swelling measuring 2 cm in diameter and moving with deglutition.

### Cytology

FNAC from the thyroid lesions was done with 23-gauge needle. Smears were stained with hematoxylin and eosin (H&E) stain. Microscopic examination of the smears revealed cellular smears with predominantly dispersed and a few clusters of plasmacytoid cells of variable sizes. The cells had abundant cytoplasm and eccentric nuclei with coarse chromatin. Bi-nucleation and multi-nucleation was also noted. Small clumps of eosinophilic amyloid-like amorphous material were seen in the background. A diagnosis of the MTC was made on the basis of these cytological findings (figure 1, 2).



**Fig-1: Hematoxylin-eosin stain (10x) cytosmear showed dispersed plasmacytoid cells with occasional binucleate cells**



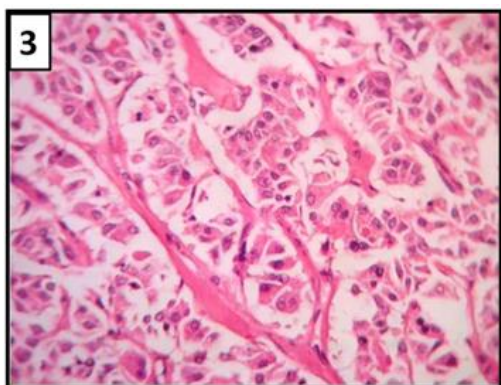
**Fig-2: Hematoxylin-eosin stain (4x) cytosmear showed eosinophilic amyloid amorphous material in the back ground**

### Histopathology

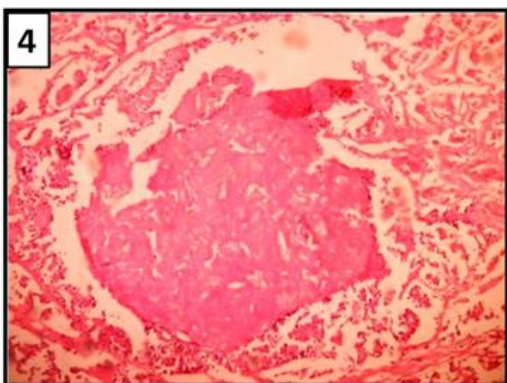
Diagnosis of medullary carcinoma of thyroid was confirmed by histopathology. The tumor tissue was arranged in syncytial, organoid, nested, micropapillae

and trabecular patterns. Individual tumor cells are round to polygonal with abundant eosinophilic cytoplasm. The nucleus is ovoid vesicular with stippled chromatin. Mitotic activity of 1-2/HPF noted. Also noted is eosinophilic amyloid like material in the background (figure 3, 4).

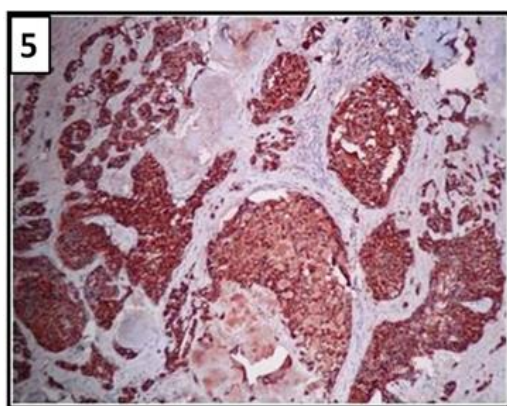
Immunohistochemistry with calcitonin revealed strong positivity in the tumour cells. Amyloid like material showed apple green birefringence under polarised microscopy (figure 5, 6).



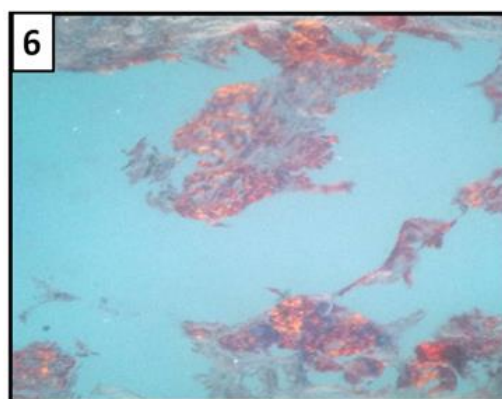
**Fig-3: Hematoxylin-eosin stain (10x) showed tumor tissue in organoid, nested pattern with vesicular nucleus**



**Fig-4: Hematoxylin-eosin stain (4x) showed eosinophilic amyloid amorphous material in the back ground**



**Fig-5: Immunohistochemistry (10x) with calcitonin revealed strong positivity in the tumour cells**



**Fig-6: Amyloid like material showed apple green birefringence under polarised microscopy**

## DISCUSSION

Medullary thyroid carcinoma is a rare thyroid carcinoma. It is associated with a tumor marker, the hormone calcitonin. The measurement of calcitonin enables diagnosis as well as prognostication, following surgical resection of the tumor [3]. Early spread to regional lymph nodes is common. Distant metastases occur in the liver, lung, bone and brain.

MTC presents as a solitary thyroid nodule. Sporadic cases are usually unilateral unlike inherited cases associated with multiple endocrine neoplasia (MEN) syndromes which are always bilateral and multicentric. MTC typically is the first abnormality observed in both MEN 2A and 2B syndromes.

RET gene is involved in the development of this tumor. RET (REarranged during Transfection) proto-oncogene is a receptor protein tyrosine kinase encoded on chromosome 10 [4]. Isolated MTC occurs in the fifth or sixth decade of life, and MTC associated with MEN syndromes occurs during the second or third decade of life.

Clinical presentation and disease outcome depends on the extent of disease, nature of tumor and overall efficacy of surgical treatment. Patient may present with a solitary thyroid nodule or with compression symptoms like hoarseness, dysphagia, and respiratory difficulty. Diarrhea may occur from increased intestinal electrolyte secretion secondary to high calcitonin levels in plasma. Distant metastases may result in weight loss, lethargy and bone pain.

FNAC smears from the plasmacytoid medullary thyroid carcinoma are usually cellular, with tumor cells that are dispersed. The individual cells are characterized by abundant cytoplasm, eccentric nucleus, neuroendocrine type chromatin, inconspicuous nucleoli. Binucleated and multinucleated cell are often noticed [5].

Apart from the classic plasmacytoid cell pattern, the tumor cells may resemble spindle cells, or

small cells with scanty cytoplasm and moulding of nuclei [6]. In such cases, the presence of eosinophilic amyloid material in the background is a valuable clue to the diagnosis. Congo Red staining helps to differentiate amyloid from colloid or hyaline fragments and is diagnostic for medullary thyroid carcinoma. Amyloid may be seen in smears from amyloid goiters as well as plasmacytoma of thyroid [7]. Hence attention to the individual cell morphology helps in the diagnosis.

The small cell pattern of tumor cells may be mistaken for a malignant lymphoma, poorly differentiated insular carcinoma or metastatic small cell carcinoma. Similarly, the spindle cell variant of tumor mimic a fibroblastic tumor or a melanoma and giant cells from anaplastic carcinoma [6]. In such cases, measurement of serum calcitonin levels are very helpful for the diagnosis of medullary carcinoma thyroid.

Calcitonin is the principal biochemical marker in MTC and it is used for detection, staging and prognosis of MTC [4]. Calcitonin levels >100 pg/mL have been found to have 100% positive predictive value for MTC [4, 8].

Identification of *RET* mutation carriers helps in early diagnosis and treatment of affected individuals. Machens et al found that in *RET* carriers, estimation of calcitonin levels can be used to determine the need for lymph node dissection [9]. In their study of 308 *RET* carriers, all patients with MTC positive lymph nodes had elevated basal calcitonin levels (91.4 pg/mL or higher).

Patients with regional lymph node involvement or calcitonin levels >400 pg/mL should undergo further imaging studies to detect metastatic disease [4]. 24-hour urinalysis for catecholamine metabolites like vanillylmandelic acid [VMA], metanephrine is done to rule out pheochromocytoma in patients with MEN type 2A or 2B. Pheochromocytoma must be treated before MTC [4].

In addition to calcitonin, MTC cells can produce other hormones like corticotropin, serotonin, melanin, and prostaglandins. Paraneoplastic syndromes like carcinoid syndrome, Cushing syndrome can occur in these patients.

## CONCLUSION

FNAC is considered a first line diagnostic test for evaluation of thyroid lesions and helps in early diagnosis and treatment. However it is not a substitute for histopathology.

## REFERENCES

1. Lombardo F, Baudin E, Chiefari E; Familial medullary thyroid carcinoma: clinical variability and low aggressiveness associated with *RET*

mutation at codon 804. *J Clin Endocrinol Metab.*, 2002; 87:1674- 80.

2. Matias-Guiu X; *RET* protooncogene analysis in diagnosis of medullary thyroid carcinoma and multiple endocrine neoplasia type 2. *Adv Anat Pathol.*, 1998; 5:196–201.
3. Jackson CE, Tashjian AH, Block MA. Detection of medullary thyroid carcinoma by calcitonin assay in families. *Ann Intern Med.*, 1973; 78:845–52.
4. Kloos RT, Eng C, Evans DB, Francis GL, Gagel RF, Gharib H; Medullary thyroid cancer: management guidelines of the American Thyroid Association. *Thyroid*, 2009; 19(6):565-612.
5. Forrest CH, Frost FA, de Boer WB, Spagnolo DV, Whitaker D, Sterrett BF; Medullary carcinoma of the thyroid: Accuracy of diagnosis of fine needle aspiration cytology. *Cancer*, 1998; 84:295–302.
6. Orell SR, Sterrett GF, Whitaker D; 4th ed. New Delhi: Elsevier. *Fine Needle Aspiration Cytology*, 2005; 125–64.
7. Bourtsos EP, Bedrossian CW, De Frias DV, Nayar R; Thyroid plasmacytoma mimicking medullary carcinoma: A potential pitfall in aspiration cytology. *Diagn Cytopath.*, 2000; 23:354–8.
8. Costante G, Meringolo D, Durante C, Bianchi D, Nocera M, Tumino S; Predictive value of serum calcitonin levels for preoperative diagnosis of medullary thyroid carcinoma in a cohort of 5817 consecutive patients with thyroid nodules. *J Clin Endocrinol Metab.*, 2007; 92(2):450-5.
9. Machens A, Lorenz K, Dralle H; Individualization of lymph node dissection in *RET* (rearranged during transfection) carriers at risk for medullary thyroid cancer: value of pretherapeutic calcitonin levels. *Ann Surg.*, 2009; 250(2):305-10.