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Oncology

A CASE REPORT OF MEDULLARY CARCINOMA OF THYROID

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ABSTRACT Medullary thyroid carcinoma originates from the thyroid parafollicular cells and accounts for 3-10% of all thyroid malignancies.A 34year old male patient presented with hoarseness of voice. Cervical lymphadenopathy is present without any palpable thyroid mass. Plain & CECT showed multiple heterogeneous enhancing lesions noted in both lobes of thyroid , and isthmus.FNAC of thyroid mass and neck nodes revealed clusters of plasmacytoid cells and few binucleate cells. Round to elongated nuclei with granular chromatin and inconspicuous nucleoli in the tumor cells with occasional pseudo-inclusions suggestive of MTC thyroid. FNAC from bilateral nodes revealed necrotic & amyloid material

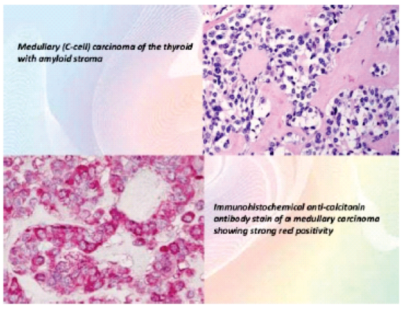
KEYWORDS : Thyroid cancer , Calcitonin , Mutations , Familial

INTRODUCTION:

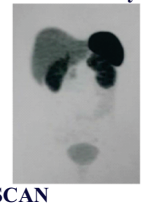
Medullary carcinoma of thyroid accounts for 4% to 10% of thyroid carcinomas, arising from the Para follicular cells (C cells). While 80% of the cases are sporadic and 20% implicated in familial MTC and associated with MEN 2 syndromes. Aggressiveness of the disease prompts early diagnosis and intervention**.**

CASE REPORT

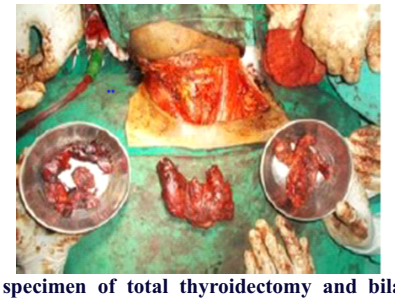
A 34 year old male patient presented with history of hoarseness of voice since 20 days. On examination cervical lymphadenopathy is present without any palpable thyroid mass.Routine investigations and thyroid profile were within normal range, Plain & CECT showed multiple heterogeneous enhancing lesions noted in both lobes of thyroid , and isthmus , largest measuring in the left lobe 4.6 * 2.8 cm showing calcifications. Lymph nodes noted : Right upper jugular-1.7cm,Right mid jugular-1.4cm,Right lower jugular-1.3cm,Left upper jugular-1.3cm ,Left mid jugular-11mm ,Left lower jugular-11mm with calcifications suggestive of bilateral metastatic cervical lymphadenopathy.FNAC of thyroid mass and neck nodes revealed clusters of plasmacytoid cells and few binucleate cells. Round to elongated nuclei with granular chromatin and inconspicuous nucleoli in the tumor cells with occasional pseudo-inclusions suggestive of MTC thyroid. FNAC from bilateral nodes revealed necrotic & amyloid material. USG abdomen and pelvis revealed no deposits. No genetic studies were done.Serum calcitonin -2000IU/L HPE of the specimen revealed polygonal to spindle shaped cells in amyloid background suggestive of MTC thyroid.



Histology of Medullary carcinoma of thyroid



68 Ga DOTONOC PET SCAN



Resected specimen of total thyroidectomy and bilateral neck dissection

MANAGEMENT

Total thyroidectomy with bilateral central and lateral neck dissection was done followed by 6000cGy of radiation by EBRT in 30 cycles.Intra operative findings showed tumor in the tracheo-esophageal groove encasing laryngeal nerve on left side ,loss of planes with trachea lateral wall & esophagus,bilateral hard nodes extending from level II to VI . Some nodes extending into the mediastinum are not removed.HPE of the specimen showed heterogeneous lesions in both lobes of thyroid and isthmus . Microscopic features are polygonal to spindle shaped tumor cells arranged in sheet like pattern. Tumor cells have coarsely clumped chromatin with inconspicuous nucleoli.8 lymph nodes on the right side and 6 lymph nodes on the left side showed deposits(pT4N1b).Post-operative 68 Ga DOTONOC PET scan is negative for residual/distant metastasis.

FOLLOW UP:

The patient was followed for 1,3,6,9 months with basal calcitonin levels with no evidence of recurrence . Follow up after 12 months showed Serum Calcitonin levels of 1724 pg/ml and all other lab investigations within normal range . CECT of neck revealed 2*2 cms hard mass in the left tracheo-oesophageal groove .USG , Plain & Contrast CT of chest ,pelvis , spine , brain showed no distant metastasis.

DISCUSSION

MTC is a rare variant among thyroid carcinomas (1 in 120 cases in this institution) involving RET mutations ,5% to 12% of all thyroid cancers and only 10 %of all MTC are familial. Three distinct familial syndromes involved with MTC are MEN2A,MEN2B,famlial non-MEN MTC.In MEN2A 42% to 60% of patients develop phaeochromocytomas . In patients with MEN2B all patients have MTC and 60% develop phaeochromocytomas .

MTC suspected cases should be evaluated for other components of MEN2 syndrome by Serum Calcium, Urinary /basal serum

catecholamines .General workup of MTC should include a)serum calcitonin b)CEA c) USG of neck including lateral compartment d) genetic testing for RET mutations and e) biochemical evaluation for Phaeochromocytoma. When a suspicion of FMTC,MEN2A,MEN2B exists , precise diagnosis depends on the detection of missense mutations in RET proto-oncogene in peripheral leukocytes . Mutations can now be classified as to their risk of aggressive MTC , based on genotype-phenotype correlation studies . screening for family members for RET mutations in exon 10 and 11for MEN2A and FMTC and exon 16 (codon 918) for MEN2B.

SURGICAL MANAGEMENT

The surgical management of familial MTC is total thyroidectomy with central neck lymph node dissection .

POST OPERATIVE FOLOW UP

The 10-year survival of MTC is 80%to90%.Detection of an elevated basal plasma calcitonin level indicates recurrent or persistent disease The average life expectancy of MTC and MEN2A is more than 50 years.

MTC Risk Group	Codons Affected	MTC phenotype features	MTC prophylactic management
Low Risk	609,768,790,791 , 804,891	Least aggresive	Thyroidectomy before 10 years of age
High Risk	611,618,620,634	MTC as early as 2 years and lymph node metastasis as early as 5 years	Thyroidectomy before 5 yeas
Highest Risk	883,918,922	Includes MEN2B mutations ,highest risk of early MTC development and metastasis.	Thyroidectomy in first month of life(6 months at most)

All cases of proven MTC should be treated by total thyroidectomy with level VI nodal dissection. Clinically detectable disease in level II, III ,IV warrants lateral compartment nodal dissection. Prophylactic thyroidectomy is advised within the first year in MEN2B RET mutations, within 5 years in patients with MEN2B,FMTC . Thyroid nodules larger than 5mm,elevated calcitonin levels ,lymph node metastasis warrant level VI neck dissection. Follow up is by basal and stimulated calcitonin tests .Because MTC is not follicular in origin ,TSH suppression ,RAI scanning and therapy have no role in MTC unless there is concomitant PTC/FTC Cabozantinib, a tyrosine kinase inhibitor, was approved by the US Food and Drug Administration in November 2012, for the treatment of metastatic medullary thyroid carcinoma. Although side effects typically include stomatitis, palmar-plantar erythrodysesthesia syndrome, hypertension and diarrhea, most patients are able to tolerate the recommended dose of 140 mg daily. Surgical resection is the primary treatment for medullary thyroid carcinoma. Patients with metastatic disease, who are not candidates for surgery, are considered candidates for systemic therapy

FUTURE TRENDS :

Motesanib, is a highly selective tyrosine kinase inhibitor that targets all three VEGF receptors, platelet derived growth factor receptor and RET. In a phase II study, 91 patients with advanced MTC were treated with motesanib (125 mg daily) for up to 48 weeks. Although partial response was noted in only two patients out of 91, 48% of the patients had stable disease for at least 24 weeks . However, more research is needed before motesanib can be widely accepted for the treatment of metastatic MTC. Radioimmunotherapy is another field that needs to be explored for treating MTC. In a non randomized trial, patients with progressive metastatic MTC were given antiCEA/anti-diethylenetriamine pentaacetic acid recombinant bispecific antibodies. The median overall survival after administration of this therapy was 110 months, compared to 60 months in the untreated cohort .

CONCLUSION :

MTC is a rare variant of thyroid carcinoma with aggressive course . A total thyroidectomy with central and lateral neck dissection gives better outcome and survival rates. Follow up is basal and stimulated calcitonin levels.

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