American Journal of Medical Case Reports, 2016, Vol. 4, No. 1, 8-11
Available online at http://pubs.sciepub.com/ajmcr/4/1/3

DOI:10.12691/ajmcr-4-1-3

A Rare Presentation of Medullary Carcinoma Thyroid

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Abstract Medullary Thyroid Carcinoma (MTC) is a rare thyroid tumor that arises from neural crest-derived Calcitonin producing Para follicular C cells and accounts for approximately 4 % of thyroid malignancies. This neuroendocrine tumor typically is an aggressive cancer, with secretion of several neuro-humoral mediators. We report a case of 49 year old male patient who presented with episodes of chest discomfort and abdominal pain associated with loud screaming of unknown etiology, on evaluation found to have Medullary Thyroid Carcinoma as its cause. MTC usually present as palpable firm to hard thyroid nodules or enlargement of regional lymph nodes. Since the systemic symptoms of MTC are nonspecific, it is challenging to diagnose MTC when patients first presents with systemic symptoms as in our patient. This case is reported to highlight the unusual presentation of this rare thyroid tumor and to emphasize the need for meticulous clinical examination and high index of suspicion to diagnose it.

Keywords: *medullary carcinoma thyroid, thyroid malignancy, neurohormones*

Cite This Article: Balakrishnan valliyot, Saroshkumar KK, Sarin SM, Kadeeja beevi B, Nirmal mathew alex, and Tency joshu thomas, "A Rare Presentation of Medullary Carcinoma Thyroid." *American Journal of Medical Case Reports*, vol. 4, no. 1 (2016): 8-11. doi: 10.12691/ajmcr-4-1-3.

1. Introduction

Medullary thyroid carcinoma (MTC) is a rare thyroid tumor that accounts for approximately 4% of all thyroid cancers [1]. MTC lesions can metastasize to regional lymph nodes but can also have hematological spread and may affect the liver, bone, lungs and skin2. Most medullary thyroid carcinomas occur sporadically (75-80%) however approximately 20-25% occur with spectrum of several inherited syndromes such as Familial MTC, MEN2A, and MEN2B. Patients usually present with a thyroid nodule that may or may not be associated with cervical lymphadenopathy. Although uncommon patients may also present with various paraneoplastic syndromes, including Cushing or carcinoid syndrome. MTC secrete not only calcitonin but also other peptides such as CEA, Calcitonin gene related peptide, prostaglandins E2 and Serotonin which are responsible for various systemic symptoms and atypical presentations. Distant metastases (eg. lung, liver, bone) may result in lethargy, weight loss and bone pain. Primary modality of treatment is surgical; total thyroidectomy with central neck dissection. This is usually followed by medications that include tyrosine kinase inhibitors that target vascular endothelial growth factor receptors which have shown partial response rates of up to 30% in single agent studies.

2. Case Report

A 49 year old male patient with no past history of any significant chronic medical illness presented with complaints of several episodes of chest and abdominal discomfort associated with sweating and palpitation for the past one month. He had retrosternal constricting type of chest discomfort with radiation to left arm associated with sweating. These episodes of chest discomfort were associated with colicky abdominal pain and an abnormal loud screaming which lasts around 2-3minutes.He was fully conscious during these episodes. No abnormal movements, up rolling of eyes or incontinence were present. Events occurred both during rest and exertion. After these episodes were over he was asymptomatic. He was evaluated in a tertiary care Centre in view of chest discomfort with ECG, TMT and Echocardiography; all were normal. His baseline investigations like blood routine, Urine routine examination, RFT, LFT, TFT and USG abdomen were normal. He was further evaluated with coronary angiogram for chest discomfort and it was also normal. Since no organic disease was detected patient was discharged with analgesic and anxiolytics but he had no relief and he consulted our institution.

Table 1.

BLOOD ROUTINE	TC-8500, N65%, L30%, Hb-14mg%; HCT, MCV, MCHC-N, Platelet-350,000, ESR-30
URINE ROUTINE	Normal
RENAL FUNCTION TESTS	Blood Urea-23mg/dL, S.Creatine-1mg/dl
LIVER FUNCTION TESTS	T.Bilirubin/D.Bilirubin-1/0.2 mg/dl SGOT/SGPT/ALP-33/29/98 IU/L T.Protein/Albumin/Globulin-7/4.4/3.6 g%
ECG	Normal
CHEST X-RAY	Normal

Table 2.

Ca2+, PHOSPHOROUS	Calcium 9.1mg/dl, Phosphorus 3mg/dl
PANCREAATIC ENZYMES	Normal
OGD SCOPY	Normal
COLONOSCOPY	Segmental colitis, biopsy taken showed nonspecific inflammation
URINE PORPHOBILINOGEN	Negative
HIV,HBsAg	Negative
THYROID FUNCTION TESTS	TSH:1.1 uU/ml, FT4:2.2ng/dl
24 HR URINE VMA AND METANEPHRINE	Normal
S.CALCITONIN	42(<10)
5-HIAA	Normal
CECT ABDOMEN	Hypodense mass in the liver, suspected metastasis; normal pancreas and suprarenals

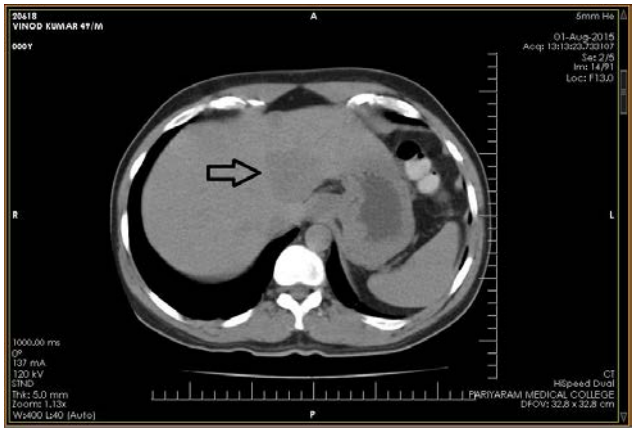

Figure 1. Plain CT showing hypodense lesions in the liver

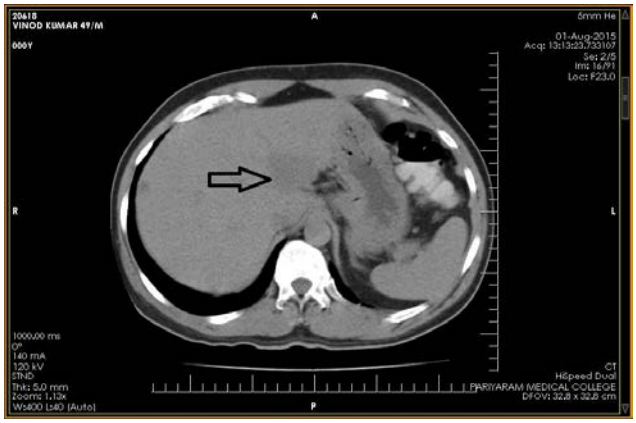

Figure 2. Plain CT showing hypodense lesions in the liver

On clinical examination, his vitals were normal and a non-tender hard nodule of 2×2 cm was palpable in the lower pole of Right lobe of thyroid. No cervical or other lymph nodes were palpable. Rest of the systems were normal and he was clinically thyroid. Like blood routine, Urinalysis, RFT, LFT, TFT (Free T4, Free T3 and TSH), Serum Calcium and Phosphorous were all normal (refer Table 1 & Table 2).

Ultra sound scan of the neck showed round nodule with hypo echogenicity and calcifications-. FNAC of the thyroid nodule was suggestive of medullary thyroid carcinoma (Figure 5 & Figure 6). Basal serum calcitonin level was 42 pg./ml(normal<10pg/ml). 24-hour urinary VMA and metanephrines done to rule out associated pheochromocytoma were normal. CECT thorax and abdomen were done to rule out any metastasis. On CT abdomen a hypodense lesion was noted in the liver suggestive of metastasis (refer Figure 1 to Figure 4). Upper GI endoscopy and esophageal manometry done during asymptomatic period showed no evidence of esophageal spasm. None of his family members and relatives had history of any endocrine neoplasms. So a diagnosis of Sporadic Medullary Thyroid Carcinoma with liver metastasis was made and patient was referred to an Oncology Centre for surgery and further management.

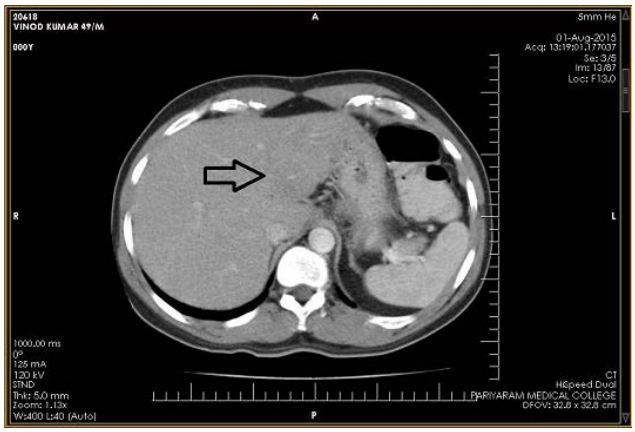

Figure 3. CECT showing non enhancement by mass lesions in the liver

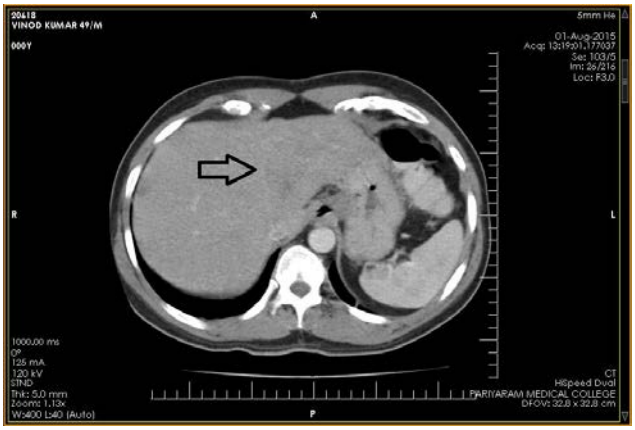

Figure 4. CECT showing non enhancement by mass lesions in the liver

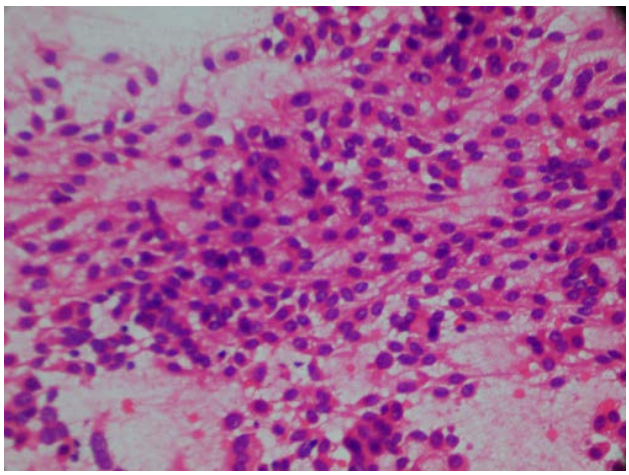

Figure 5. FNAC from Thyroid nodule showing cellular histology of Medullary Carcinoma Thyroid

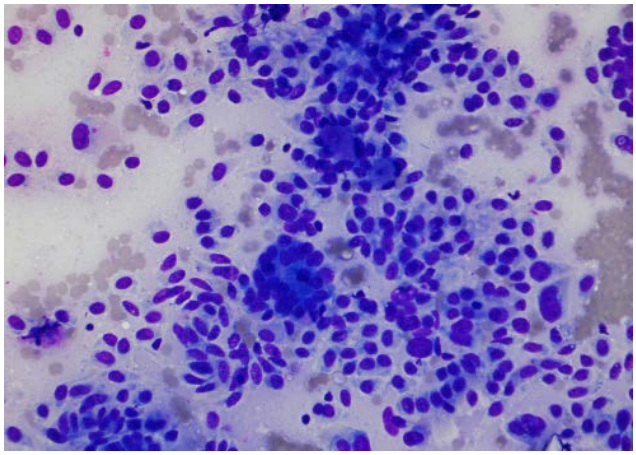

Figure 6. FNAC from Thyroid nodule showing cellular histology of Medullary Carcinoma Thyroid

3. Discussion

Thyroid carcinoma is the most common endocrine malignancy [2]. Medullary thyroid cancer (MTC) is a neuroendocrine tumor of the Para follicular C cells of the thyroid gland and accounts for approximately 4% of thyroid carcinomas. The typical age of presentation is in the fifth or sixth decade, and there may be a slight female preponderance.

Sporadic medullary thyroid cancer (MTC) accounts for about 75-80 % and rest of them may occur in hereditary syndromes such as Familial MTC, MEN2A, and MEN2B [3]. MEN syndrome is caused by activating germ line mutations of the RET proto-oncogene, where this tumor is isolated (Familial MTC – FMTC) or is associated to other tumors MEN 2A (parathyroid adenoma, pheochromocytoma and cutaneous lichen amyloidosis) and MEN 2B (Pheochromocytoma, mucosal and intestinal ganglioneuromatosis, marfanoid habitus).

The most common presentation of sporadic MTC is that of a solitary thyroid nodule, which occurs in 75 to 95 percent of patients'. In most patients with MTC, the disease has already metastasized at the time of diagnosis. Distant metastases may occur in the liver, lung, bones [4,5], and less often, brain and skin. Survival rates of MTC are 40-50% at 10 years [6].

Calcitonin a small peptide secreted by C-cells is the most specific and sensitive marker of MTC useful in the diagnosis and follow-up of this tumor. Another tumor marker used in the follow-up of MTC is carcino-embryonic antigen (CEA)- considered to have lower diagnostic accuracy than calcitonin [7,8] Systemic symptoms occur due to the neurohumoral secretion by the tumor. Tumor secretion of calcitonin, calcitonin-gene related peptide, or other substances can cause diarrhea, abdominal pain or facial flushing in patients with advanced disease.

Primary treatment of both hereditary and sporadic MTC is total thyroidectomy with lymph node dissection, with the intention of remove all neoplastic tissue present in the neck. The postoperative follow-up of patients with MTC should be performed to early identify recovery or persistence/relapse of MTC in patients with elevated concentrations of biochemical markers after surgery. For localization of the recurrence or residue of the MTC, various scintigraphic methods are used with **t**he radio-labeled molecules [9].

Systemic chemotherapy [10,11] is poorly efficient and may be indicated only in cases of rapid tumor progression. Chemoembolization of liver metastases with Adriamycin were reported to provide a high response rate for both symptoms and tumor mass [12]. Kinase inhibitors directed against tumor cells (RET and other kinases) and endothelial cells (VEGFRs) provide a significantly higher response rate than cytotoxic chemotherapy and should be proposed to MTC patients who have progressive disease as first-line treatment [13,14].

MTC usually present as palpable thyroid nodules or enlargement of regional lymph nodes, since the systemic symptoms of MTC are non-specific, it is challenging to diagnose MTC when patients first present with systemic symptoms as in our case. A detailed cardiac evaluation including coronary angiography did not reveal any cardiac cause for the discomfort. No structural lesion was detected in the abdominal sonogram, upper G.I. endoscopy and CECT abdomen to account for the episodic colicky abdominal pain. Patient was evaluated for the possibility of associated pheochromocytoma but 24 hour urine VMA and metanephrines were normal. So considering the episodic colicky nature of abdominal pain and chest discomfort with a back ground of elevated calcitonin level and no evidence of any structural lesion, a neurohumoral mediated esophageal and intestinal spasmodic pain was considered as the possible explanation. Since the systemic symptoms of MTC are nonspecific, it is challenging to diagnose MTC when patients first presents with systemic symptoms as in our patient, So a high index of suspicion is needed to diagnose it.

Competing Interest

Authors have no competing interests.

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