CASE REPORT

ISOLATED FAMILIAL MEDULLARY THYROID CARCINOMA AS PART OF MULTIPLE ENDOCRINE NEOPLASM (MEN-2A)

Muhammad Ashraf Sharif, Asad Mahmood*, Badar Murtaza*, Zunera Asghar**

AFIP Rawalpindi, *CMH Bahawalnagar, **KRL Hospital Islamabad

INTRODUCTION

Medullary carcinoma of the thyroid (MTC) is a distinct thyroid carcinoma that originates from the parafollicular C cells of the thyroid gland which produce calcitonin. MTC has a genetic association with multiple endocrine neoplasia (MEN) type 2A and 2B syndromes. Sporadic, or isolated, MTC occurs in 75% of patients[1].

CASE REPORT

A 70 years lady reported with progressively increasing symptoms of lethargy, dysphagia, dyspnoea and swelling at the base of neck for the last three years. She had history of intermittent diarrhoea, abdominal pain, weight loss and pain left shoulder girdle. There was no history of palpitations, sweating, pain in the swelling or any skin changes. She was being treated symptomatically for the last three years. Her physical examination demonstrated a pale emaciated normotensive lady with visible goiter having two dominant non-tender firm nodules moving with deglutition without audible bruit or retrosternal extension. Variable sized firm, fixed, nontender bilateral cervical lymph nodes were palpable. Her chest ausculatation revealed bilateral coarse crepitations with rhonci. There was marked tenderness of sternum and left shoulder joint. An audible stridor was present. However there was no jaundice, abdominal mass or any focal neurological deficit. Her laboratory work up showed normal serum T4, T3 & TSH levels. Serum calcium levels were raised at 10.46mg/dL against serum albumin levels of 44 gm/L. Her fine needle aspiration cytology (FNAC) of the thyroid nodules and associated lymph nodes revealed dyshesive clusters of oval to spindle plasmacytoid cells with eccentric nuclei and abundant amphophillic cytoplasm. Deposits of eosinophillic material resembling amyloid were also seen (Fig. 1). These findings were suggestive of medullary carcinoma of thyroid with metastasis to the cervical lymph nodes. Her serum Calcitonin levels were 30,440 pg/mL(normal ref range: <5.0 pg/mL) which supported the FNAC diagnosis of medullary carcinoma. Her serum CEA levels were 448 ng/mL (normal ref range: <3.0ng/mL). On her staging work up, chest radiograph showed multiple hyperdense opacities of variable sizes predominantly at the bases in both lung fields suggestive of metastatic lesions. A computed tomography (CT) scan of the chest revealed variable sized small nodules scattered in all the segments of both lungs favoring the possibility of metastasis while abdominal ultrasonography and CT scan did not show any evidence of hepatic, adrenal or pancreatic pathology. Her investigations including full blood count, liver function tests, renal profile and bone scans were within normal limits. Upon further inquiry, a striking revelation was made in the family history. The eldest daughter of the patient aged 46 years and a son aged 43 years had died of complications due to metastatic medullary carcinoma of the thyroid.

DISCUSSION

MTC comprises less than 10% of all thyroid cancers and has a genetic association with MEN syndromes types 2A and 2B. It is derived from neural crest cells with RET gene mutation. There are 25% patients with a familial mode of inheritance while the rest are sporadic. MTC associated with MEN 2A or 2B have a peak incidence in the 2nd and 3rd decades of life while sporadic cases occur in the 5th or 6th decade[2].

Clinically patients present with a swelling in the neck prominent during swallowing while cases with locally advanced disease have

Correspondence: Dr Muhammad Ashraf Sharif, House No. 107, St No. 110, Sector G-11/3 Islamabad
Email: ashrafof@gmail.com
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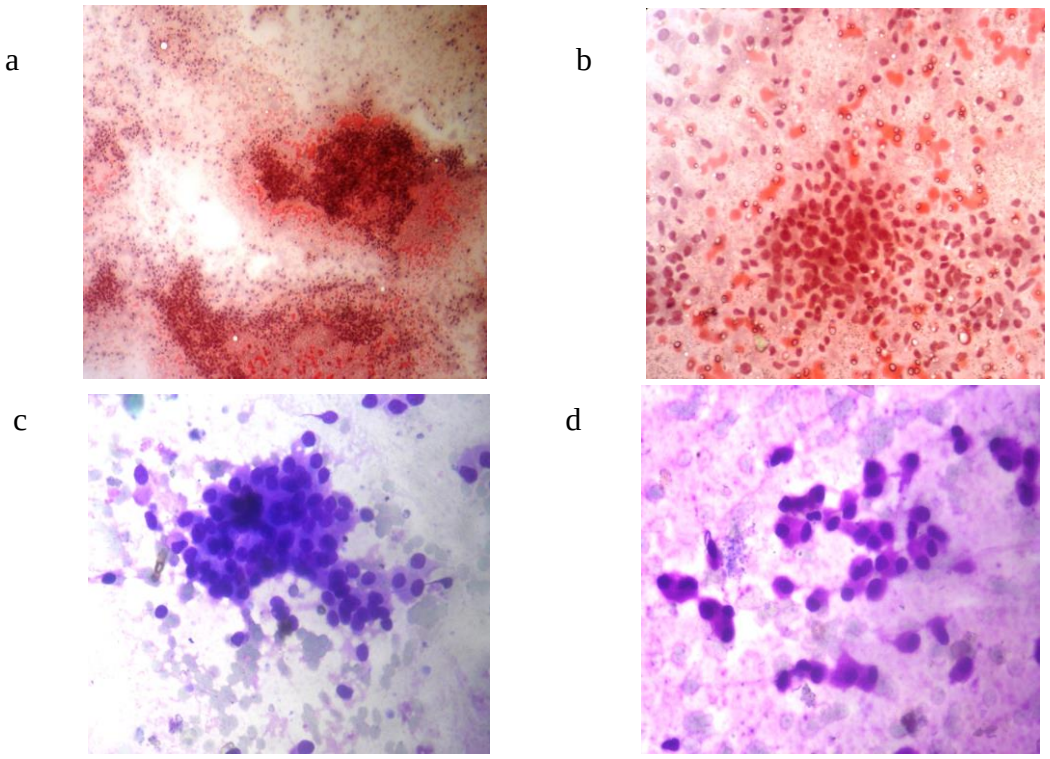

Figure: Photomicrographs showing fine needle aspirate of the thyroid. a & b showing hematoxylin & eosin stained preparation with hypercellular smears having pale cytoplasm and diffuse nuclear chromatin in a dyshesive pattern. c&d showing hemacolor stain with plasmacytoid appearance of the cells characteristic of medullary carcinoma of thyroid in the back drop of raised serum calcitonin levels. (a&c H*E x200 , b&d at MGAx400 magnification).

hoarseness, dysphagia, or respiratory difficulty. Paraneoplastic syndromes like Cushing or carcinoid syndrome may be seen in a few cases. Diarrhoea may be seen due to increased intestinal electrolyte secretion because of high serum calcitonin levels. Abdominal pain, jaundice, and rarely, bone tenderness may occur in patients with systemic metastases. Physical examination usually shows a dominant thyroid nodule while the presence of cervical lymphadenopathy signifies locally advanced disease[3] as was also seen in our case.

Laboratory evaluation by serum calcitonin levels are used to diagnose overt as well as subclinical cases of FMC. High levels of carcinoembryonic antigen like the present case are also seen in medullary carcinomas. A 24-hour urinalysis for vanillylmandelic acid & metanephrine is done to rule out concomitant pheochromocytoma in patients diagnosed with MEN type 2A or 2B[4].

Fine-needle aspiration yields cytologic information, allowing diagnosis of MTC. Histopathological examination of the resected gross specimen reveals a well-circumscribed gray white nodule with a coarse texture. Microscopically, it contains nests of round or ovoid cells. A fibrovascular stroma is usually intercalated between cells. Sometimes, amyloid material, consisting of calcitonin prohormone, may occur in the MTC stroma. Immunohistochemical demonstration of calcitonin and negativity for thyroglobulin supports the diagnosis of medullary carcinoma over other neoplastic lesions of the thyroid[5].

Cytogenetic analysis has revolutionized the diagnosis of familial cases by DNA testing for RET gene. An asymptomatic family member with a positive RET gene in should be evaluated and searched for occult neoplasm, carrying out radiological scans for primary and distant malignancy[6].

Preclinical patients of MEN 2A syndrome are treated by simple total thyroidectomy without cervical lymph node dissection while total thyroidectomy and modified radical neck dissection is recommended for lymph node positive cases of medullary carcinoma. Patients

with positive surgical margins or mediastinal extension are candidates of adjuvant radiotherapy while symptoms of bony metastases are controlled by external beam radiotherapy[7].

Prognosis depends on patient age, histologic grade, and status of surgical resection. Elderly patients as our case, higher-grade lesions or incomplete surgical resection of the lesion are poor prognostic indicators[3].

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