Case Report

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Multiple Endocrine Neoplasia Type 2b: A Rare Case Report

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Abstract

Multiple endocrine neoplasia Type 2b is a rare syndrome caused by mutations in RET proto oncogene. It is a rare case, which is found 1 in 30,000. We report a case of 23-year-old male patient with goiter, right lower chest pain, paroxysmal spells and hypertension. On examination, mucosal neuromas and Grade 2 hard goiter were observed. Patient's thyroid profile was normal. Fine-needle aspiration cytology thyroid showed medullary carcinoma of the thyroid. Calcitonin levels were found to be elevated. Contrast enhanced computed tomography neck showed 28 mm × 20 mm heterogeneous mass in the right lobe of the thyroid. Histopathology and immune histochemistry confirmed the pheochromocytoma.

Key words: Medullary carcinoma thyroid, Multiple endocrine neoplasia TYPE 2B, Pheochromocytoma

INTRODUCTION

Multiple endocrine neoplasia Type 2B is a rare syndrome caused by mutations in RET proto oncogene. The genetic defect in MEN 2 is on chromosome 10 (10q 11.2). MEN Type 2B is transmitted as autosomal dominant trait associated with various endocrine tumors. Multiple endocrine neoplasia affects 1 in 30,000 people.[1] Incidence of MEN Type 2A is 80%, familial medullary thyroid carcinoma 15%, MEN Type 2B 5%. Among sub types - Type 2A is most common followed by familial medullary thyroid carcinoma. MEN Type 2B is relatively uncommon, accounting for 5% of all cases of MEN. MEN Type 2B is associated with medullary carcinoma thyroid, pheochromocytoma, mucosal neuromas, gangliomatosis of intestinal tract and marfonoid habitus, whereas hyperparathyroidism is absent.[2]

We report a rare case of MEN Type 2B presented with pheochromocytoma, medullary thyroid carcinoma and mucosal neuromas of lips and tongue with no marfanoid habitus.

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CASE REPORT

A 23-year-old male patient presented with goiter of 1 year duration with no compressive symptoms with no history suggestive of hypothyrodism or hyper thyroidism. He had pain in right lower chest region of 6 months duration with no history of respiratory tract infections. He also had a history of three episodes of paroxysmal spells during past 6 months. Each spell was characterized by headache, sweating and palpitations. Examination revealed mucosal neuromas of lips and tongue (Figure 1), high arched palate, Grade 2 hard goiter with no marfanoid habitus. He had hypertension. Systemic examination was normal.

Table 1 shows baseline biochemical profile.

Thyroid profile was normal. Fine needle aspiration cytology (FNAC) of thyroid showed medullary carcinoma. Ultrasonography of thyroid showed solitary nodule of the right lobe of the thyroid in view of low sensitivity of U/S we did contrast enhanced computer tomography (CECT) (Figure 2). CECT neck showed mass of size 28 mm × 20 mm in the right lobe of the thyroid with lymph node metastasis (Figure 3) and calcitonin levels were elevated. In view of the presence of paroxysmal spells, we evaluated

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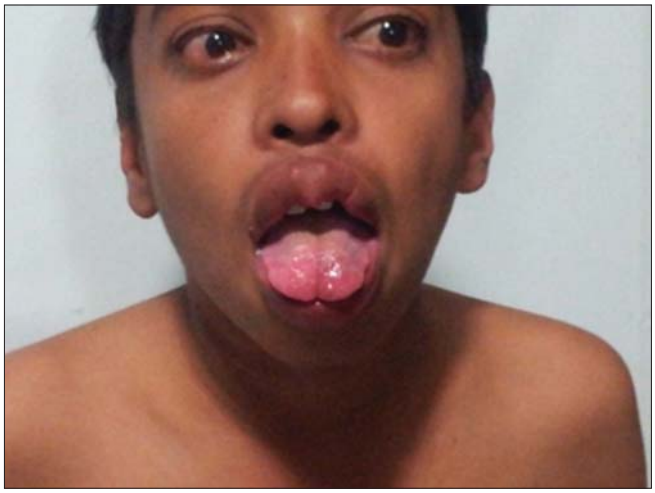

Figure 1: Mucosal neuromas of tongue and lips

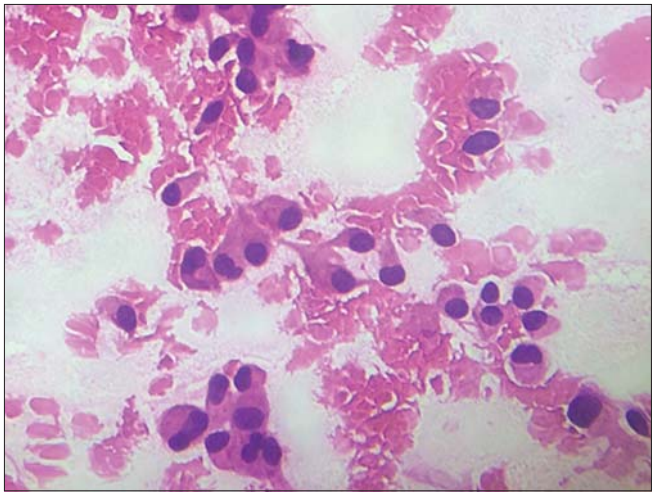

Figure 2: Fine needle aspiration cytology of thyroid showing medullary carcinoma of thyroid

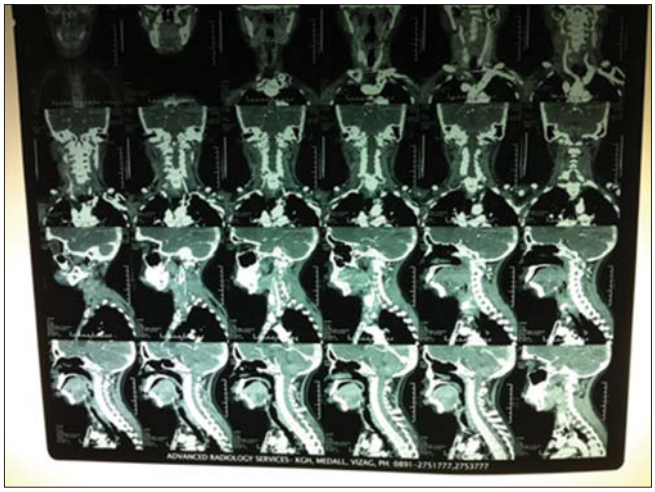

Figure 3: Contrast enhanced computed tomography neck showing heterogenously enhancing hypodense lobulated mass lesion of 28 mm × 20 mm seen in right Level II/III station, right trachea esophaeal groove, inseparable from hypopharynx, cricoids and proximal esophagus

for pheochroma cytoma. Elevated plasma metanephrines, nor-metanephrines and were noticed (Table 2). Magnetic resonance imaging abdomen revealed right supra renal mass. Pre-operatively patient was managed with an alpha blocker (prazosin) for hyper tension. He underwent laparotomy and right adrenalectomy. Specimen was taken out and sent for biopsy (Figure 4). Immunohistochemistry and histopathology (Figure 5) confirmed pheochroma cytoma. Post-operatively he was managed with 2.5 mg of

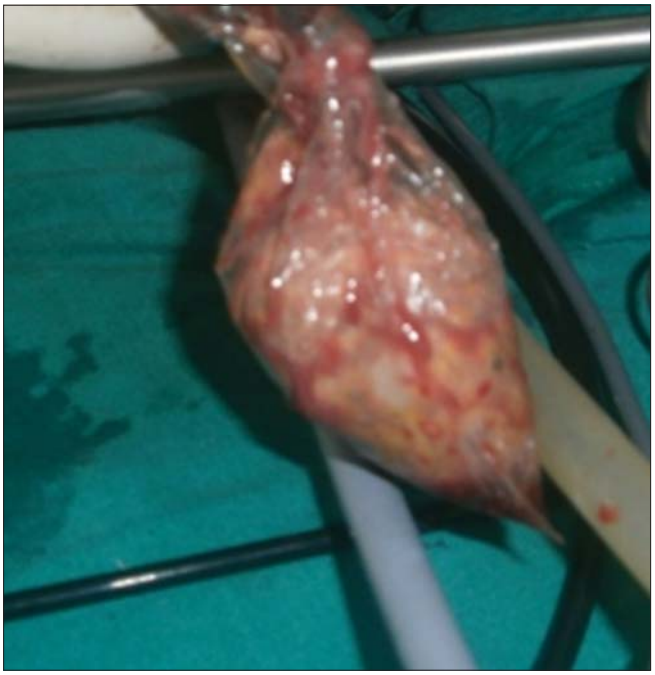

Figure 4: Biopsy specimen of pheochromocytoma

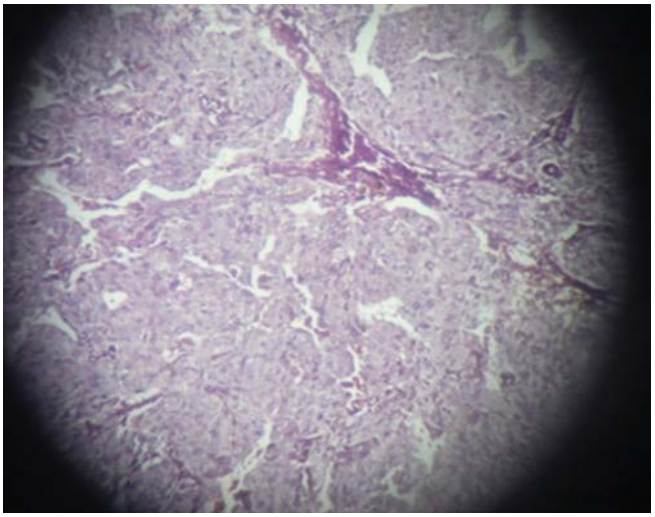

Figure 5: Histopathological examination shows uniform polygonal cells arranged as well-defined nests (zell ballen pattern) separated by thin fibrovascular septae. Individual cells show basophilic granular cytoplasm with round to oval nuclei. At places tumor cells show clear cytoplasm. The surrounding fibrofatty tissue shows congested vascular space

Table 1: Biochemical profile

Hemoglobin %	11.8 g/dl
Total leucocyte count	17,700/mm^3
Differential count	N - 81%, L - 12%, M - 1%, E - 1%
Random blood sugar	133 mg/dl
Blood urea	21 mg/dl
Serum creatine	0.6 mg/dl
SGOT	29 U/L
SGPT	28 U/L
Serum bilirubin (total)	0.4 mg/dl
Serum proteins (total)	7.8 mg/dl
Albumin	4.4 mg/dl

SGOT: Serum glutamine oxalo acetyl transamanases, SGPT: Serum glutamine pyruvate transaminases

Table 2: Hormone profile

Serumcalcitonin	1515 pg/ml
Tri ido thyronine (T3)	1.25 ng/ml
Tetra ido thyronine (T4)	10.75 µg/dl
Thyroid stimulating hormone	1.30 µIU/dl
Metanephrine	743 pg/ml
Nor-metanephrine	405.6 pg/ml

prazosin once daily. Patient deferred surgery for medullary carcinoma of the thyroid.

DISCUSSION

We report a case of multiple endocrine neoplasia (MEN Type 2B) who presented with mucosal neuromas, medullary carcinoma thyroid, pheochromocytoma. Williams and Pollock[3] reported first case of MEN TypE 2B. Chong first named this disease as MEN Type 2B. Patient with MEN Type 2B usually present in the first decade of life. Recent studies revealed age at diagnosis may range from 1 to 31 years,[4] but our case was presented at the age of 23 years.

Among 100% of patients with MEN Type 2B develop mucosal neuromas in the lips, tongue and oral cavity, conjunctiva eye lids and within cornea. Our case had mucosal neuromas over tongue and lips several years after birth.[5,6] Ganglio neuromas in the gastrointestinal tract are usually seen in 30% of MEN Type 2B. Ganglion eurromas are most commonly seen in a large bowel, small bowel, liver, gallbladder and pancreas. Marfanoid habitus is present in 75% of MEN Type 2B as are skeletal abnormalities such as kyphosis, pectus excavatum and talipes supinatus. Our case did not have marfonid habitus. Medullary thyroid cancers are usually seen in 90-95% of MEN 2B and are commonly multiple this malignant tumor appears in late teens or twenties. Hyperplasia of C-cells of thyroid and hyperplasia of the adrenal medulla are thought to be pre malignant lesions of medullary thyroid cancer and pheochroma cytoma. Our patient had medullary carcinoma thyroid with lymph node metastasis. Patient deferred surgery for medullary carcinoma of the thyroid. Medullary carcinoma of the thyroid in MEN Type 2B carries a poor prognosis compared with sporadic cases.[7]

Pheochromocytoma is usually manifested in 45-50% of patients with MEN Type 2B occurring during second and third decade of life. It is frequently multicentric and bilateral. Our patient had right adrenal pheochromacytoma. 50% of MEN Type 2B are autosomal dominant, others are sporadic. Our case did not have any family history, and so it could be sporadic.

CONCLUSIONS

Finally, we report a rare case of MEN Type 2B who presented with pheochromocytoma, mucosal neuromas medullary carcinoma of the thyroid.

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