

Young woman with Multiple Endocrine Neoplasia 2B (MEN 2B) Diagnosed by PET-CT-A Case Report

¹Rawnak Afrin, ¹Shankar Biswas, ¹Shaila Sharmin, ²A.B.M Golam Mostofa, ¹Jasmine Ara Haque

¹Institute of Nuclear medicine & Allied Sciences, Dhaka.

²Department of Medicine, DMCH

Correspondence Address: Dr. Rawnak Afrin, Associate Professor & PMO, Institute of Nuclear Medicine & Allied Sciences, Dhaka. Bangladesh Atomic Energy Commission. Email: afrinrawnak@gmail.com

ABSTRACT

Multiple endocrine neoplasia, type 2B (MEN2B) is an autosomal dominant syndrome characterized by medullary thyroid carcinoma, pheochromocytoma, multiple mucosal neuromas & intestinal ganglioneuromas. A young woman of 20 years presented with irregularity of both lips since childhood and a midline neck swelling which gradually increased in size within last 1 year. She had hypertension and history of three episodes of paroxysmal spells characterized by headache, palpitations and excessive sweating during past 5 months. On physical examination, patient was having tachycardia, high blood pressure level (140/100 mmHg), sweaty with no tremor or exophthalmos. She had bumpy lips, multiple mucosal neuromas in lip & buccal mucosae, a hard nodular goiter and no marfanoid habitus. Core biopsy from right thyroid lobe revealed medullary thyroid carcinoma. Calcitonin level were markedly elevated. 18F-FDG PET-CT scan showed heterogeneous mixed density soft tissue mass involving both lobes and isthmus of thyroid gland with intense FDG uptake and FDG avid enlarged right cervical lymph nodes. A well circumscribed complex mass was found in the left upper abdomen adjacent to pancreas. Left adrenal gland showed a heterogeneous mass with mild FDG uptake and according to PET-CT findings, patient was diagnosed as a case of MEN 2B.

Keywords: MEN 2B, ¹⁸F-FDG PET-CT

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INTRODUCTION

Multiple Endocrine Neoplasia (MEN), shows occurrence of tumors involving two or more endocrine glands in a single patient (1). Two major types of multiple endocrine neoplasia affects an estimated 1 in 30,000 people (2). Type 2 A is the most common variety among the subtypes of MEN type 2. Type 2B is relatively uncommon, about 5 percent of all cases of MEN. About 50% of MEN Type 2B are autosomal dominant, others are sporadic. Multiple

endocrine neoplasia, type 2B (MEN 2B) is characterized by medullary thyroid carcinoma, pheochromocytoma, multiple mucosal neuromas and intestinal ganglioneuromas, whereas parathyroid tumors do not usually occur in MEN 2B (2).

CASE REPORT

A young woman of 20 years presented with irregular, bumpy lips since childhood and a midline neck swelling which gradually increased in size within last 1 year. There was no pressure effect or breathlessness. She had hypertension and history of three episodes of paroxysmal spells characterized by headache, palpitations and excessive sweating during past 5 months. On physical examination, patient had tachycardia with a pulse rate of 88, high blood pressure (140/100 mmHg), sweaty, moist hands and skin with no tremor or exophthalmos. Her lips were irregular, swollen and bumpy with multiple mucosal neuromas in lip & buccal mucosae. On neck examination, a hard nodular goiter of about 3X3 cm size and few enlarged neck nodes were seen. Patient had no marfanoid habitus. Core biopsy from right thyroid lobe revealed medullary thyroid carcinoma. Serum Calcitonin level were markedly elevated. High resolution ultrasound of neck revealed heterogeneous thyroid mass and multiple enlarged neck nodes on both sides.

Core biopsy of thyroid nodule was positive and histopathology also reported medullary carcinoma of thyroid gland. The patient was advised a whole body PET-CT scan and referred to Institute of Nuclear medicine & Allied Sciences (INMAS), Dhaka. After proper preparations and fasting PET-CT images were acquired from vertex to mid-thigh in a whole-body

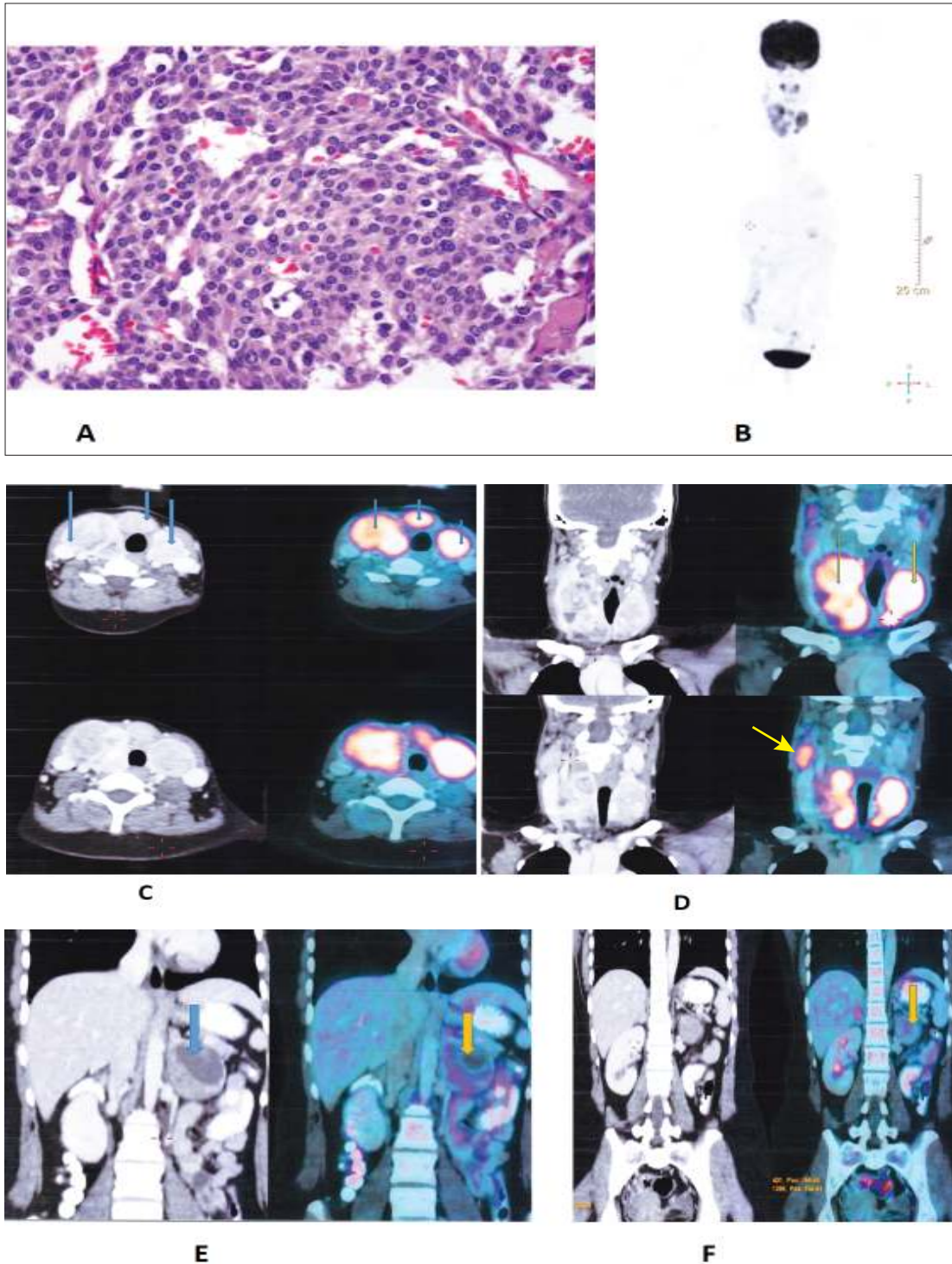


Figure 1 : Young female patient of 20 years having goiter, hypertension, headache, tachycardia and diaphoresis showed following findings. A) Histopathological section from right thyroid lobe showing tumor cells having amphophilic granular cytoplasm and rounded nuclei; amyloid accumulation seen as a pink coloured amorphous material typical for medullary thyroid cancer. B) Maximum Intensity Projection (MIP) image of PET- CT showed areas of physiological & pathological accumulation of 18F-FDG. C) and D) Axial, coronal CT and Fused PET-CT images revealed hypermetabolic heterogeneous soft tissue masses involving both lobes of thyroid and isthmus. FDG avid enlarged right cervical lymph node is also noted (arrow). E) and F) Coronal CT and Fused PET-CT images of a well circumscribed mixed density mass consisting both solid and central cystic components detected at the left upper abdomen adjacent to pancreas and mild FDG avid left adrenal mass.

PET-CT scanner (Philips 128 slice ingenuity TF PET CT), one hour after intravenous injection of ^{18}F -FDG. Diagnostic CT images of whole body with 2 mm slices was also obtained with and without intravenous contrast injection. Images were reconstructed using List mode TF HD algorithm and slices were reformatted into trans axial, coronal and sagittal views. Semi-quantitative estimation of FDG uptake was performed by calculating SUVmax value, corrected for dose administered and body weight (g/ml). Adequate patient preparation rules were strictly followed.

PET CT images revealed hypermetabolic heterogeneous soft tissue mass involving both lobes of thyroid and isthmus compatible with thyroid malignancy, hypermetabolic cervical nodal metastases and mild FDG avid left adrenal mass – suggest pheochromocytoma, right adrenal hyperplasia and a complex upper abdominal mass – likely ganglioneuroma. The patient was reported as a case of MEN 2B. Her plasma free metanephrine level was elevated, 28 nmol/L and urinary vanillylmandelic acid (VMA) was also elevated 90 $\mu\text{mol}/24$ hr.

DISCUSSION

Multiple endocrine neoplasia (MEN) syndromes usually present as two or more endocrine gland tumors in a patient, either simultaneously or successively. The clinical manifestations of MEN are complex and diverse due to involvement of multiple endocrine glands and associated non endocrine organ lesions. Due to the diversity of manifestations, it is not easy to diagnose MEN clinically. MEN 2 is divided into three subtypes according to different phenotypes, including MEN 2A, MEN 2B, and familial medullary thyroid carcinoma (FMTC) and the prevalence is 2–5 per 100,000 people (3). The main feature of MEN 2 are medullary thyroid carcinoma (MTC), and pheochromocytoma. Almost 100% of MEN 2B patients will develop MTC. The age of onset of MTC related to MEN 2 is younger than that of sporadic MTC cases (4). MTC related to MEN 2B are more aggressive and penetrative (5). MTC secrete too much calcitonin, often multicentric and bilateral (6). MEN 2B patients generally do not develop parathyroid

disease. Some special clinical manifestations can be found in patients with MEN 2B (such as “Marfanoid” body habitus, multiple mucosal neuromas on lips and tongue) (7) and provide important clues for the early diagnosis. Mutations of the RET gene are present in 98% of MEN 2 patients. Mutations in exon 16 are usually found in patients with MEN 2B (5).

The reported case of MEN Type 2B presented with mucosal neuromas, MTC, pheochromocytoma and ganglioneuromas. Chong et al. first named this disease as MEN Type 2B (8). Patients with MEN Type 2B usually present in the first decade of life with few more references of recent studies where it was reported between 1 to 31 years (9). This reported case was aged 20 years and had medullary thyroid carcinoma with lymph node metastases. Medullary thyroid carcinomas of MEN 2B carries a poor prognosis compared with sporadic cases (10). Almost 100% of cases with MEN Type 2B presents mucosal neuromas in the lips, tongue, oral cavity, conjunctiva, eye lids and within cornea (11). This reported case had mucosal neuromas in lips & buccal mucosa. Ganglioneuromas in the gastrointestinal tract are usually detected in 30% of MEN Type 2B but most commonly seen in large and small intestines, liver, gallbladder and pancreas. Marfanoid habitus is present in almost 75% cases although this patient had not. Pheochromocytoma is usually manifested in 50% of patients with MEN Type 2B occurring during second and third decade of life (12).

CONCLUSION

This reported case showed some unusual history, classic clinical findings and helped us diagnose with the hybrid imaging modality PET-CT that corresponded to the imaging findings of MEN 2B syndrome, including pheochromocytoma, mucosal neuromas, ganglioneuroma & medullary carcinoma of the thyroid. Endocrine evaluation, appropriate laboratory tests and targeted imaging evaluation of the typical endocrine organs can provide clues for the diagnosis of this rare clinical suspicion. Accurate and comprehensive diagnosis will enable patients to receive appropriate treatment and clinical management.

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