CASE REPORT

Case Report of Rare Hereditary Endocrine Cancer Syndrome: Multiple Endocrine Neoplasia Type 2B

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Abstract

Multiple endocrine neoplasia type 2B (MEN2B) is an extremely rare hereditary thyroid cancer syndrome. The individuals are presented with an aggressive form of medullary thyroid carcinoma (MTC). They have classic morphology features that aid in the diagnosis of the syndrome.

Keywords: Medullary thyroid carcinoma, Mucosal neuromas, Multiple endocrine neoplasia type 2B.

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Introduction

Williams and Pollock in 1966 first described the association of MTC with mucosal neuromas.[1] Chong et al. in 1975 termed this association as subtype 2B of MEN syndrome.[2] M918T codon mutation is the most common genetic mutation (>95%).[2] The unique extra endocrine features include marfanoid habitus, ganglioneuromas of the gastrointestinal tract, and ectropion of eyelids. There is 50% lifetime risk of developing pheochromocytoma.

Medullary thyroid carcinoma is aggressive at the time of presentation as the onset is early but most often with delay in recognition and diagnosis of this rare entity.

Case Capsule

A 14-year-old girl presented to the pediatric surgery department with a history of upper lip swelling since 2 years of age, neck swelling since 4 years of age, and increased frequency of formed stools despite normal appetite since 5 years of age. She was evaluated elsewhere for the thyroid swelling with ultrasound neck at 4 years and was told to be benign, kept on follow-up.

The treating physician noticed marfanoid habitus Taller for age (Fig. 1), upper lip swelling, tongue mass–mucosal neuromas (Fig. 2), bilateral upper eyelid eversion (Fig. 3), and left thyroid nodule with restricted mobility (Fig. 4), and hyperlaxity of joints (Fig. 5).

Based on physical features with associated thyroid swelling, a diagnosis of probable MEN2B syndrome was made.

On further evaluation, she had FNA-proven MTC with significant left cervical lymph node metastasis. Serum calcitonin was 9036 pg/mL (11.5 pg/mL) and carcinoembryonic antigen (CEA) was 284 ng/mL (<5 ng/mL). Workup for pheochromocytoma, the 24 hours urinary metanephrines and normetanephrines, CT abdomen, and metaiodobenzylguanidine (MIBG) scan were negative.

There was no significant family history. Rearranged during transfection (RET) gene mutation testing was counseled, but the parents did not agree with the same.

She underwent total thyroidectomy with central compartment and left functional neck dissection. Final histopathology was suggestive of MTC with metastasis to cervical lymph nodes.

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Fig. 1: Marfanoid habitus – tall for age, slender arms, and leg

Discussion

Multiple endocrine neoplasia type 2B is an autosomal dominant condition with a mutation in RET gene in chromosome 10q that transcribes for Tyrosine Kinase receptor. Often the mutation is *de novo*, with more than 95% showing mutation in codon 918T (ATA highest risk).[3]

Medullary thyroid carcinoma is expressed 100% in affected individuals. The clinical presentation of thyroid swelling may

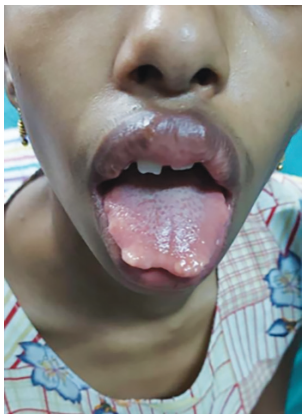

Fig. 2: Mucosal neuromas in upper lip and tongue

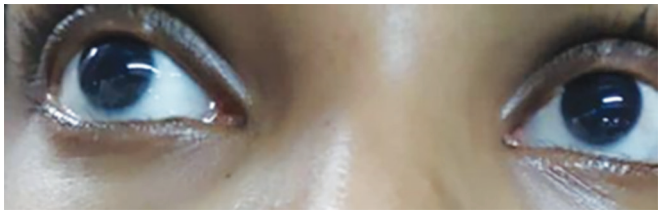

Fig. 3: Eversion of upper eyelids

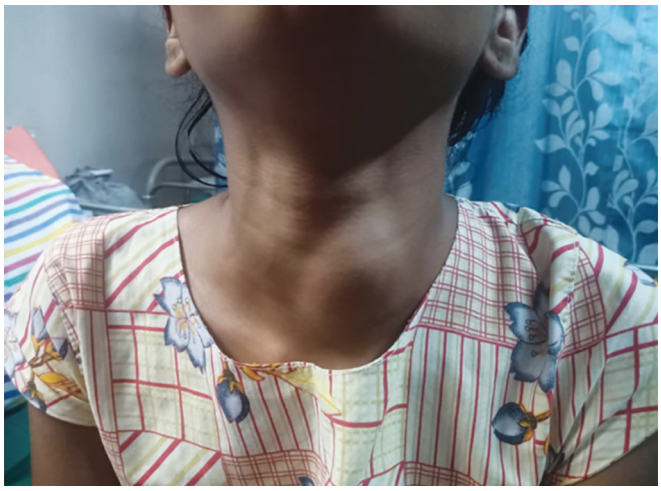

Fig. 4: Left thyroid nodule

be evident as early as infancy. Zenaty et al.[4] described 2 of 3 patients with lymph node metastasis in hereditary MEN2B operated prophylactically during infancy. The tumor most commonly involves bilateral thyroid lobes and multifocal. The parafollicular C cells may show hyperplasia even before the manifestation of tumor itself.

Medullary thyroid carcinoma is the main cause of death in MEN2B[5] as the stage of tumor forms the main factor at diagnosis. Due to their aggressive nature, ATA recommends prophylactic thyroidectomy in hereditary MTC as early as infancy.[3]

The largest published series of MEN2B by Brauckhoff et al.[6] showed cancer-specific death at mean age of 18.2 ± 10.7 years. The delay in recognizing the clinical features in MEN2B is the most

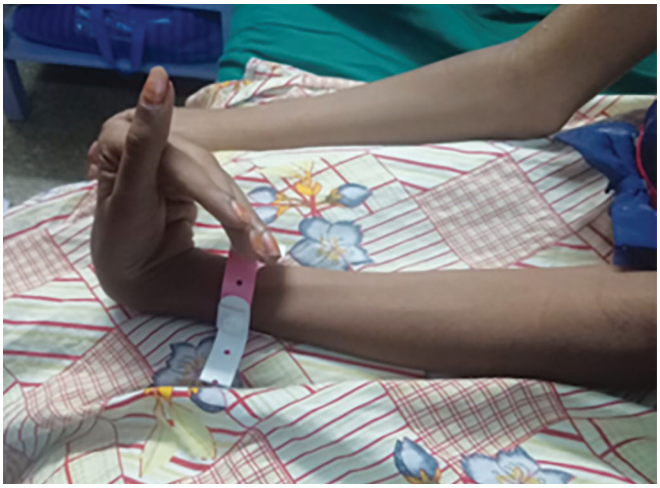

Fig. 5: Hyperlaxity of wrist joint

common reason stated in literature resulting in the aggressive presentation of MTC with lymph node or distant metastasis.

These patients are at 50% risk of developing pheochromocytoma. Thosani et al.[7] described 15 patients of MEN2B diagnosed and treated for pheochromocytoma at a median age of 25 years.

The extra endocrine physical manifestation in MEN2B is unique.

Mucosal neuromas, a hallmark in MEN2B,[8] may be evident at birth, with the majority manifesting by 1st decade of life. They appear as 2–7 mm yellow painless flat or sessile nodules.

Marfanoid habitus like taller for age, high arched palpate, slender arms and legs, joint laxity, and scoliosis can manifest.

"Tearless crying" alacrimia, eversion on upper eyelids, conjunctival neuromas, thickened corneal nerves, and mild ptosis are some of the ophthalmologic signs.

Feeding intolerance in infancy, constipation or diarrhea, abdominal distension (mega-colon) due to enteric and extrinsic nerve hyperplasia, and ganglioneuromas of the submucosa and myenteric plexuses lead by loss of normal bowel tone.

Conclusion

Physicians and other health care workers' awareness and recognition of various phenotypic presentations in MEN2B are of utmost importance. The early development of MTC, its recognition with appropriate surgical intervention as early as infancy, and constant surveillance for the development of pheochromocytoma in affected individuals are to be considered.

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