Pediatric Multiple Endocrine Neoplasia Type 2B: Clinicopathological Correlation of Perilimbal Mucosal Neuromas and Treatment of Secondary Open-Angle Glaucoma

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Established Facts

- Mucosal neuromas are associated with multiple endocrine neoplasia type 2B (MEN 2B), the histopathology of which is well described.
- Open-angle glaucoma can rarely occur with MEN 2B.
- Surgical treatment approach of MEN 2B-associated glaucoma is not well established.

Novel Insights

- High-resolution anterior segment optical coherence tomographic findings of mucosal neuroma can help in its diagnosis.
- Gonioscopy-assisted transluminal trabeculotomy may be safe and effective in the treatment of juvenile-onset open-angle glaucoma associated with MEN 2B.

Keywords

Multiple endocrine neoplasia type 2B · Mucosal neuromas · Juvenile open-angle glaucoma · Anterior segment optical coherence tomography · Gonioscopy-assisted transluminal trabeculotomy

Abstract

Ocular findings of multiple endocrine neoplasia type 2B (MEN 2B) include prominent corneal nerves, mucosal neuromas of the conjunctiva, glaucoma, and dry eyes. A 15-year-old girl with MEN 2B presents with advanced secondary open-angle glaucoma and bilateral perilimbal masses. High-resolution optical coherence tomography (HR-OCT) of the perilimbal lesions showed normal epithelial thickness and subepithelial lobular areas of mixed reflectivity, which correlates well with histo-

pathologic findings of benign mucosal neuromas. The patient underwent bilateral gonioscopy-assisted transluminal trabeculotomy (GATT) in both eyes, which achieved adequate intraocular pressure control at short-term follow-up. To the authors' knowledge, this is the first report correlating HR-OCT and histopathologic findings in benign mucosal neuroma associated with MEN 2B, and the first description of secondary open-angle glaucoma associated with MEN 2B treated with GATT.

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Introduction

Ocular manifestations of multiple endocrine neoplasia type 2B (MEN 2B), a rare, autosomal-dominant tumor syndrome, include prominent corneal nerves, mucosal

Fig. 1. **a** Slit lamp photograph of a perilimbal serpentine subconjunctival lesion. **b** Intraoperative gonioscopy showing open angle with moderate pigmentation.

neuromas of the conjunctiva, glaucoma, and dry eyes [1, 2]. We report the high-resolution optical coherence tomographic (HR-OCT) features and clinicopathological correlation of perilimbal mucosal neuroma in a case of pediatric MEN 2B, and the treatment of the associated secondary open-angle glaucoma with gonioscopy-assisted transluminal trabeculotomy (GATT).

Case Report

A 15-year-old girl with a history of metastatic medullary thyroid cancer was referred to the Bascom Palmer Eye Institute Emergency Room, after elevated intraocular pressures (IOPs) were noted during a routine eye examination by a pediatric ophthalmologist. A molecular diagnosis of MEN 2B syndrome was made 2 years prior with a pMet918Thr pathogenic mutation in the RET gene. There is no family history of glaucomatous diseases, and the patient has never received systemic or topical steroids. On examination, she had a best-corrected visual acuity (BCVA) of 20/100 in both eyes (OU), constricted visual field by confrontation, and sluggishly reactive pupils. IOP by Tonopen was 28 mm Hg in the right eye (OD) and 29 mm Hg in the left eye (OS). She was discharged on dorzolamide/timolol-fixed combination (OU, twice daily) and latanoprost (OU, once at bedtime), and urgently referred to the pediatric glaucoma service.

The patient was lost to follow-up and returned 20 months later. On follow-up examination, BCVA were 20/200 OD and 20/100 OS. IOPs by Goldmann applanation were 52 mm Hg OD and 44 mm Hg OS on dorzolamide/timolol-fixed combination (OU, twice daily) and latanoprost (OU, once at bedtime). Central corneal thicknesses were 632 μ m OD, 616 μ m OS. On slit lamp examination, she had multiple, elevated, serpentine, perilimbal subconjunctival lesions (Fig. 1a) and prominent corneal nerves, but otherwise normal anterior segments in both eyes. Gonioscopy revealed Shaffer grade IV open angles with moderate pigmentation (Fig. 1b). Dilated examination revealed significant cupping and pallor of the optic discs. Color slit lamp photos and HR-OCT of the perilimbal masses were obtained (Fig. 2a), which revealed normal epithelial thickness and reflectivity, and subepithelial lesions of mixed reflectivity with lobular and whirling cellular features.

Due to the poorly controlled IOP, GATT was performed sequentially in both eyes with concurrent excisional biopsies of the perilimbal lesions. Pathological examination revealed neural tumors composed of spindle-shaped Schwann cells (Fig. 2b) that stained with epithelial membrane antigen (Fig. 2c) and S100 protein (Fig. 2d), consistent with benign mucosal neuroma.

Three months following GATT in the second eye, BCVA has improved to 20/150 OD and 20/60 OS, and IOPs were 11 and 12 mm Hg without the use of IOP-lowering medications. The neuromas have not recurred.

Discussion

HR-OCT is a noninvasive, adjunctive tool in the diagnosis of corneal and conjunctival pathology [3]. To our knowledge, we present the first correlation between the HR-OCT and histopathologic findings of a mucosal neuroma. The HR-OCT features of normal epithelium with subepithelial and whirling, lobular masses of mixed reflectivity differ from that of ocular surface squamous neoplasm, pingueculum, pterygium, lymphoma, Salzmann's nodular degeneration, nevi, and melanoma [3] and may help differentiate a mucosal neuroma from these other entities.

Glaucoma associated with MEN 2B has been reported in both adults and children [2, 4]. GATT, a microincisional trabeculotomy technique that allows the circumferential incision of trabecular meshwork through two clear-corneal incisions, has demonstrated fair short-term safety and efficacy in juvenile and secondary open-angle glaucoma [5]. Our patient has responded favorably to GATT in both eyes, with IOP controlled without the use of IOP-lowering medication 3 months following the procedure. Longer follow-up is needed to assess the long-term efficacy of GATT in juvenile-onset glaucoma secondary to MEN 2B.

Fig. 2. **a** High-resolution anterior segment optical coherence tomography of the perilimbal serpentine subconjunctival lesion. The epithelium (red arrowheads) has normal thickness. There are subepithelial lobular areas of mixed reflectivity (asterisks). **b** Hematoxylin and eosin stain showing spindle-shaped cells (inset)

that are variably encapsulated. **c** Positive epithelial membrane antigen stain at the tumor periphery (red arrowheads). **d** Positive S100 stain within the substance of the tumor. The constellation of histopathologic findings is consistent with benign mucosal neuroma.

In conclusion, HR-OCT may be a useful tool in the confirmation of conjunctival mucosal neuromas in patients with MEN 2B. GATT may be a safe and effective surgical option in children with glaucoma associated with this condition.

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Statement of Ethics

Subject and guardian have given their informed consent for the use of clinical and pathology photographs.

Disclosure Statement

None of the authors have any possible conflicts of interest to disclose.

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