Late-Onset Unilateral Primary Developmental Glaucoma Associated With Iridotrabecular Dysgenesis, Congenital Ectropion Uveae and Thickened Corneal Nerves: A New Neural Crest Syndrome?

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Abstract. The association of unilateral primary developmental glaucoma with iridotrabecular dysgenesis and congenital ectropion uveae has been well documented in the literature.1,2 The glaucoma in this entity may present at birth, infancy or may develop at a later stage in life. I report the case of a child with late-onset unilateral primary developmental glaucoma due to iridotrabecular dysgenesis, congenital ectropion uveae, and who had a previously undescribed association with ipsilateral thickened corneal nerves in the stroma. [Ophthalmic Surg Lasers 1999;30:567-570.]

CASE REPORT

A 9-year-old girl with late onset primary developmental glaucoma on her right eye underwent complete ocular and systemic examination. Her visual acuity was corrected to 20/25 with −1.00 −2.5 × 180°

Figure 1. Clinical appearance of the child with obvious enlargement of the right cornea.

Figure 2. Anterior segment photograph of the right eye showing pigment epithelial hyperplasia extending 360° around the pupillary border.

right eye; 20/15 unaided, left eye. Her intraocular pressures were 36 mm Hg and 14 mm Hg in right and left eye, respectively. Gonioscopy revealed anterior iris insertion on the trabecular meshwork typical of primary developmental glaucoma. Figure 1 shows obvious enlargement of the right cornea; horizontal corneal diameters were 12.5 mm and 11 mm in the right and left eye, respectively. Congenital ectropion uveae (CEU) was present 360° around the pupil, extending only a short distance onto the right iris surface (Figure 2), while the left eye showed no abnormality of the pupillary border (Figure 3).

Fundus evaluation revealed 0.5:1 cupping with thinning and pallor of the temporal neuroretinal rim on the right side (Figure 4), while the left eye disc showed no abnormality (Figure 5). Slit lamp examination showed multiple grayish-white, prominent, thickened corneal nerves in the stroma of the right cornea.
only (Figures 6 and 7). No evidence of neurofibromatosis or other systemic abnormality was present. The patient was successfully managed with primary combined trabeculotomy and trabeculectomy.3

COMMENT

In normal eyes, corneal nerves are not thick enough to visualize by slit-lamp biomicroscopy, partly because of the absence of myelinated fibers.4 Increased

visibility of corneal nerves, however, is recognized in some ocular and systemic diseases.5 The differential diagnosis of prominent corneal nerves includes disease states in which the nerves become more visible because of intrinsic corneal disease or secondary thickening of the corneal nerves. This may be caused by nerve regeneration or regional inflammation such as anterior keratoconus, Fuch’s dystrophy with bullous keratopathy, posterior polymorphous dystrophy, herpes zoster and simplex keratitis, and failed grafts.5,6 The visibility itself, however, is mild and localized. In contrast, the corneal nerves in the present case were readily visible, appeared thickened, and extended into the central cornea in all meridians.

Prominent corneal nerves over the entire cornea are thought to be associated with congenital ichthyosis, Refsum’s disease, multiple endocrine neoplasia7-16 and leprosy.11,12 Neurofibromatosis13 has also been included in the differential diagnosis of prominent corneal nerves; however, the patients described were all from the early part of this century and may have actually had multiple endocrine neoplasia type IIB.10 Among the 3 multiple endocrine neoplasia syndromes, it is generally

Figure 3. Anterior segment photograph of the left eye showing normal pupillary margin.

Figure 4. Fundus photograph (3D) of the right eye showing significant optic disc cupping.

Figure 5. Fundus photograph (3D) of the left eye showing normal disc appearance.

Figure 6. Slit-lamp examination shows grayish-white, thickened corneal nerves (seen within slit-beam).

Figure 7. Magnified (x 25) view of the thickened corneal nerves.
accepted that type II B consistently shows the most prominent corneal nerves in both corneas. The presence of prominent corneal nerves has been reported in 100% of multiple endocrine neoplasia type II B cases undergoing slit-lamp examination.

The present case had prominent corneal nerves in 1 eye only. Both multiple endocrine neoplasia type II B and multiple neurofibromatosis are genetically determined disorders of neural crest derivatives. Congenital medullation of the nerve fibers and prominent corneal nerves have also been described in multiple neurofibromatosis. The association between prominent corneal nerves and neurofibromatosis has been documented histologically in 1 patient with congenital buphthalmos and bullous keratopathy. In the present case, the prominent and thickened corneal nerves were present within an otherwise normal corneal stroma in a 9-year-old girl who had ipsilateral late-onset primary developmental glaucoma due to iridotrabecular dysgenesis and congenital ectropion uveae. The possibility of other ocular or systemic diseases were excluded by thorough ocular and systemic examination and necessary investigations by internists.

Congenital ectropion uveae is a rare, non-progressive anomaly which may be associated with angle dysgenesis and anterior insertion of the iris root manifested as primary developmental glaucoma. Various other congenital ocular and systemic anomalies may be associated with this disorder. Quigley and Stanley described a patient with unilateral congenital iris pigment epithelial hyperplasia in whom glaucoma associated with extensive pigment deposition in the angle was observed at age 41.

The exact etiology of developmental glaucoma with CEU is unknown. Abnormalities in neural crest cell migration may have a major role in the pathogenesis of developmental glaucomas. Despite the neuroectodermal origin, these cells make a major contribution to the mesenchyma, which helps in the development of iris epithelium, corneal endothelium and nerve sheaths. Three successive waves of ingrowth of neural crest cells are associated with differentiation of the anterior chamber. The first wave forms the corneal endothelium, the second wave forms the iris and pupillary membrane and the third wave forms the keratocytes. The triad of primary developmental glaucoma, congenital ectropion uveae and prominent corneal nerves as seen in the present case are embryologically related and lay a strong clinical credence to neural crest cell theory of anterior segment development. To our knowledge, this is the first report on the association of thickened corneal nerves with primary developmental glaucoma due to iridotrabecular dysgenesis and congenital ectropion uveae.

REFERENCES


