Congenital Iris Ectropion and Glaucoma Associated With Intestinal Neuronal Dysplasia: A Manifestation of a Neural Crest Syndrome

Congenital iris ectropion (CIE) associated with glaucoma is a rare ocular manifestation of a neural crest syndrome. We describe a 5-year-old boy with unilateral congenital iris ectropion, glaucoma, and features of intestinal neuronal dysplasia (IND) on rectal mucosal biopsy. The affected eye was buphthalmic and displayed an iridotrabecular dysgenesis with advanced glaucomatous damage. The contralateral eye showed a mild trabeculodysgenesis without ectropion uveae, coloboma, or sector heterochromia of the iris. The association of iridotrabecular dysgenesis and IND is suggested to represent a manifestation, to our knowledge not previously described, of a new neural crest syndrome.

Congenital iris ectropion is a rare, usually nonprogressive anomaly characterized by the posterior iris pigment epithelium on the anterior surface of the iris stroma, anterior insertion of the iris root, and trabecular dysgenesis. It is frequently associated with developmental glaucoma and may occur as part of a systemic disorder including neurofibromatosis, primary facial hemihypertrophy, Rieger anomaly, and Prader-Willi syndrome.1

We report a case of unilateral CIE with iridotrabecular dysgenesis and congenital glaucoma associated with

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best-corrected visual acuity</td>
<td>20/200</td>
<td>20/20</td>
</tr>
<tr>
<td>Intraocular pressure, mm Hg</td>
<td>36</td>
<td>12</td>
</tr>
<tr>
<td>Corneal thickness, µm</td>
<td>585</td>
<td>615</td>
</tr>
<tr>
<td>Horizontal corneal diameter, mm</td>
<td>14</td>
<td>11</td>
</tr>
</tbody>
</table>

Table. Summary of Clinical Ophthalmic Findings

Figure 1. Anterior segment photograph of the right eye. A, Wide pupil and striking smoothness of the anterior surface of the iris, absence of the circular contraction furrows, and absence of radial folds are shown. Arrows indicate the iris ectropion. B, Higher magnification and illumination of the iris to better differentiate the pupillary margin from the iris ectropion (arrows).

Figure 2. Gonioscopic view of the high insertion of the iris (arrowheads) without any detectable differentiation of the anterior chamber angle. Black arrows indicate iris ectropion; white arrows, iris atrophy.

Figure 3. Ultrasound biomicroscopy shows the anterior insertion of the iris root and the deep posterior chamber.
features of IND. Intestinal neuronal dysplasia is considered the mildest form of malformation of the enteric nervous system and is currently regarded as retarded maturation of submucosal ganglia.\(^2\)\(^-\)\(^4\)

Clinically, IND may resemble Hirschsprung disease (congenital aganglionosis megacolon) with severe chronic constipation. To our knowledge, the combination of CIE and IND has not been described previously. It is of interest since both diseases are considered to be linked to neural crest disorders.\(^3\)\(^-\)\(^5\)

**Report of a Case.** A 5-year-old boy was referred to us with gradual visual loss for 6 months and a painful buphthalmic right eye. The pupil reaction to light was sluggish in the right eye but normal in the left eye. Findings at initial examination are summarized in the **Table**.

On examination under general anesthesia, the cornea was clear and did not have posterior embryotoxon or breaks in the Descemet membrane in either eye. There was CIE in the right eye extending 360° around the pupil, and it was limited by a sharply demarcated round border with the rest of the iris having a strikingly smooth, cryptless anterior surface (**Figure 1**). The anterior chamber was deeper in the right eye than in the left eye. On gonioscopy, the anterior insertion of the iris root was positioned above the Schwalbe line. No angular structure was discernible (**Figure 2**). On ultrasound biomicroscopy, the anterior chamber depth was 4.0 mm, the trabeculo-iris angle was 42.3°, and the anterior insertion of the iris root was confirmed (**Figure 3**). The left eye did not have major pathological findings of the iris (**Figure 4**), but there was an increased number of iris processes reaching above the Schwalbe line. The iris was inserted relatively posterior with a discernible ciliary body band. Funduscopy showed a largely excavated glaucomatous optic disc in the right eye but no disc cupping in the left eye (**Figure 5**).

The patient had a history of gastrointestinal problems with severe constipation since birth. He underwent a colonoscopy with full-thickness rectal biopsy at the age of 2.25 years, and it showed characteristic histologic features of IND type B with several giant ganglia showing up to 13 nerve cells (**Figure 6**). Specifically, the nerve cells were polymorphous with little cytoplasm. This is in contrast to normal ganglia that have up to 8 monomorphous nerve cells per ganglion. The patient was treated conservatively with a stool softener and enemas, as the clinical problem is manageable in this way in most patients with IND. The fact that defecation became regular and rhythmic at age 4 years underscores the concept of a developmental retardation of the enteric nervous system in IND. At his last visit on November 15, 2005, no other systemic (ie, cardiovascular, neurologic) abnormality and no developmental delay were found. After informed consent was signed by the parents, an uneventful deep sclerectomy combined with trabeculotomy was performed in the right eye. The intraocular pressure after surgery was between 12 and 14 mm Hg at follow-up at 3 months.

**Comment.** Congenital iris ectropion is an uncommon malformation of the iris resulting from proliferation of the iris pigment epithelium on the anterior surface of the iris from the pigment ruff. Additional major features are a smooth

![Figure 4. Anterior segment photograph of the left eye showing no pathological findings of the iris.](image)

![Figure 5. Funduscopy shows large glaucomatous cupping of the optic nerve head with an overall narrowing of the neuroretinal rim.](image)

![Figure 6. Histopathological examination of the rectum revealed multiple giant ganglia with up to 13 nerve cells (arrowheads), heterotopic ganglia in the muscularis mucosae (white arrows), and small polymorphous nerve cells (black arrows), which is suggestive of intestinal neuronal dysplasia type B (enzyme histochemistry for lactic acid dehydrogenase, original magnification x100).](image)
cryptless iris surface, anterior iris insertion, and dysgenesis of the iridoconveal angle often leading to glaucoma. Although the exact etiology is unknown, CIE arises from late developmental arrest of the posterior migration of neural crest cells. Likewise, abnormal migration and differentiation of cells derived from the neural crest are implied in IND, a disease of the submucous enteric plexus characterized histologically by a large proportion of giant ganglia. In contrast, classic Hirschsprung disease is characterized by the absence of ganglia of the myenteric plexus and submucous plexus in the rectosigmoid. At the molecular level, different factors that may be involved in the development and migration of neural crest cells have been described. The transcription factor Hox11L.1 is thought to be involved in peripheral nervous system development and is expressed by enteric neurons. In addition, genes encoding endothelin 3 or its receptor influence the migration of neuronal crest–derived progenitors. An overexpression of Hox 4 has been found to lead to a misdirection of migratory neuronal progenitors. The association of Hirschsprung disease and iris defects including herochromia and coloboma is known. However, to our knowledge, the combination of CIE, iridotrabecular dysgenesis, and glaucoma with IND has not been previously described. The combination of both disorders, CIE and IND, underscores their pathogenesis as disorders of neural crest cell migration and differentiation. A genetic defect and the molecular pathogenesis, however, remain to be elucidated.

Matthias C. Grieshaber, MD
Selim Orgul, MD
Elisabeth Bruder, MD
Faruk Hadziselimovic, MD
Josef Flammer, MD

Correspondence: Dr Grieshaber, Department of Ophthalmology, University of Basel, Mittlere Strasse 91, PO Box, CH-4031 Basel, Switzerland (mgrieshaber@ubbs.ch).

Financial Disclosure: None reported.

Iris Ectopic Thyroid Tissue: Report of a Case

Ectopic benign thyroid tissue outside the normal migration path of the thyroid is an extremely rare condition that, to our knowledge, has never been described in the eye. A 15-year-old boy was seen with a pink, multifocal lesion with an intraocular tumor in his right eye. This lesion was detected on routine eye examination when he reported a 6-week history of floaters and headaches. The patient was not previously aware of this tumor, and no prior ocular disease was reported. Systemic assessment was unremarkable apart from mild asthma. At his first visit to us, his visual acuity was 20/20 OD and 20/20 OS. Slitlamp examination of the right eye showed a temporal, pink, multinodular lesion that involved the iris root and anterior chamber angle (Figure 1). At gonioscopic examination, the mass obstructed the view into the anterior chamber angle from the 8- to 9-o'clock positions. The intraocular pressure was 19 mm Hg OD and 15 mm Hg OS. The fundus and the left eye were healthy. On ultrasonography, the tumor measured approximately 3.8 mm longitudinally and 2.5 mm transversely with a thickness of 1.2 mm. The internal acoustic reflectivity suggested small cystic spaces within the lesion (Figure 2). The differential diagnosis included lacrimal gland choristoma and medulloepithelioma. An excision biopsy consisting of iridocyclectomy was performed under general anesthesia without complications. The postoperative recovery was uneventful. At follow-up examination 9 months after surgery, the unaided visual acuity was 20/20 OD. The intraocular pressure was 15 mm Hg OD and 14 mm Hg OS. Biomicroscopy showed a small surgical coloboma corresponding to the excised lesion. There were no complications.

Histopathological Examination. Histopathological examination confirmed that the specimen comprised inner corneoscleral tissue including the peripheral Descemet membrane, trabecular meshwork, Schlemm canal, ciliary muscle, ciliary processes, and peripheral iris.