Leukocoria Caused by Intraocular Heterotopic Brain Tissue

Leukocoria caused by diverse ocular conditions is distinguishable by history, characteristic clinical findings, and ancillary imaging. Atypical cases pose a diagnostic dilemma necessitating enucleation if retinoblastoma or malignancy cannot be excluded. We report a newborn with leukocoria in a microphthalmic eye containing an uncalcified subretinal mass. Teratoid medulloepithelioma was suspected. Instead, benign heterotopic brain tissue was found, which to our knowledge has only been reported once before, due to aberrant differentiation of the neuroectoderm into cerebral gray matter instead of the retina.

Report of a Case. A 5-day-old, healthy baby girl with leukocoria of the microphthalmic right eye was seen in the Retinoblastoma Program at the Hospital for Sick Children, Toronto, Ontario. Perinatal and family histories were unremarkable. The left eye was normal, but the right eye appeared blind. Under general anesthesia, intraocular pressure and ocular movements were normal. The 8-mm-diameter right cornea was clear and the anterior chamber, deep. The iris was hypoplastic with persistent tunica vasculosa lentis bridging the pupil. The irregularly shaped lens was small but clear. Zonules were incomplete (Figure 1). A large, nasal, creamy-white, elevated subretinal mass, obscuring the retina and optic nerve, extended into the clear vitreous until just behind the lens. B-scan ultrasonography results revealed a homogeneous, uncalcified tumor filling two thirds of the eye (Figure 2). Sclera underlying the tumor bulged like a staphyloma. The medial rectus muscle moved freely.Computed tomography results showed an abnormal-shaped, small eye with ectatic or deficient sclera underlying the uncalcified tumor and medial rectus (Figure 3). Coronal T2-weighted magnetic resonance imaging results showed no melanin or blood in the tumor, which was isodense with cerebral cortex (Figure 4). The tumor border was smooth and concave with a vitreous band, possibly persistent hyaloid, extending across the vitreous/subretinal space to the sclera. There was no extraocular extension. The optic nerves and brain appeared normal.

Malignant teratoid medulloepithelioma with persistent hyperplastic primary vitreous was suspected. Serial B-scans during 2 weeks suggested growth and change in vitreous density. Eye Cancer Network and International Tumor Board (New York, NY) consultations all recommended enucleation of this blind eye with possible malignancy. The 16 × 17 × 16-mm eye showed no scleral defects. On opening the eye through an inferior, horizontal pupil-optic nerve incision, a solid, uncalcified, homogeneously grayish-white tumor unlike retinoblastoma was found arising in a staphylomatous choroidal coloboma, filling much of the vitreous and abutting the lens anteriorly (Figure 5). Where imaging suggested deficient sclera was a choroid coloboma with scleral ectasia.

The tumor, eosinophilic on hematoxylin-eosin stain, resting di-

Figure 2. B-scan ultrasonography results show a homogeneous, uncalcified mass occupying two thirds of the vitreous cavity, overlying the optic nerve, and extending anteriorly to abut the lens. Sclera beneath the tumor suggested a staphyloma. A vitreous band (arrow) was present on the temporal side of the mass.

Figure 3. Nonenhanced axial computed tomography results show a small right eye with irregular, possibly deficient sclera adjacent to the tumor under the medial rectus muscle (white arrow). The tumor mass was not calcified and did not show extraocular extension.

Figure 4. Coronal T2-weighted magnetic resonance imaging results confirmed that the tumor did not contain melanin or blood but was isodense with gray matter. A vitreous band, possibly persistent hyaloid, extended supero-temporally from the smooth tumor border to the sclera. The eye appears egg-shaped with a bulge in the sclera beneath the tumor medially (white arrow).
rectly on ectatic sclera in the anterior retina/ciliary region, extended backward across the choroid to the optic nerve (Figure 6A). Areas of dysplastic retina were thrown into focal pseudorosettes in their periphery (Figure 6A). The tumor was composed of brain tissue strongly positive for synaptophysin (Figure 6B). Large, mature, crystal violet–positive neurons (Figure 7A, B, and D); glial, fibrillary, acidic, protein–positive, plump oligodendrocytes; and spindle-shaped astrocytes (Figure 7A and C) were admixed with neuropil containing rare focal calcification. The cornea and anterior chamber were unremarkable. Lens epithelial and bladder cells had migrated into the posterior subcapsular area. The ciliary body was attenuated. The tumor appeared to arise from the retina in some areas (Figure 8A) and the retinal pigment epithelium in others (Figure 8B). The 6-mm tumor-free optic nerve was atrophic, drawn into the globe under traction (Figure 8B).

Comment. Normal brain tissue not communicating with the central nervous system (brain heterotopia) has been reported in the head and neck, rarely in the orbit,2–5 at the limbus,6,7 and in 1 case in the anterior segment of an infant’s eye.8 Intraocular heterotopic brain tissue arising from the retina or anterior retinal pigment epithelium was reported recently.1 To our knowledge, this is the second report.

Previous authors proposed that when embryonal neuroectodermal
stem cells segregated outside the central nervous system during development, teratomatous proliferation or true astrocytomas or benign brain heterotopia could result. In our patient, the tumor appeared to arise from both the retina and retinal pigment epithelium within a coloboma, suggesting abnormal neur ectoderm dif-

Figure 7. A, High-power photomicrograph of the tumor demonstrating mature neurons (arrow), oligodendrocytes (diamond-headed arrow), and astrocytes (open arrow) interspersed in neuropil, typical of cerebral gray matter (hematoxylin-eosin). B, Crystal violet stain of mature neurons within the tumor (arrow). The stain bound very strongly to RNA in the rough endoplasmic reticulum of the neuron. Note the prominent nucleolus. C, Glial fibrillary acidic protein in astrocytes (arrows), the most common glia in the tumor. D, A single neuron within the tumor immunolabeled with neurofilament antibody. Note the dendritic processes (D) and large central nucleus (N) typical of most neurons (all images original magnification ×400).

Figure 8. A, Relationship between the tumor (T), choroid (C), and normal retina (R) with the tumor appearing contiguous with the outer retina (arrow) (hematoxylin-eosin, original magnification ×40). B, The tumor (T) appeared to have drawn the optic nerve (ON) into the eye. Note the displacement of the retina (R) and apparent continuity of the tumor with the retinal pigment epithelium (RPE) (arrows) (hematoxylin-eosin, original magnification ×100).
differentiation within the optic cup in the embryonic fissure, causing subsequent microphthalmia and anterior segment maldevelopment. The pathogenesis is uncertain; failure of a clone of pluripotential stem cells in the embryonic fissure to initiate normal retinal development may have occurred. This may be due to a somatic mutation in a gene involved in the retinal signaling pathway, such as CHX-10\(^{9}\), PAX6\(^{10}\), PAX2\(^{11}\), Rx\(^{12}\), or sonic hedgehog, SHH\(^{13}\), which are required for vertebrate retinal development. These mutations potentially could leave cortical development as a default pathway for retinal differentiation. Thus, a local cerebrocortical cell mass arising in the anterior retina/ciliary region may be analogous to experimental eye formation in ectopic locations when the Drosophila gene, eyeless (ey), homologous to mammalian PAX6, drives eye development wherever ectopic expression occurs.\(^{14}\) A germline deletion in SHH has been associated with iris and uveoretinal colobomas.\(^{15}\) We hypothesize in the present case that somatic mutation in such a gene may be causative.

The finding of leukocoria in a child requires thorough evaluation to exclude retinoblastoma or other intraocular malignancies. This neonatal development of an uncalcified, homogenous intraocular mass in a microphthalmic eye was more consistent with a developmental anomaly than retinoblastoma. With no possible useful vision but potential malignancy, including atypical teratoid medulloepithelioma or retinoblastoma, enucleation of the eye was indicated. This child continued to thrive without needing further medical tests or interventions.

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Orbital Myositis in Churg-Strauss Syndrome

A case of orbital myositis in a patient with Churg-Strauss syndrome (CSS) is reported herein. To our knowledge, this association has been reported only once previously.\(^{1}\) We also describe the previously reported ophthalmic manifestations of CSS.

Report of a Case. A 55-year-old woman was referred to our unit with a 1-week history of redness and pain behind the right eye, which worsened on eye movement.

Her medical history included adult-onset, steroid-dependent asthma, diagnosed at 30 years of age and currently stabilized with inhaled corticosteroid use. She also had, from allergic rhinitis, nasal polyps and severe sinus disease requiring repeated surgery. She had been noted to have peripheral blood eosinophilia on several occasions for the last 7 years and had a recurrent rash for the last 4 years involving her trunk and back, responsive to corticosteroid treatment and found to be interstitial granuloma annulare on tissue biopsy results obtained 4 years earlier. A repeated biopsy 1 year later revealed an intense urticarial inflammatory reaction with perivascular eosinophilic and lymphohytic inflammatory infiltrates. Peripheral blood eosinophil levels, 4 and 3 years previously, were raised at 2300/µL and 2060/µL, respectively. A bone marrow biopsy obtained 3 years earlier revealed a marrow eosinophilia and an elevation of eosinophil precursor populations (eosinophil and eosinophil precursors, 10%) with normal erythropoiesis, myelopoiesis, marrow cells, and marrow architecture. Findings from bone marrow lymphocyte surface marker analysis and gene rearrangement studies were normal. Allergies included sulfur, aspirin, and certain foods, for which she had undergone desensitization therapy.

On examination, she had swelling and tenderness of the right upper lid and bony tenderness over the right cheek. Her right conjunctiva was inflamed and edematous with
A 25-year-old white man was initially seen with a 1-week history of floaters and decreased vision in his left eye. The patient had been diagnosed with Tourette syndrome at age 7 years, obsessive-compulsive disorder at age 11 years, and depression at age 24 years. His motor tics involved excessive blinking, blepharospasm, clapping, jabbing his fingers into his eyes, and punching himself in the periorbital area. The patient was taking buspirone hydrochloride (10 mg twice a day) and clomipramine hydrochloride (25 mg twice a day). On examination, the patient was alert and oriented, and he had no evidence of cognitive impairment. Visual acuity was 20/200 OD and hand motion OS. There was no afferent pupillary defect. Intraocular pressures were 18 OD and 16 OS. Slit-lamp examination findings of the right eye demonstrated pigment deposits on the corneal endothelium, moderate (2+) aqueous pigmented cells, and posterior subcapsular cataract. The left eye had a less than 1-mm hyphema and many (4+) circulating red blood cells in the anterior chamber, as well as a dense posterior subcapsular cataract. Fundoscopy results revealed a retinal dialysis from the 1:30 to the 4:30 clock position with 4 long radial extensions to the temporal macula and from the 6-o’clock to the 11-o’clock position with 1 long radial extension to the optic disc. There was an additional radially oriented posterior retinal break. Postoperatively, the retinas were attached in both eyes. One month later, the left eye developed proliferative vitreoretinopathy with retinal detachment and underwent reoperation. At 6 months, the retinas remained attached and the visual acuity was 20/100 OU.

Comment. Ophthalmic manifestations of Tourette syndrome include frequent blinking and blepharospasm, gaze deviations and abnormal saccades, and accidental and self-inflicted ocular injuries. The retinal detachments in our patient were most likely the result of repeated, self-induced finger jabbing to the eyes since the patient had no other risk factors for retinal detachment. In patients with retinal detachment, factors suggesting a traumatic etiology typically include unilateral vitreoretinal findings, retinal dialysis or giant retinal tear, and age younger than 40 years. However, in patients with self-induced or repeated trauma, the vitreoretinal pathologic features may be bilateral, as demonstrated by our patient. To prevent further self-injury, patients should wear protective polycarbonate goggles, and they should be monitored closely in conjunction with the psychiatry service. Treatment of the underlying disorder with behavior modification and pharmacotherapy is essential, and pharmacological agents that antagonize dopamine are most effective in reducing the severity of motor and vocal tics.

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