Ectopic Cerebrospinal-like Fluid From Retrobulbar Cysts as a Possible Cause of Pediatric Retinal Detachment Associated With Optic Disc Coloboma: New Implications for Management

Retinal detachment in adults with posterior segment coloboma is thought to be rhegmatogenous. Vitrectomy techniques are therefore used therapeutically. There is indirect evidence that subretinal fluid in retinal detachment, associated with optic nerve cavitation, is cerebrospinal fluid (CSF).\(^1\) We report 2 pediatric cases, referred for the management of coloboma-related retinal detachment, that provide direct evidence that the fluid is like CSF.

**Report of Cases.** Case 1. A white female infant was born at 29 weeks’ gestational age (GA) weighing 1200 g following spontaneous vaginal delivery after a normal pregnancy. Chromosome 1 harbored a p32.3 deletion. There was associated cleft lip, ventriculo-septal defect, and patent ductus arteriosus. Hydrocephalus required ventricular lavage at 34 weeks’ GA followed by repeated drainage from a cranial subcutaneous reservoir.

During screening for retinopathy of prematurity, the left retina was found attached at 33 weeks’ GA (Figure 1A). Nasal retinal detachment in the left eye was first noted at 38 weeks’ GA (Figure 1B). An examination under anesthetic was performed at 41 weeks’ GA. The horizontal corneal diameter and axial length were 4 and 12.3 mm in the right eye and 8.0 and 16.2 mm in the left eye. There were bilateral colobomas of the iris, posterior choroid, retina, and optic nerve with subtotal retinal detachment in the left eye (Figure 1C) and an attached retina in the right eye (Figure 1D).

Case 2. A white female infant born at term, following uneventful pregnancy and spontaneous vaginal delivery, was examined at 6 weeks of age and found to have bilateral microphthalmos (horizontal corneal diameter and axial length: 8.5 and 14.32 mm in the right eye and 9.0 and 16.98 mm in the left eye), colobomas similar to the first case, and attached retinas in both eyes. Other than microcephaly, findings of the pediatric workup, including genetic/chromosome studies, thoracoabdominal ultrasonography, and brain magnetic resonance imaging, were negative. An examination under anesthetic at 4 months of age showed subtotal retinal detachment in the right eye and an attached retina in the left eye (Figure 2A and B).

In both cases, rhegmatogenous etiology was not obvious and a conservative approach was agreed on because spontaneous reattachment is known to occur.\(^2\) There was, however, no change in case 1 two months later. Six months later in case 2, there

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**Figure 1.** Retcam images of case 1 showing the left eye at 33 (A), 38 (B), and 41 (C) weeks’ gestational age developing subtotal retinal detachment and the right eye (D) with disc and chorioretinal detachment without retinal detachment.

**Figure 2.** Retcam images of case 2 at 4 months of age showing retinal detachment in the right eye (A) and an attached retina in the left eye (B). The left eye developed subtotal retinal detachment 6 months later (C) associated with closure of excavation (compare the black arrows in parts B and C), pigmentary retinopathy (C, white arrow), and herniation of the retina into the excavation (C, green line). Corresponding optical coherence tomography in the left eye (D).
was no improvement in the right eye and the left eye had developed subtotal retinal detachment (Figure 2C) that was herniating into the entrance of the disc coloboma (Figure 2D). Visual evoked potentials in case 2 indicated no response from the right eye and a partial response from the left eye.

In both cases, the potential role of left vitrectomy was considered for persistent retinal detachment, on the assumption that unseen retinal breaks were present and associated with a pigmentary response identifiable in the left eye of case 2 (Figure 2C). It was agreed to proceed in this way if we could demonstrate the absence of CSF from the subretinal space of the left eye.

With informed consent, a general anesthetic was administered; aqueous humor, sampled; and an anterior chamber maintainer, used to pressurize each left eye. Trans-scleral aspiration of subretinal fluid into a 1-mL syringe attached to a 27-gauge needle was performed under indirect ophthalmoscopic control. Subretinal fluid was positive and aqueous was negative for asialotransferrin, which is also known as β₂-transferrin, a specific marker of CSF. A computed tomography cisternogram performed before sampling of fluid in case 1 showed retrobulbar cysts that were larger and more intimately related to the optic nerve in the left eye than the right eye but importantly failed to show a connection between the intracranial cistern and the subretinal space (Figure 3A-C) of the left eye. Magnetic resonance imaging in case 2 showed bilateral cysts adjacent to the optic nerve entrance (Figure 3D-F).

Comment. Failure of the optic fissure to close adequately results in typical coloboma. Retinal detachment is a complication that has been well characterized in chorioretinal coloboma in adults. Optical coherence tomography has verified that breaks occur at the margins of the coloboma allowing syneretic vitreous access to the subretinal space. As such, conventional approaches using vitrectomy techniques are able to cure these patients. However, pediatric vitreous that is less syneretic is theoretically unlikely to accumulate rapidly, as observed in case 1, through unseen small breaks. Morning glory disc-associated retinal detachment is thought to be secondary to CSF fistula between the subretinal and subarachnoid spaces and has been cured with nerve sheath fenestration. To the best of our knowledge, our group is the first to demonstrate that subretinal fluid in retinal detachment
associated with microphthalmos and a cyst contains CSF-like fluid based on positivity for β₂-transferrin, an assay used routinely to detect CSF leak following basal skull fracture. It was a surprise, therefore, that, in case 1, cisternography failed to verify a communication between the subretinal space and intracranial CSF. The most likely source of the fluid is the orbital cysts that are intimately related to the retrobulbar optic nerve in all 3 eyes with retinal detachment. The right eye of case 1 has not yet developed retinal detachment and has a small cyst anteriorinferiorly in the orbit. This hypothesis is supported by clinicopathological correlation in which a blind microphthalmic eye-cyst complex was excised. The cyst contained β₂-transferrin–rich fluid that was lined by ependymal cells, similar to those of the choroid plexus, which produce CSF intracranially. In normal eyes, the outer retina, including the retinal pigment epithelium, terminates at the edge of the optic disc. Case 2 confirms that the retina herniates posteriorly through the disc excavation where the subretinal space presumably communicates with the cyst cavity. The series of fundus changes in the left eye of case 2 suggests that the continuous presence of subretinal fluid is potentially detrimental because it is associated with a pigmentedary response from the retinal pigment epithelium. Based on our hypothesis, the net removal of fluid from the subretinal space could be favored by reducing CSF production using oral acetazolamide or by surgically shunting subretinal fluid, for example by a guarded posterior sclerostomy. If an isolated chord-like connection exists between the eye and cyst, its ligation is another therapeutic option that has been used to preserve a nonseeing eye.

In summary, we have a new hypothesis explaining retinal detachment in some cases of optic nerve colobomas, which in our view mandates orbital imaging to determine the presence of cysts that could be producing a β₂-transferrin–rich fluid. Vitrectomy may be an inappropriate technique to use. Other techniques could be considered if spontaneous improvement does not occur because the retinal pigment epithelium may be compromised and result in poor visual outcome.

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