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Congenital Fibrovascular Pupillary Membranes: Clinical and Histopathological Findings

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Abstract

Purpose—To report the clinical and histopathological findings associated with congenital fibrovascular pupillary membranes.

Design—Case series.

Participants—Seven infants; six with a unilateral congenital pupillary membrane and one with classic persistent fetal vasculature (PFV).

Methods—Patients underwent a membranectomy, pupilloplasty and/or a lensectomy. Histopathological examination was performed on the excised membranes.

Main Outcome Measures—Visual acuity and pupil size.

Results—Four of the 6 patients with a unilateral congenital pupillary membrane had one or more recurrences after a membranectomy and pupilloplasty. The most recent pupil size ranged from 2 to 5 mm in the affected eye. When last tested, the vision in the affected eye was excellent in 4 of the 6 patients. The two patients without recurrences of the pupillary membranes underwent multiple iris spincterotomies at the time of the initial surgery. Histopathological examination of two primary pupillary membranes showed fibrovascular tissue that did not stain for neuron specific enolase. Smooth muscle actin was only present in vascular walls. In contrast, histopathology of a recurrent pupillary membrane revealed collagenized fibrovascular tissue that was immunoreactive for smooth muscle actin. Finally, histopathology of the retrolenticular membrane excised from an infant with classic PFV was similar to the latter aside from hypercellularity.

Conclusions—Congenital fibrovascular pupillary membranes in infants are likely a variant of PFV that may recur if incompletely excised. The risk of these membranes recurring may be reduced by excising as much as the membrane as possible and enlarging the pupil with iris spincterotomies. A lensectomy should be avoided if possible.

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A unilateral anterior segment disorder associated with a congenital white pupillary membrane and anterior chamber angle abnormalities was first reported by Cibis in 1986.¹ Cibis and coworkers² postulated that these membranes arise from ectopic iris tissue. This entity has been called by a variety of names including congenital pupillary-iris-lens membrane with goniodysgenesis, congenital idiopathic microcoria, and fibrous congenital iris membranes.³⁻⁵ In some cases, progressive miosis has been documented.⁴ When the red reflex is no longer visible or severely compromised, these eyes are usually treated with a membranectomy and pupilloplasty with or without a lensectomy. Histopathological examination of one of these pupillary membranes revealed a fibrovascular membrane with elongated spindle cells immunoreactive for smooth muscle actin.⁶ A recurrence of these pupillary membranes has not been reported previously.

We report one or more recurrences of a fibrovascular pupillary membrane in 4 of 6 children with this condition and propose that it is an anterior variant of persistent fetal vasculature (PFV) based on the histopathological and clinical findings in these eyes. We also report on the histopathology of a retrolenticular membrane excised from an infant with classic PFV.

Methods

The study was submitted to the institutional review board (IRB) of Emory University who determined that the study did not need IRB approval since as a retrospective chart review it was determined to be exempt from IRB review. The study was in compliance with the Health Insurance Portability and Accountability Act. Prior to initiating the study, we searched PubMed for all citations referring to congenital pupillary-iris-lens membrane with goniodysgenesis, congenital idiopathic microcoria, and fibrous congenital iris membranes. We reviewed the clinical course of 6 infants with a congenital fibrovascular pupillary membrane by performing a chart review. Histopathological examination was performed on specimens from 4 of these 6 patients. We also studied histopathologically a retrolenticular membrane from an infant with classic PFV. The specimens studied histopathologically were fixed in 10% neutral-buffered formalin, dehydrated in increasing concentrations of alcohol, cleared in xylene and embedded in paraffin. The paraffin block was then sectioned in 7-micron-thick slices, stained with hematoxylin-eosin and periodic acid-Schiff, and examined using light microscopy (Olympus BH-2, Tokyo, Japan). Immunohistochemical stains were performed on the specimens using the peroxidase anti-peroxidase technique for neuron specific enolase (DAKO, Carpinteria, California) to identify neural crest derived cells, smooth muscle actin (DAKO), CD31 (DAKO) to identify pericytes, myofibroblasts and vascular smooth muscle cells, leukocyte common antigen (LCA) (DAKO) to identify the contribution of bone marrow-derived progenitor cells to the membranes, platelet-derived growth factor (PDGF) beta receptor (Santa Cruz, Santa Cruz, CA) to identify nascent pericytes, and glial fibrillary acidic protein (GFAP) (DAKO) to identify the contributions of glial cells to the fibrovascular membranes.

Results

The 6 patients with congenital fibrovascular membranes were a mean of 1.7 months of age (range, 4 days to 3 months) at the time they underwent the primary excision of their pupillary membrane (Table 1). The condition was unilateral in all 6 patients. All of the patients had miosis relative to their fellow eye. In all cases, the pupils only dilated minimally after the instillation of mydriatic agents due to adhesions between the pupillary membrane and the iris or posterior synechiae. Two patients had anterior capsular cataracts. In the other 4 patients, the pupillary membrane was not adherent to the crystalline lens. The corneal diameter of the affected eye was the same as the fellow eye in 5 of the 6 cases. In one patient (Patient 3), the cornea of the affected eye was 1 mm smaller. In 3 patients, radial vessels

could be seen extending onto the surface of the pupillary membrane from the iris stroma. Three of the patients had mild corectopia and 3 patients had posterior embryotoxon in the affected eye. In 2 patients (Patients 5 and 6), B-scan immersion ultrasonography with a 20 Hz probe was performed. The resolution was poor in one patient, but a membrane extending behind the iris to the ciliary processes could be identified in Patient 5.

Four of the patients initially underwent a membranectomy and pupilloplasty. At the time of surgery it was noted that the membranes were adherent to the iris pigment epithelium and that they extended behind the iris. One patient (Patient 1) underwent synechialysis only. However, the miosis recurred in this eye so a pupilloplasty was subsequently performed as a second procedure. Another patient (Patient 4) with a pupillary membrane and an anterior capsular cataract underwent synechialysis, a lensectomy and a pupilloplasty. Postoperatively, this patient developed severe miosis and subsequently underwent two additional membranectomies and pupilloplasties. A limbal approach was used for the first reoperation, whereas a pars plana approach was used for the second reoperation.

Finally, a patient with classic PFV underwent cataract surgery when 7 weeks of age. Preoperatively, the right eye was noted on a B-scan to have a hyaloid vessel extending from the lens to the optic disc. After aspirating the lens, the patient was noted to have a highly vascularized retrolenticular membrane attached to the ciliary processes (Fig 1). This membrane was excised and submitted for histopathological examination.

Case Reports

Patient 1

A 4-day-old girl was referred for evaluation of a poor red reflex in the right eye. Prior to dilation, only a thin crescent of a red reflex was visible temporally in the right eye. After dilation, a 3 mm white fibrovascular membrane with radial vessels extending onto its surface from 1 to 3 o'clock was noted in the superonasal quadrant of the pupil. In addition, iris strands were adherent to the inferotemporal margin of the pupillary membrane (Fig 2a). The child weighed 5 pounds at birth and had been delivered after a 35 gestational week pregnancy complicated by preeclampsia. Aside from mild jaundice, the medical history was otherwise unremarkable. When the child was 13 days old, surgery was performed. After filling the anterior chamber with an ophthalmic viscosurgical device (OVD), the posterior synechiae and iris strands were lysed and the pupil dilated to 6 mm. Because of the eccentric location of the plaque on the anterior lens capsule, a lensectomy was not performed. At the end of the surgery, a good red reflex was present. The right eye was treated postoperatively with prednisolone acetate 1% and atropine 1%. After discontinuing the atropine drops, the right pupil became progressively smaller until a red reflex was barely visible even after pharmacological dilation (Fig 2b). When the child was 8 months old, a second membranectomy and pupilloplasty were performed. After filling the anterior chamber with an OVD, the adhesions between the iris and the fibrovascular membrane were severed with straight horizontal opening vitrectomy scissors. The pupil was then enlarged to 4 mm by creating multiple iris spincterotomies. Postoperatively, the right eye was treated with prednisolone acetate 1% and atropine 1% drops. The child was subsequently prescribed spectacles and part-time patching therapy of the fellow eye. At the last follow-up at age 10 years, the best corrected visual acuity was 20/50-2 in the right eye and 20/20 in the left eye. The right pupil was 2 mm in size.

Patient 2

A 3-month-old girl was referred for evaluation of anisocoria. The parents had noted a white spot in one corner of the pupil when the child was 2 days old. They also noted that the right

pupil was eccentric and smaller in size than the left pupil. The patient's medical history was otherwise unremarkable. Visual acuity was central, steady and maintained in both eyes. On slit-lamp examination, the right pupil was 0.5 mm in diameter and displaced temporally. There was a white nodule in the nasal corner of the right pupil and a posterior embryotoxon superiorly. The right pupil only dilated to 1.5 mm after the instillation of mydriatic agents (Fig 3a). The left anterior segment was normal. The diameter of both corneas was 10 mm and the intraocular pressure was 7 mmHg bilaterally.

After a discussion of the risks and benefits of observation versus surgery, the parents elected to have their child undergo a membranectomy and pupilloplasty. After filling the anterior chamber with an OVD, straight horizontal opening and 60° angled vertical opening vitrectomy scissors were used to create iris spincterotomies and to open a white fibrovascular membrane that was attached to the undersurface of the iris nasally, but not to the crystalline lens (Video 1, available at <http://aaojournal.org>). A vitreous cutting instrument was then used to excise the visible portion of the pupillary membrane. At the end of the procedure, the right pupil was 5 mm in size; only a small fragment of the fibrovascular membrane was visible at 12 o'clock. Postoperatively, the right eye was treated with prednisolone acetate 1% and atropine 1% drops for 6 weeks. Two months after surgery, no red reflex was visible in the right eye even after the instillation of mydriatic agents. A second surgery was then performed. The pupil was mechanically enlarged after filling the anterior chamber with an OVD. Next, the fibrovascular membrane was excised and the pupil was enlarged with multiple iris spincterotomies. At the end of the surgery, the right pupil was 4 mm in diameter and a good red reflex was present. Postoperatively, the right eye was treated with prednisolone acetate 1% and atropine 1% for 6 weeks. At age 10 months, the red reflex was absent in the right eye even after the instillation of mydriatic agents (Fig 3b). The patient underwent a third membranectomy and pupilloplasty during which a retro-irido nodule was excised and sent for histopathological examination (Video 2, available at <http://aaojournal.org>). Postoperatively, the right eye was treated with prednisolone acetate 1% and atropine 1%. At the last follow-up at age 3 years, HOTV acuity was 20/250 in the right eye and 20/20 in the left eye. The right pupil was 5 mm in size and the left pupil 3 mm. The cycloplegic refraction was +6.00 +2.75 × 90 in the right eye and +1.50 +0.50 × 70 in the left eye. The crystalline lenses were clear in both eyes. The child was orthotropic. The left eye was being treated with part-time patching therapy.

Patient 6

A 2-month-old girl was referred for evaluation of pupillary abnormality in the left eye. The parents first became aware of the pupillary abnormality when she was age 1 month, but after reviewing photographs they determined that it was present even at age 1 week. The parents believed the abnormality was worsening. The child was delivered after a full-term pregnancy with a birth weight of 7 pounds 12 ounces. The child's medical history was otherwise unremarkable. Vision was central, steady and maintained in both eyes. The right anterior segment was normal. In the left eye, a white membrane covered all but the infero-temporal corner of the pupil. Radial vessels extended from the iris onto the fibrovascular membrane (Fig 4a). The underlying crystalline lens was clear. The child was treated with topical 1% atropine in the left eye for 2 months. The parents then elected to have a pupilloplasty performed. Both pupils were 11.8 mm in diameter. The intraocular pressure was 16 mmHg in the left eye. After filling the anterior chamber with an OVD, the pupillary membrane was excised with straight horizontal opening and 60° angled vertical opening vitrectomy scissors. The specimen was sent for histopathological examination. Multiple iris spincterotomies were then created to enlarge the pupil. At the end of the procedure, it was noted that there was additional fibrovascular membrane present that extended underneath the iris between 7 o'clock and 1 o'clock (Fig 4b). Postoperatively, the right eye was treated with

prednisolone acetate 1% and atropine 1% for 4 weeks and part-time patching therapy of the right eye. At last follow-up at age 8 months, the left pupil was 3 mm in size and reactive to light. The vision was central, steady and maintained in both eyes.

Histopathological Findings

Both primary pupillary membrane specimens (Patients 5 and 6) consisted of fibrovascular tissue containing endothelial lined venules and arterioles, fibrocytes and extracellular collagen (Table 2) (Fig 5). In addition, iris pigment epithelial cells had migrated onto the surface of the membranes closest to the pupillary margin (Fig 6). Immunohistochemical stains were positive for platelet-derived growth factor (PDGF) beta receptor. Immunohistochemical stains for CD31 and smooth muscle actin were only positive in the walls of vascular channels and in the iris pigment epithelium on the surface of the membranes. Immunostains for neuronal specific enolase, leukocyte common antigen (LCA) and fibrillary acidic protein (GFAP) were negative. Normal iris pigment epithelium and stroma was present overlying the fibrovascular tissue in Case 6. However, in Case 5 the stroma of the iris overlying the fibrovascular membrane was normal, but the iris pigment epithelium was absent.

Histopathologic examination of a recurrent pupillary membrane from Patient 2 showed collagenized fibrovascular tissue with overlying iris pigment epithelium (Fig 7). The anterior portion of the membrane stained positively for smooth muscle actin. The immunostaining for Patient 2 was otherwise the same as for Patients 5 and 6. The vitrectomy specimens from Patient 4 showed a hypocellular membrane consisting of pigmented and nonpigmented cells and extracellular material.

Immunohistochemistry staining of the specimen from the eye with classical PFV was the same as the specimens from the eyes with primary pupillary membranes. However, this specimen (Fig 8) was more hypercellular than the pupillary membrane specimens from Patients 5 and 6.

Discussion

We report 6 infants who underwent the surgical excision of a fibrovascular pupillary membrane. The membranes recurred in 4 of the 6 patients from 1 week to 6 months after the primary membranectomy. In the two eyes that did not have a recurrence of the pupillary membranes, iris spincterotomies had been performed at the time of the primary membranectomy. If a fibrovascular membrane is incompletely excised, progressive miosis of the pupil may occur due to postoperative tissue proliferation. By enlarging the pupil with iris spincterotomies at the time of the initial membranectomy, a pupil size that was adequate to allow for the development of normal vision could be maintained. In our experience, it is usually not possible to remove all of the fibrovascular tissue without also performing a lensectomy. However, we advise against a lensectomy in most cases. In four of our patients, the pupillary membrane was not attached to the lens so that the crystalline lens could be separated from the pupillary membrane using an OVD obviating the need for a lensectomy. However, in the other two cases, the pupillary membranes were adherent to anterior lens opacities. In one patient, the lens opacity was eccentric and the child has developed good vision even though a lensectomy was not performed. In the other patient, the lens opacity was centrally located and a lensectomy was performed. This child now has dense amblyopia which is likely compounded by aphakia.

Congenital fibrovascular pupillary membranes have been described by a variety of names including congenital pupillary-iris-lens membrane with goniodysgenesis, congenital

idiopathic microcoria, and fibrous congenital iris membranes.³⁻⁵ Various theories have been postulated to explain the etiology of these membranes. Cibis and coworkers² postulated that these membranes are derived from ectopic iris tissue arising from aberrant migration of neural crest cells to the anterior segment. They interpreted one of these membranes that they studied histopathologically as ectopic iris stroma. The authors cited the coexistence of Schwalbe's line and an abnormal appearance of the iris stroma in some eyes with congenital fibrovascular pupillary membranes as further evidence that this disorder represents a neurocristopathy. However, if these membranes arose from neural crest cells, they should stain for neuron specific enolase which is a marker for neural crest derived cells. None of the membranes we studied histopathologically stained positively for neuron specific enolase. In addition, if the membranes truly arose from ectopic iris we would have expected to have found the membranes on the anterior rather than the posterior surface of the iris and we would have expected them to contain elements of normal iris architecture. This was not the case for any of the pupillary membranes we examined histopathologically—2 cases after the primary excision of a pupillary membrane and 2 cases after the recurrence of a pupillary membrane. In one of the recurrent cases, the membrane specimens were fragmented so we were unable to identify their relationship to the iris. However, in the other 3 cases the membranes were posterior rather than anterior to the surface of the iris. In one primary case, the iris pigment epithelium overlying the pupillary membranes was normal. In the other primary case, the overlying iris stroma was normal, but the iris pigment epithelium was absent presumably because it had migrated onto the surface of the pupillary membrane. In the recurrent case, the iris pigment epithelium overlying the pupillary membrane was in its normal location, but hypertrophic.

Goldberg⁷ first coined the term persistent fetal vasculature (PFV) to refer to a group of disorders associated with the persistence of various components of the hyaloid vascular system. He suggested the condition be referred to as PFV rather than PHPV (persistent hyperplastic primary vitreous) to emphasize the fact that the fetal vessels in this disorder can persist in the anterior segment of the eye as well as the retrolenticular location. The hyaloid vascular system is present during early embryogenesis and includes the hyaloid artery, the vasa hyaloidea propria, the tunica vasculosa lentis and the pupillary membrane. Branches of the hyaloid artery in the vitreous are referred to as the vasa hyaloidea propria. The tunica vasculosa lentis is an anastomotic network of vascular channels encircling the lens that also arising from the hyaloids vascular system. The most anterior portion of the hyaloid vascular system is the pupillary membrane which consists of loops of blood vessels and a diaphanous sheet of mesoderm. Normally, the hyaloidal vascular system regresses during the second trimester. However, in premature infants the tunica vasculosa lentis may persist for 1–2 months after birth and radial iris vessels may be visible as long as 5–6 weeks after birth in full-term infants. Vestiges of the tunica vasculosa lentis are commonly observed in children with unilateral congenital cataracts and have been referred to as minimal fetal vascular remnants.⁸

Robb⁵ first suggested that congenital fibrovascular pupillary membranes may represent a variant of PFV. We agree that the clinical and histopathological findings of these congenital pupillary membranes are most consistent with PFV. Like PFV, they are associated with prominent iris vessels often extending into the pupillary membranes. Goldberg⁷ noted that iridohyaloid vessels in the iris stroma are important clues to the correct diagnosis of PFV. Like PFV, congenital fibrovascular pupillary membranes are almost always unilateral and idiopathic. The histopathological appearance and immunohistochemical staining properties of these fibrovascular pupillary membranes were also similar to the immunohistochemical staining of a retrolenticular membrane we studied from an eye with classic PFV, albeit the retrolenticular membrane was more hypercellular than fibrovascular pupillary membranes, presumably due to the presence of hyalocytes. The immunohistochemical

staining profile in our cases suggests a mesenchymal origin for the endothelial/pericyte-lined venules and arterioles in the pupillary membranes. In addition, the presence of platelet-derived growth factor (PDGFR) positive pericytes in the venules and arterioles in these membranes suggests that they arose in utero, as would be expected in eyes with PFV, rather than from neovascularization secondary to trauma or inflammation.

It is well known that retrolenticular membranes in eyes with PFV may recur if incompletely excised. Stark et al⁹ reported the recurrence of a pupillary membrane in 2 of 7 infants with PFV after the surgical excision of a dense retrolenticular membrane. Similarly, Hunt et al¹⁰ reported the recurrence of a pupillary membrane in two infants with PFV after a lensectomy. We have also found that congenital fibrovascular pupillary membranes may recur if incompletely excised. The progressive miosis associated with the recurrence of these membranes is likely mediated by myofibroblasts. It is most likely that myofibroblasts arise from smooth muscle differentiation of fibroblasts. One of the recurrent membranes we studied histopathologically had many features suggestive of a keloid. A keloid is a dermal fibroproliferative abnormality with excessive deposition of extracellular matrix components, including glycoproteins, collagen and fibronectin. Smooth muscle actin is often expressed in keloid-derived dermal fibroblasts. Smooth muscle actin was highly expressed in one of the recurrent membrane we studied histopathologically. Kesarwani and coworkers⁶ also reported immunoreactivity for smooth muscle actin in a pupillary membrane that they studied histopathologically. Smooth muscle actin was only present in the vascular walls of the two primary pupillary membranes we studied histopathologically.

Persistent pupillary membranes are pigmented strands that extend across the pupil (Table 3).¹¹ They also likely arise from remnants of the hyaloid vascular system. Interestingly, Patient 2 had both persistent pupillary strands as well as a congenital fibrovascular pupillary membrane (Fig 2). Congenital fibrovascular pupillary membranes are often associated with posterior embryotoxon and other abnormalities of the anterior chamber angle. They differ from Axenfeld-Rieger Syndrome in that they are unilateral and have not been reported to be associated with glaucoma. In addition, corectopia is not a common finding in eyes with a congenital fibrovascular pupillary membrane whereas it is often present in eyes with Axenfeld-Rieger syndrome.

In conclusion, congenital fibrovascular pupillary membranes are likely a variant of PFV. To prevent visually significant miosis from developing in these eyes after the excision of these membranes, it is important to excise as much of the membranes as possible and to enlarge the pupil to 4 or 5 mm by creating iris spincteromies. If visually significant miosis does develop postoperatively, a reoperation should be performed promptly to prevent amblyopia from developing.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.
Intraoperative photograph of the right eye of a 7 week old child with classic PFV. The lens has been aspirated revealing a highly vascularized retrolenticular membrane attached to the ciliary processes.

Figure 2.

Figure 2a (on left) Right eye of Patient 1 at age 2 weeks after pharmacological dilation. A fibrovascular membrane blocks the pupil nasally. The membrane is attached to the pupil inferiorly by iris strands (white arrows). Radial iris vessels (black arrows) extend onto the surface of the membrane.

Figure 2b (on right) Right eye of Patient 1 at age 8 months after pharmacological dilation. The pupil is adherent to the fibrovascular membrane except for one small sector inferotemporally.

Figure 3.

Figure 3a (on left) Right eye of Patient 2 at age 3 months after pharmacological dilation. All but the temporal margin of the pupil is adherent to white fibrovascular tissue. A posterior embryotoxon is present superiorly (arrows).

Figure 3b (on right) Right eye of Patient 2 at age 10 months after two recurrence of miosis. After pharmacological dilation, the pupil was still only a narrow slit (arrow) and no red reflex was visible.

Figure 4.

Figure 4a (on left) Left eye of Patient 6 after pharmacological dilation. A fibrovascular membrane covers most of the pupil. Radial vessels (arrows) extend on to the membrane superiorly and vascular channels can be seen coursing through the membrane.

Figure 4b (on right) Left eye of Patient 6 after a membranectomy and pupilloplasty. Multiple spincterotomies have been made circumferentially around the pupil. A white membrane (arrows) which is adherent to the iris pigment epithelium extends beneath the iris for 180 degrees.

Figure 5.
The pupillary membrane excised from Case 6 shows fibrovascular tissue composed of vascular channels (arrows), spindle-shaped cells, round cells, and extracellular collagen. (hematoxylin and eosin 40X)

Figure 6.

Iris with melanocytes (*) on its surface. Its posterior interface (arrowheads) is adherent to fibrovascular tissue. Vascular channels in the fibrovascular tissue are highlighted with smooth muscle actin (arrow). Melanocytes from the iris have migrated onto the surface of the fibrovascular tissue in one area (**). (peroxidase anti-peroxidase, 100X)

Figure 7. Histopathological section from retro-irido nodule excised from the right eye of Patient 2 at age 10 months. The fibrovascular tissue is collagenized and contains spindle-shaped cells that were immunoreactive for smooth muscle actin consistent with myofibroblasts. The overlying iris pigment epithelium is hypertrophic. (hematoxylin and eosin 100X)

Figure 8. Histopathological section of a retrolenticular membrane excised from a 7 week old child with classic PFV. It contains multiple vascular channels and is hypercellular. (hematoxylin and eosin 25X)

Clinical Findings

Table 1

Patient/Affected Eye	Age at Presentation	Ocular Findings	Initial Surgery	# of Re-operations	Follow-up (months)	Initial Pupil Size (mm)	Last Pupil Size (mm)	Last Visual Acuity
1/RE	4 days	miosis, anterior capsular cataract, persistent iris vessels	synechialysis	1	120	1	2	RE: 20/50 LE: 20/20
2/RE	3 months	miosis, corectopia, posterior embryotoxon	membranectomy, pupilloplasty	2	34	0.5	5	RE: 20/250 LE: 20/20
3/RE	2 months	miosis, corectopia, posterior embryotoxon, microphthalmos (9.0 mm)	membranectomy, pupilloplasty	1	10	1	2.5	RE: CSM LE: CSM
4/LE	5 weeks	miosis, corectopia anterior capsular cataract, pupillary membrane, posterior embryotoxon	synechialysis, lensectomy pupilloplasty,	2	4	1	5	RE: CSM LE: CSNM
5/LE	3 months	miosis, pupillary membrane, persistent iris vessels	membranectomy, pupilloplasty	0	5	1	3	RE: CSM LE: CSM
6/LE	2 months	miosis, pupillary membrane, persistent iris vessels	membranectomy, pupilloplasty	0	5	1	3	RE: CSM LE: CSM

RE, right eye; LE, left eye; CSM, central, steady and maintained; CSNM, central, steady and not maintained.

Table 2

Histopathologic Findings and Immunohistochemical Staining

Patient #	Surgical Sample	Pupillary Membrane	Overlying Iris	Smooth Muscle Actin	CD31	Neuronal Specific Endolase	PDGF Beta Receptor	LCA	GFAP
2	Recurrent pupillary membrane	Collagenized Fibrovascular tissue	Normal iris pigment epithelium	+ in anterior portion of tissue	Only + in walls of vascular channels	-	+	-	-
4	Vitreous Aspirate x 2	Fragments of hypocellular material	NA	NA	NA	NA	NA	NA	NA
5	Primary pupillary membrane	Thin fibrovascular membrane	Absence of iris pigment epithelium, Iris stroma normal	Only + in walls of vascular channels	Only + in walls of vascular channels	-	+	-	-
6	Primary pupillary membrane	Thin fibrovascular membrane	Normal iris pigment epithelium and iris stroma	Only + in walls of vascular channels	Only + in walls of vascular channels	-	+	-	-
Classic PFV	Retro-lenticular membrane	NA	NA	Only + in walls of vascular channels	Only + in walls of vascular channels	-	+	-	-

PFV, persistent fetal vasculature; PDGF, platelet-derived growth factor; LCA, leukocyte common antigen; GFAP, glia fibrillary acidic protein; NA, not available

Table 3

Clinical Conditions Causing Congenital Pupillary Abnormalities

Condition	Ocular Findings	Etiology	Inheritance	Laterality	Glaucoma	Effect on Vision
Axenveld-Rieger Syndrome	Posterior embryotoxon, peripheral Iridocorneal adhesions, iris atrophy, ectropion uveae, corectopia	Neural crest disorder	Autosomal dominant (RIEG2, FOXC1, PITX2 genes)	Bilateral	50%	Minimal
Persistent Pupillary Membrane	Pigmented strands or membrane bridging pupil	Incomplete degeneration of tunica vasculosa lentis	None	Bilateral	no	Minimal
Congenital Fibrovascular Pupillary Membrane	Miosis, corectopia, fibrovascular pupillary membrane attached to ciliary processes $\pm$ anterior capsular cataract, $\pm$ posterior embryotoxon	Anterior variant of Persistent Fetal Vasculature	None	Unilateral	no	Severe if untreated