• Letter to the Editor •

Congenital fibrovascular pupillary membranes: case series with pathological correlation and surgical treatment

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Dear Editor,

We present three cases of congenital fibrovascular pupillary membranes (CFPM) with pathological correlation and surgical treatment. CFPM was first described by Cibis *et al*[1] as a new entity of anterior segment malformation termed "congenital pupillary-iris-lens membrane with goniodysgenesis". This entity was later identified under different names, including "congenital idiopathic microcoria"[2] and "fibrous congenital iris membranes"[3]. Lambert *et al*[4] reported similar cases of CFPM. Histopathological findings suggested that this condition was an anterior variant of persistent fetal vasculature (PFV). However, there was still a lack of histological evidence to support the pathological origins of CFPM. The cases presented herein described the histopathological examinations of CFPM and provided surgical strategies. We obtained the written informed consent from the patients, and this case study is in accordance with the tenets of the Declaration of Helsinki.

In Case 1, a 9-year-old boy with a white opacity was suspected to have congenital cataract. A distorted slit-like pupil was noted, and a white membrane was seen posterior to the iris, completely occluding the pupil (Figure 1A). Corrected visual acuity of the left eye was 20/400, while that of the right eye was 20/13. Non-contact tonometry (NCT) yielded an intraocular pressure (IOP) of 16 mm Hg. An ultrasonic biological microscope (UBM) revealed a central anterior chamber depth of 2.84 mm in the left eye, with posterior synechiae inferiorly (Figure 1C). Anterior chamber angle was open, and the lens was transparent.

The patient underwent membranectomy and pupilloplasty. Ophthalmic viscosurgical devices (OVDs) were injected into the anterior chamber to separate the posterior synechiae from the membrane. The membrane was further removed using intraocular scissors and an anterior vitrector. The lens was intact and transparent; thus, cataract surgery was not performed.

The pupillary membrane specimen of Case 1 showed cellularity in the iris epithelium embedded in fibrovascular tissue. In addition, the membranes consisted of endothelial-lined blood vessels, fibrocytes, and extracellular collagen (Figure 2A). Immunohistochemical staining was positive for CD31 and α-SMA in the blood vessel walls and in the iris pigment epithelium, which adhered to the fibrovascular tissue. Immunostaining for neuron-specific enolase (NSE) and glial fibrillary acidic protein was negative (Figure 2B).

During the follow up visits, the best corrected visual acuity (BCVA) of the left eye was 20/200, and patching therapy was recommended. The pseudopupillary opening remained rounded with a diameter of 4 mm. IOP measured by NCT was normal in the left eye. No angle closure or lens opacity was noted at that time.

In Case 2, a 7-year-old boy had a "white dot" in the left eye. A thick white membrane occluded the distorted pupil. A strand of the membrane extended to the root of the iris at 1 o'clock. When the pupil was maximally dilated to 4 mm, the membrane attached to the temporal lesser ring of the iris, and a transparent lens was observed (Figure 1B). BCVA of the left eye was 20/70, while that of the right eye was 20/20. IOP was within normal range. UBM revealed that the anterior chamber angle was closed in all directions, except temporally. Wide posterior synechiae were noted (Figure 1D). The patient underwent pupilloplasty and membranectomy, which was similar to Case 1. Histopathological examination revealed that normal iris pigment epithelium and stroma were present overlying the

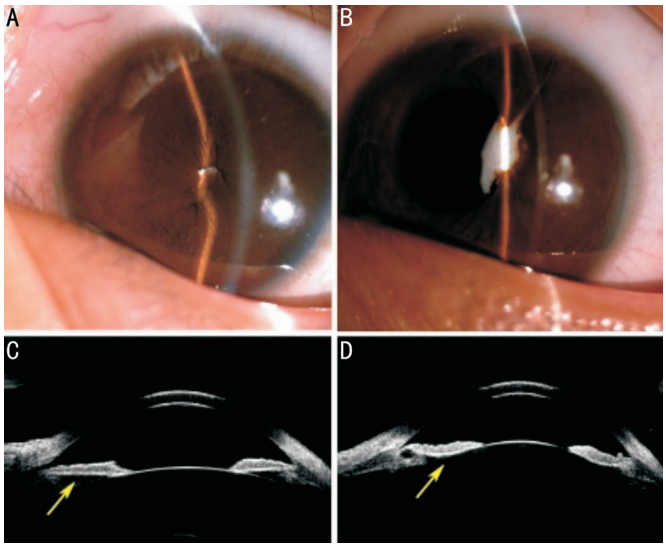

Figure 1 Structural characteristics of the anterior segment A, C: Case 1, age 9 at initial examination. The pupil is distorted and completely occluded by the membrane, extending onto the lens from the iris. UBM revealed central anterior chamber depth of 2.84 mm in the left eye, with posterior synechiae inferiorly (arrow). B, D: Case 2, age 7 at initial examination. The pupil is distorted and completely occluded by the membrane, extending onto the lens from the iris. The iris-lens membrane extends to the anterior chamber angle. UBM revealed central anterior chamber depth of 2.44 mm in the left eye. The anterior chamber angle was closed in all directions except temporally. Wide posterior synechiae was noted (arrow). UBM: Ultrasonic biological microscope.

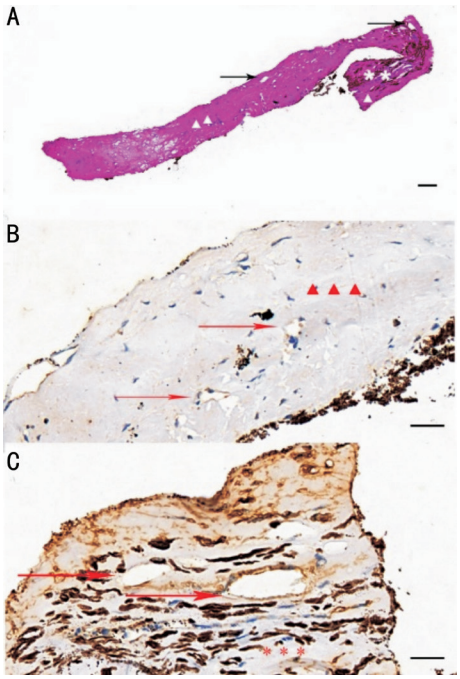

Figure 2 Immunohistochemical staining of the removed membranes A: The pupillary membrane excised from Case 1 shows hypercellular iris epithelium (asterisk) embedded within fibrovascular tissue, which is composed of vascular channels (black arrows) and collagen (white triangles). H&E, 20×, bar=50 μm. B: Vascular channels are scattered in the collagenized fibrovascular tissue (triangles) with positive staining of CD-31 in the vascular walls (arrows). CD-31, 100×, bar=20 μm. C: Vascular channels (arrows) in the fibrovascular tissue are stained with smooth muscle actin. Iris tissue with melanocytes (asterisk) are adhered posteriorly to the fibrovascular tissue interface. α-SMA, 100×, bar=20 μm.

fibrovascular tissue, and extracellular collagen deposits could also be seen in the iris stroma (Figure 2C).

In Case 3, a 5-month-old boy had a "white pupil" in the left eye. A distorted pupil with a diameter of 1 mm was noted. A white membrane was seen posterior to the iris through the lens. The patient underwent membranectomy, pupilloplasty, and cataract surgery. The fibrotic membrane was calcified, embedded in pigmented iris-like tissue, and firmly adhered to the anterior capsule. The lens was exposed, and cortex opacity was noted. Capsulorhexis and phacoemulsification were performed to remove the cataract. Posterior capsulorhexis and anterior vitrectomy were also performed to prevent posterior capsular opacification. The patient had subsequent intraocular lens implantation after 18mo. During surgery, the peripheral capsule was fibrotic and firmly adhered to the posterior iris. The intraocular lens was implanted in the ciliary sulcus. In the postoperative evaluation, the pseudopupillary opening was rounded with a diameter of 4 mm and was associated with some fibrinous exudates.

The most controversial topic of CFPM is its pathological origin. Cibis *et al*[1] concluded that the membranes originate from ectopic iris tissue after aberrant migration of the neural crest. Additionally, the membranes contain abnormal iris stroma and involve Schwalbe's line, which is a disorder of neurocristopathy. In our immunostaining studies, however, membranes were negative for NSE, which is a biomarker for neural crest-derived cells. Therefore, we conclude that congenital CFPM is not derived from neural crest cells.

In our study, the clinical and histopathologic findings of CFPM are most consistent with PFV, which are associated with blood vessels in the iris tissue extending into the pupillary membranes. Like PFV, CFPM is mostly unilateral and idiopathic. Goldberg[5] found that to diagnose PFV, iridohyaloid vessels in the iris stroma should be used as important clues. The immunostaining profile in our study revealed that endothelial cells and pericytes of blood vessels stained positive for CD31, which is a mesenchymal origin biomarker. However, more evidence is needed to determine whether these blood vessels arise in utero, as is the case in PFV, or from neovascularisation due to inflammation.

There are different approaches to treatment depending on the severity of the disorder. Observation is described for eyes with a sufficient pupillary size[1,3,5-8]. However, most cases undergo

surgical intervention[9-11], especially in cases with secondary glaucoma[12]. In our study, the membranes did not recur, nor was progressive miosis of the pupil observed during follow-up visits. By enlarging the pupil with pupilloplasty during initial surgery, the pupil size remained at 4 mm and was adequate for light to come through and allow for normal visual development in younger children (Case 3). However, the fibrovascular membrane firmly adhered to the normal iris tissue and posteriorly to the lens capsule, making membrane removal difficult. In addition, it was not possible to completely remove the membrane without cataract surgery if the adhesion could not be easily separated using OVDs. In Case 3, cataract surgery was performed during the initial surgery to completely excise the membrane. In follow-up visits, the iris was adherent to the lens capsule because of postoperative tissue proliferation. We advise against cataract surgery in most cases to avoid membrane recurrence and miosis and minimise postoperative tissue proliferation. In our experience, OVDs are strongly recommended to separate the pupillary membrane from the lens and iris so that cataract surgery can be obviated. However, if lens opacity is severe or centrally located, cataract surgery should be considered to enable the development of normal vision.

In conclusion, CFPM is often associated with miosis and are likely a variant of PFV. The anterior segment should be examined carefully to exclude cataracts and glaucoma. In immunohistological studies, α-SMA and CD31 are observed in membrane fibrovascular tissue. It is essential to remove the membranes as completely as possible, and pupilloplasty to enlarge the pupil to approximately 4 mm is important for visual development. Cataract surgery is not necessary in most cases and should be avoided due to the risk of membrane recurrence and progressive miosis.

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