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ORIGINAL PAPER

# Management of severe persistent fetal vasculature: case series and review of the literature

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**Abstract**
*Purpose* Persistent fetal vasculature (PFV) is a unique ocular disorder usually presenting early in life. The unregressed embryonal hyaloid vasculature poses a risk of severe ocular complications leading to decreased visual acuity. Surgery is the mainstay of therapy in complicated cases. We describe the clinical presentation and surgical treatment of PFV managed at our center from 2012 to 2015.
*Methods* The study is a case series comprised eight patients who were diagnosed with complicated severe PFV. All were managed with a tailored surgical approach. The clinical characteristics, medical and surgical treatment, and follow-up findings of each case are described.
*Results* There were six males and two females. Surgical intervention involved anterior or posterior vitrectomy, lens extraction, and intraocular lens implantation. Hyaloid stalk removal with release of ciliary traction was variably utilized in selected cases. Endodiathermy controlled intraocular bleeding, and intraocular scissors proved helpful in anterior PFV for disinserting the ciliary process from an abnormally thickened posterior lens capsule. Visual outcomes differed in each case, depending on multiple clinical factors.
*Conclusion* Severe complex PFV presents a therapeutic challenge. A tailored surgical approach with meticulous postoperative management is essential for visual rehabilitation.

**Keywords** Congenital cataract · Persistent fetal vasculature · Surgery · Endodiathermy

## Introduction

Persistent fetal vasculature (PFV) is a mostly sporadic congenital developmental disorder [1]. It is caused by the failure of regression of the embryonal hyaloid vasculature [1, 2] and often presents as an intravitreal fibrovascular tissue [1, 2]. It has been associated with different genetic and systemic disorders. PFV can cause permanent damage to visual functions and therefore warrants prompt diagnosis, evaluation, and treatment. The mainstay of treatment is surgical removal of the fibrovascular membrane and opacified lens followed by intraocular lens (IOL) implantation [1, 3].

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We describe eight cases of complicated severe PFV managed at a tertiary pediatric medical center over a 3-year period. The clinical presentation and tailored surgical treatment were different in each case.

## Patients and methods

The study group included eight patients, six male and two female, diagnosed with PFV in our department between 2012 and 2015. PFV was defined as a cataractous lens with a retrolental fibrovascular membrane. The patient and disease-related characteristics are summarized in Table 1.

The study was approved by the Institutional Review Board and was in compliance with the tenets of the Declaration of Helsinki.

### Case 1

Patient one, described in our previous report [4], was a male infant born at gestational age 25 weeks. Since birth, he had been treated in the perinatal intensive care unit for multiple systemic conditions including duodenal atresia, recurrent sepsis, hydronephrosis, and hypothyroidism. The duodenal atresia was repaired surgically, and subsequent genetic testing revealed no abnormalities.

The patient was routinely evaluated for retinopathy of prematurity (ROP). The initial ophthalmologic examination showed incomplete retinal vascularization up to zone 2 bilaterally. There were no other abnormal findings. On follow-up 2 weeks later, the ROP had progressed to stage two without plus disease. Three weeks after diagnosis of ROP, at age 9 weeks, mild posterior opacification of the left capsular lens was noted, with a vitreal strand compatible with PFV. The findings were confirmed sonographically. This was published as a case report since the PFV was observed developing in conjunction with ROP rather than present at birth. The lens opacity increased gradually until the retina was no longer visible clinically, and ultrasound was used thereafter for follow-up.

At age 50 weeks, the patient underwent cataract extraction with IOL implantation and pars plana vitrectomy. The surgery was delayed after consulting the retina service and the danger involved in performing intraocular surgery in the presence of ROP. Endodiathermy was used to control bleeding from the impressive anterior blood vessel and remove the posterior vascularized plaque adherent to the posterior capsule in order to disinsert the posterior stalk. No bleeding was noted during or after surgery. There were no other intraoperative complications. During follow-up, glaucoma was diagnosed and treated surgically; an Ahmed valve was implanted yielding good control of intraocular pressure. At the last follow-up at age 2 years and 7 months, the left eye showed good anatomical results with flat retina and a posterior chamber IOL. Visual acuity at last follow-up was 1/60 with intermittent esotropia.

### Case 2

A 2.6-year-old boy diagnosed at a different hospital with right PFV at age 4 months presented for consultation. The PFV had been treated conservatively with mydriatic drops and occlusions. Surgical treatment was ruled out at the time because it was considered too challenging and posed a risk of complications.

Ophthalmologic evaluation revealed a right dense posterior capsular opacification blocking the visual axis, with a visual acuity of 1/60. The retina was not visualized. Ultrasound scan demonstrated a thick vitreal strand extending from the cataractous lens to the optic disc, a concentric retinal detachment surrounding the optic disc as was observed by an experienced ophthalmic ultrasonographer and an attached posterior pole. Owing to the ineffectiveness of conservative treatment and the occluded visual axis, a surgical alternative was proposed. The parents deferred operative intervention until age 3.3 years, by which time vision in the right eye had deteriorated to hand motion.

The patient underwent lensectomy with posterior polar cataract removal and posterior chamber IOL implantation, followed by hyaloid stem resection (Fig. 1). Endodiathermy was used to control bleeding from the anterior and posterior PFV. No postoperative complications were noted on repeated examinations during 1.2 years' follow-up. The concentric retinal detachment surrounding the optic disc resolved spontaneously after the thickened hyaloid stem was released. Final visual acuity was 6/24 with orthophoria. IOP was within normal limits.

**Table 1** Demographics, disease-related characteristics, surgery and outcome of study series

| Pt. no./sex | Medical history | Ophthalmic history | PFV Dx. age | Unilateral/bilateral PFV | Anterior, posterior, combined PFV | Surgery age | IOL implant | F-U age (years) | Postoperative complications | Final visual acuity | Final ocular motility |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1/M | Prematurity, duodenal atresia, recurrent E. coli urosepsis, hydronephrosis, hypothyroidism, intubated 63 days in perinatal ICU | ROP Dx at 6 weeks | 9 weeks | Unilateral left | Anterior | 11.6 months | Yes | 2.6 | Glaucoma | 1/60 | Left intermittent esotropia |
| 2/M | None | None | 4 months | Unilateral right | Combined | 3.3 years | Yes | 4.6 | None | 6/24 | Orthophoria |
| 3/M | None | None | 10 days | Unilateral left | Anterior | 7 weeks | No | 1 | None | Left fix and follow | Left esotropia 5° |
| 4/F | None | Microcornea | 5 days | Unilateral right | Anterior | 9 weeks | No | 2.4 | Secondary cataract | Right deep amblyopia | Right esotropia 0°–5° |
| 5/F | None | Microcornea | 9 weeks | Unilateral left | Anterior | 3 months | No | 2.5 | Shallow retinal detachment | Left deep amblyopia | Left esotropia 20 prism diopters, after strabismus surgery |
| 6/M | Pyloric stenosis | None | 4 weeks | Unilateral right | Anterior | 8 weeks | No | 1.6 | None | Right fix and follow | Orthophoria |
| 7/M | Triplet pregnancy | None | 8 weeks | Unilateral left | Anterior | 9 weeks | No | 1.3 | None | Left intermittent fix and follow | Left esotropia 5° |
| 8/M | None | None | 6 weeks | Unilateral right | Anterior | 7 weeks | No | 1.2 | None | Right fix and follow | Orthophoria |

*Dx* diagnosis, *F-U* follow-up, *ICU* intensive care unit, *Implant* implantation, *IOL* intraocular lens, *PFV* persistent fetal vasculature

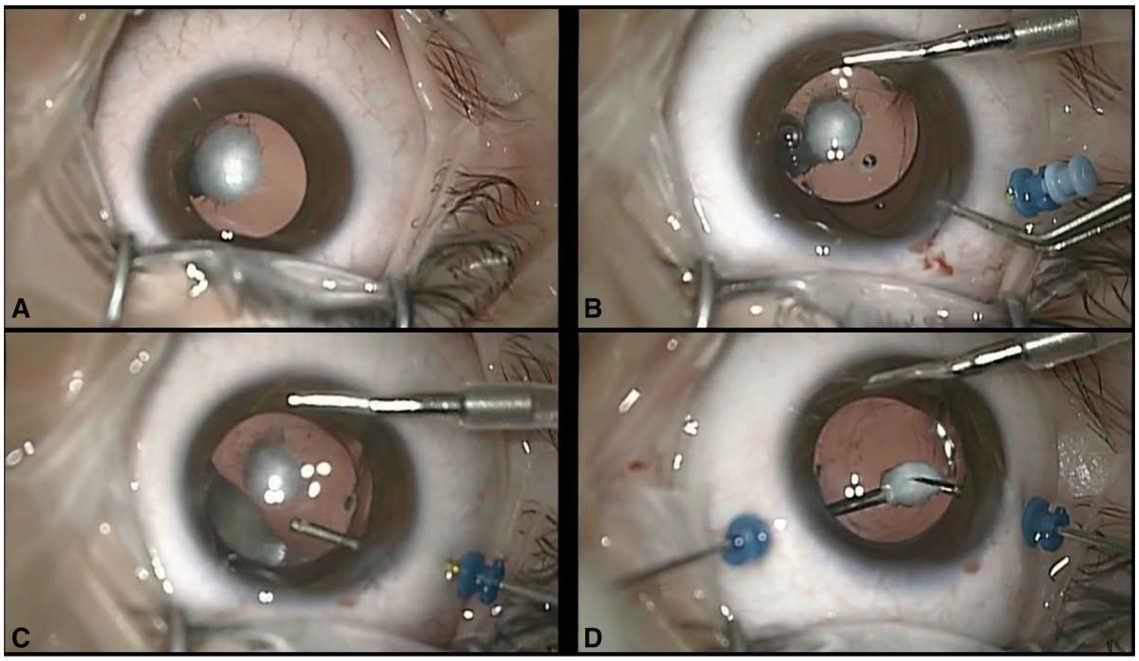


**Fig. 1** Case 2, intraoperative images of PFV and cataractous lens. **a** Dense cataract. **b** IOL insertion. **c** Hyaloid stem resection. **d** Cataract removal

Case 3

A male infant born at 40 weeks' gestation was referred for evaluation of a white pupillary reflex identified on routine pediatric examination. He was diagnosed at age 10 days with left eye cataract blocking the visual axis with vascularization of the posterior capsule. An ultrasound scan demonstrated an attached retina with a delicate PFV strand. At age 7 weeks, lensectomy and PFV resection were performed. The anterior part of the PFV was adherent to the ciliary processes without any apparent zonules. The abnormal thickened posterior capsule was removed completely by separating it from the ciliary processes using intraocular scissors. No postoperative complications were noted on follow-up. Further treatment included contralateral eye patching and a corrective left eye contact lens. The last follow-up examination at age 1 year showed residual left eye esotropia of five prism diopters (PD) and fix-and-follow visual acuity. IOP was within normal limits.

Case 4

A female infant born at 40 weeks' gestation was referred for evaluation. She was diagnosed with right microcornea, cataract, and PFV at age 5 days. At age 9 weeks, lensectomy and PFV resection were performed without IOL implantation (Fig. 2). The PFV consisted of an extremely thick abnormal posterior capsule. The visual axis was cleared, and the peripheral anterior and posterior capsules were left intact for future possible IOL implantation. Postoperative treatment included a corrective contact lens. During follow-up, the remnant posterior and anterior capsule constricted thus blocking the visual axis and retracting the ciliary processes. The peripheral remnants of the capsule were excised completely by disinserting the capsule from the ciliary processes using intraocular scissors at age 5 months. This was done in order to release the traction from the ciliary processes and to prevent further constriction of the capsule. A temporary postoperative ocular hypotony resolved spontaneously.

The patient was followed for 2 years. Findings included good anatomical results with a clear visual axis. Deep amblyopia developed due to poor compliance with occlusion. IOP was within normal limits.

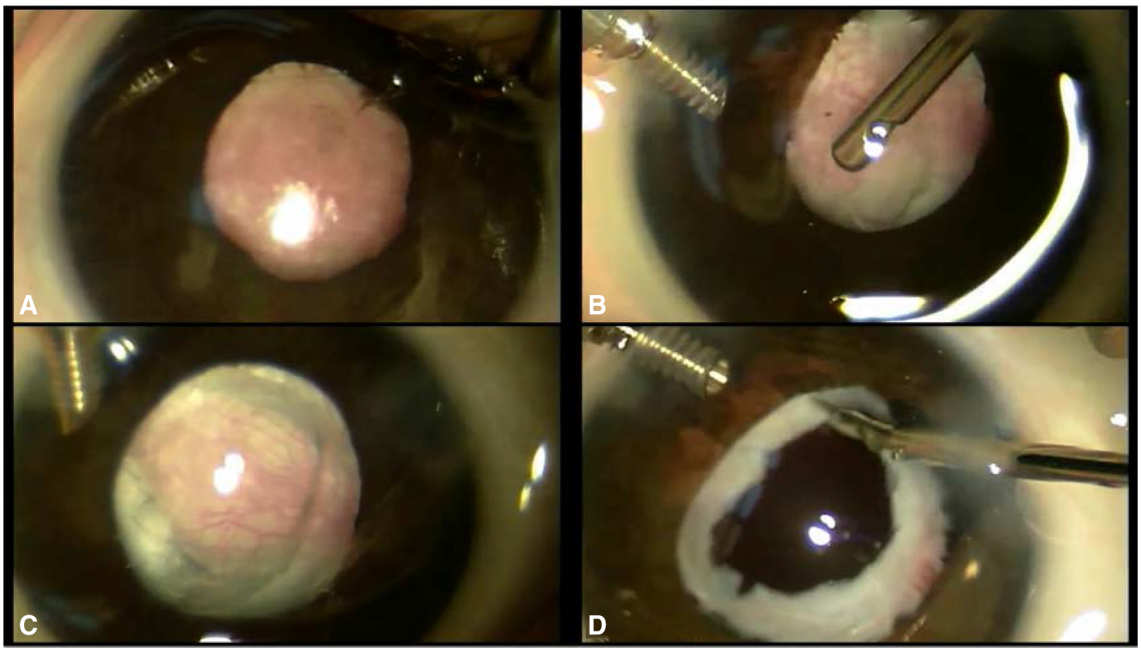


**Fig. 2** Case 4, intraoperative images of PFV and cataractous lens. **a** Dense cataract. **b** Cataract removal. **c** Fibrovascular tissue. **d** Cleared visual axis, intraocular scissors

Case 5

A female infant was referred for consultation at age 9 weeks for a "small" left eye without fixation on objects. Examination revealed a left microcornea with a vascular membrane blocking the visual axis. Very long and abnormal ciliary processes were noted.

Lensectomy, separation of the ciliary processes using intraocular scissors, and PFV resection without IOL implantation were performed at age 3 months, without immediate postoperative complications (Fig. 3). Further treatment included a corrective contact lens and intermittent patching of the contralateral eye.

Examination at the 7-month follow-up revealed a shallow left nasal retinal detachment and a colobomatous optic disc. The retinal detachment resolved over time without additional surgical intervention. At age 1.8 years, left esotropia of 50° and intermittent fix-and-follow visual acuity were noted, and the patient was referred for left medial rectus recession.

At the last follow-up at age 2.5 years, deep left amblyopia and residual left esotropia of 20 PD were noted. Nevertheless, with patching, the child demonstrated functional visual behavior. IOP was within normal limits.

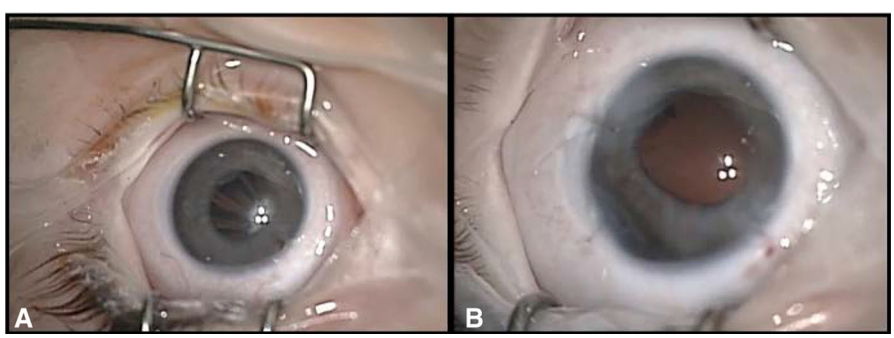


**Fig. 3** Case 5, intraoperative images of PFV and cataractous lens. **a** Microcornea and cataract with long abnormal ciliary processes. **b** Postoperative aphakia

Case 6

A male infant was referred for evaluation at age 4 weeks. He was diagnosed with a right cataract and anterior PFV. Two very long ciliary processes were stretched across the posterior capsule, and there were vascular structures on the anterior capsule. Lensectomy and PFV resection without IOL implantation were performed at 8 weeks. The whole capsule was separated from the ciliary process. A very displaced hyaloid artery was noted and cut. There was postoperative vitreous hemorrhage which resolved spontaneously within 2 weeks. Further treatment included a corrective contact lens.

The last follow-up at age 20 months showed an aphakic right eye with normal anterior and posterior segments and fix-and-follow visual acuity. IOP was within normal limits.

Case 7

A male infant born at 35 weeks following a triplet pregnancy was referred at 8 weeks for evaluation of a white pupillary reflex. He was diagnosed with left cataract and anterior PFV. The anterior part of the PFV was adherent to the ciliary processes, without any apparent zonules. The abnormal thickened posterior capsule was removed completely by separating it from the ciliary processes using intraocular scissors. Lensectomy and PFV resection were performed at 9 weeks, without postoperative complications (Fig. 4).

The last follow-up at age 15 months demonstrated an aphakic left eye with good anatomical results, a residual thin vitreal strand and intermittent fix-and-follow visual acuity with esotropia of 5 PD. IOP was within normal limits.

Case 8

A male infant born at 34 weeks' gestation was referred at age 2 weeks for evaluation of a nuclear cataract completely obscuring the visual axis in the right eye. Workup included an ultrasound examination performed at age 6 weeks, which revealed an anterior PFV with attached retina. At 7 weeks, the child underwent lensectomy and PFV resection with separation of the ciliary processes using intraocular scissors, without intraocular lens implantation. There were no postoperative complications. The last follow-up at age 14 months demonstrated an aphakic right eye with normal anterior and posterior segments and fix-and-follow visual acuity. IOP was within normal limits.

## Results

PFV ocular involvement

1. Anterior and posterior ocular involvement—seven patients presented with isolated anterior involvement and one with combined anterior and posterior involvement. One patient (case 1) had a significant PFV that caused a break in the posterior or anterior lens capsule, leading to swelling and opacification of the lens.
2. Microcornea—seen in two patients (cases 4 and 5).
3. Abnormally positioned or centrally dragged ciliary processes—seen in six patients (cases 3–8).
4. Intraocular hemorrhage, retinal folds, and lenticular opacification—seen in all patients.

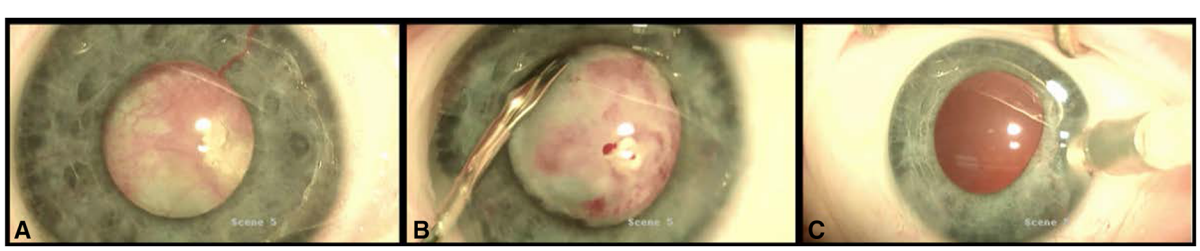


**Fig. 4** Case 7, intraoperative images of PFV and cataractous lens. **a** Dense fibrovascular tissue. **b** Separating ciliary processes with intraocular scissors. **c** Cleared visual axis

Surgical intervention

1. Intraocular lens implantation—performed during surgery in two patients (cases 1 and 2).
2. Endodiathermy—used in all cases to control intraocular bleeding.

Postoperative complications

1. Glaucoma—treated surgically (case 1).
2. Vitreous hemorrhage—resolved with no other complications (case 6).
3. Secondary cataract—necessitating additional surgery (case 4).
4. Shallow retinal detachment—resolved spontaneously (case 5).
5. Strabismus—demonstrated in five patients during follow-up, to some degree. One patient required strabismus surgery.

Visual outcomes

The last visual acuity recorded depended on the extent and severity of the PFV as well as on the intial visual acuity and parent adherence to postoperative amblyopia prevention measures.

One patient achieved visual acuity of 1/60; one achieved visual acuity of 6/24; four patients achieved visual acuity of fix and follow; and two patients remained with deep amblyopia.

## Discussion

We describe eight cases of complex PFV with severe involvement and distortion of the lens and adjacent structures necessitating a nontraditional surgical approach. The surgical technique employed intraocular scissors and intraocular diathermy that are usually used in retina surgeries in order to decrease complications.

The development of the human eye is a highly complex process. A vital part of this process is the formation and regression of the vascular network supplying the developing ocular structures. The vascular network includes the intravitreal hyaloid vessels which form the tunica vasculosa lentis and supply the anterior segment of the eye, including the lens. They reach a peak at 10 weeks' gestation and undergo apoptosis at 5–6 months' gestation, becoming obsolete at 8 months [2]. If these vessels do not regress, fibrosis ensues, leading to the formation of PFV.

The diagnosis of PFV is based on clinical findings of an opaque vascularized retrolental tissue [4]. Demonstration of the fibrovascular stalk on ultrasound scan can be confirmatory [5]. PFV is classified as anterior, posterior, or combined depending on the anatomic configuration. The extent of involvement correlates with the clinical severity [6, 7]. A unilateral clinical presentation is typical, although bilateral PFV has been described in up to 15% of patients [6, 8]. Seven of our patients presented with isolated anterior involvement and one with combined anterior and posterior involvement. The retrolental tissue connecting the optic disc to the posterior lens capsule may obscure the visual axis. Significant PFV can also cause a break in the posterior or anterior lens capsule, leading to swelling and opacification of the lens [6], as found in our patient one. Additional findings include microcornea, seen in two of our patients (4 and 5), abnormally positioned or centrally dragged ciliary processes, seen in six of our patients (nos. 3–8), and intraocular hemorrhage, retinal folds, and lenticular opacification [8, 9], seen in all our patients.

Our patient one had an atypical presentation, with PFV manifesting only after multiple assessments for ROP followed by gradual opacification of the lens. To the best of our knowledge, this is the first description in the English literature of delayed development of PFV after ROP [4].

Surgical intervention is the mainstay of therapy in PFV management. Anterior or posterior vitrectomy combined with lens extraction is essential to clear the obstructed visual axis and to prevent amblyopia and consequent functional impairment. In addition, removal of the hyaloid stalk releases retinal and ciliary body traction, reducing the chances of eye growth restriction, hypotony, or phthisis bulbi [5]. Lens extraction with or without IOL implantation also deepens the anterior chamber, thereby lowering the risk of secondary glaucoma [3]. In the present series, IOL implantation was performed during surgery in two patients (nos. 1 and 2). Endodiathermy was used in all cases to control intraocular bleeding. Intraocular scissors were found to be very helpful in removing

anterior PFV with a very thick and abnormal posterior lens capsule. When severe involvement was noted, the capsule had to be separated from the ciliary processes. The ROP in patient one and microcornea in patients four and five warranted a change in the planned therapeutic approach and its timing.

Combined cataract and PFV resection have been associated with postoperative complications in 27–50% of cases. These include retinal detachment, hyphema, intraocular hemorrhage, glaucoma, secondary cataract, inflammatory response, and phthisis bulbi [3, 10]. In our series, postoperative complications consisted of glaucoma which was treated surgically (patient 1), vitreous hemorrhage which resolved with no other complications (patient 6), secondary cataract necessitating additional surgery (patient 4), and the development of a shallow retinal detachment that resolved spontaneously during follow-up (patient 5). Five patients demonstrated a certain degree of strabismus during follow-up, and one required strabismus surgery.

Visual outcomes of surgically treated PFV depend on patient age at cataract occurrence and at surgery and macular involvement [6]. Past studies report some degree of visual improvement in 66–80% of surgically treated patients [6, 10]. Untreated patients do not show visual improvement, and approximately 40% have visual deterioration [6]. In the present study, visual outcomes varied by extent of PFV and cataract formation, initial visual acuity, and parent adherence to postoperative amblyopia prevention measures. The extent and severity of the PFV in this case series may explain the visual outcomes.

Although most cases of PFV are sporadic, there are descriptions of autosomal dominant and autosomal recessive inheritance in previous studies [1]. The pathophysiology of PFV has been attributed to mutations in *ARF* p53 suppressor, Norrie disease, pseudoglioma, and mutations in *LRP5* genes [1]. Associations were suggested with maternal protein C deficiency, clomiphene use, and cocaine abuse [2, 11]. All our cases were sporadic in nature.

In rare instances, PFV may be associated with systemic and ocular disorders, including Axenfeld-Rieger syndrome, neurofibromatosis, Aicardi syndrome, acute angle closure glaucoma, myopia, ROP, microcornea, trisomy 13/15/18, and other rare conditions [1, 10]. Conditions that can mimic PFV include familial exudative vitreoretinopathy, Norrie disease (pseudoglioma), Coat's disease, incontinentia pigmenti, and retinoblastoma; all of these should be considered in the differential diagnosis. We did not find these systemic associations with PFV in our patients.

Severe PFV poses a therapeutic challenge. A high index of clinical suspicion is important in the early detection of PFV. Ultrasonography has diagnostic value when there is lenticular opacification with a limited view of the posterior segments. An individually tailored surgical approach and postoperative treatment are required in each case. Together, early diagnosis, carefully selected surgical approach, and appropriate postsurgical management are vital for maximal visual rehabilitation.

**Compliance with ethical standards**

**Conflict of interest** All authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

**Informed consent** The need for informed consent was waved by the IRB committee, (retrospective study).

## References

1. Shastry BS (2009) Persistent hyperplastic primary vitreous: congenital malformation of the eye. Clin Exp Ophthalmol 37:884–890
2. Pau H (2010) Hypothesis on the pathogenesis of retinopathy of prematurity—it is not VEGF alone but anatomical structures that are crucial. Graefes Arch Clin Exp Ophthalmol 248:1–3
3. Walsh MK, Drenser KA, Capone A, Trese MT (2010) Early vitrectomy effective for bilateral combined anterior and posterior persistent fetal vasculature syndrome. Retina 30(4 Suppl):S2–S8
4. Zahavi A, Hilely A, Weinberger D, Snir M, Kella YR (2015) Unusual persistent fetal vasculature presentation in a premature baby. Adv Pediatr Res 2:26
5. Hu A, Pei X, Ding X, Li J, Li Y, Liu F et al (2015) Combined persistent fetal vasculature: a classification based on high-resolution B-mode ultrasound and color doppler imaging. Ophthalmology 123:19–25
6. Tartarella MB, Takahagi RU, Braga AP, Fortes Filho JB (2013) Persistent fetal vasculature: ocular features,

management of cataract and outcomes. Arq Bras Oftalmol 76:185–188
7. Müllner-Eidenböck A, Amon M, Moser E, Klebermass N (2004) Persistent fetal vasculature and minimal fetal vascular remnants: a frequent cause of unilateral congenital cataracts. Ophthalmology 111:906–913
8. Tartarella MB, Britez-Colombi GF, Milhomem S, Lopes MCE, Fortes Filho JB (2014) Pediatric cataracts: clinical aspects, frequency of strabismus and chronological, etiological, and morphological features. Arq Bras Oftalmol 77:143–147
9. Hunt A, Rowe N, Lam A, Martin F (2005) Outcomes in persistent hyperplastic primary vitreous. Br J Ophthalmol 89:859–863
10. Vasavada AR, Vasavada SA, Bobrova N, Praveen MR, Shah SK, Vasavada VA et al (2012) Outcomes of pediatric cataract surgery in anterior persistent fetal vasculature. J Cataract Refract Surg 38:849–857
11. Teske MP, Trese MT (1987) Retinopathy of prematurity-like fundus and persistent hyperplastic primary vitreous associated with maternal cocaine use. Am J Ophthalmol 103(5):719–720