

## Unusual persistent fetal vasculature presentation in a premature baby

Alon Zahavi<sup>1,2\*</sup>, Assaf Hilely<sup>3</sup>, Dov Weinberger<sup>1,2</sup>, Moshe Snir<sup>1,2,4</sup>, Yonina R. Kella<sup>1,3,4</sup>

**1** Department of Ophthalmology, Rabin Medical Center, Petah Tiqwa, Israel **2** Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel **3** Department of Ophthalmology, Kaplan Medical Center, Rehovot, Israel **4** Pediatric Ophthalmology Unit, Schneider Children's Medical Center of Israel, Petah Tiqwa, Israel

### Abstract

Persistent fetal vasculature (PFV) is a congenital developmental disorder manifesting as a fibrovascular remnant of the embryonal hyaloid vascular system within the vitreal space. Retinopathy of prematurity (ROP) presents as varying degrees of non-vascularized retinal tissue with potentially devastating ocular complications. Both pathologies arise from ocular vascular system abnormalities, and various treatment modalities have been attempted in the past. In this report we describe a unique case of a late manifesting PFV that may be associated with the development of ROP, complicated by a visually significant cataract.

**Citation:** 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. doi:10.12715/apr.2015.2.26

**Received:** March 8, 2015; **Accepted:** August 13, 2015; **Published:** November 30, 2015

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**Competing interests:** The authors have declared that no competing interests exist.

\* Email: alonzahavi@gmail.com

### Case Report

A male infant born prematurely at gestational age of 25 weeks was routinely evaluated for ROP. At a birth weight of 818g the infant suffered from duodenal atresia, which was repaired surgically, recurrent *E. coli* urosepsis, hydronephrosis, and hypothyroidism. Genetic testing performed in response to the duodenal atresia yielded no abnormalities. He was intubated for 63 days in the perinatal intensive care unit.

Ophthalmologic examination performed at six weeks of biological age revealed bilateral incomplete retinal vascularization up to middle zone 2, with normal anterior segments, clear lenses, and normal optic discs (Fig. 1A and B). During the following two weeks the condition deteriorated to ROP stage 2. The retina remained flat, without any plus disease or neovascularization.

Routine ROP follow-up examinations were frequently performed, and three weeks later a mild posterior capsular opacification of the lens was detected in the left eye for the first time. A visible strand of PFV was

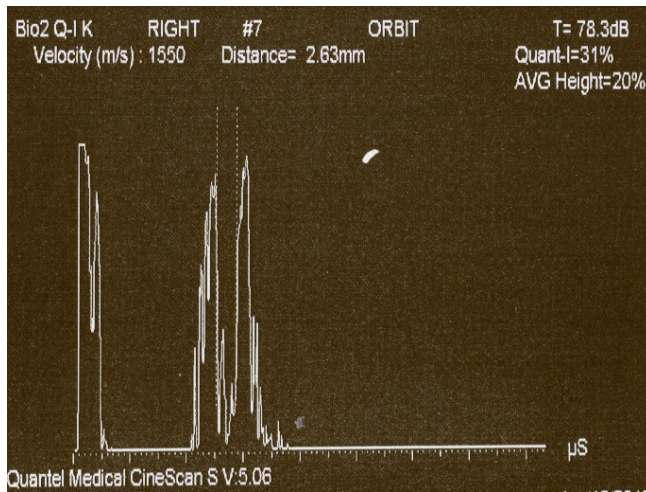
noted and confirmed sonographically (Fig. 2). During follow-up the left retina was no longer visible due to lens opacities, and ocular ultrasound scans were performed to rule out retinal detachment as a complication of ROP and PFV.

At the age of 50 weeks, the infant underwent vitrectomy with cataract extraction and intraocular lens implantation (Fig. 3A and B). There were no intraoperative complications. Postoperative glaucoma was diagnosed and treated operatively.

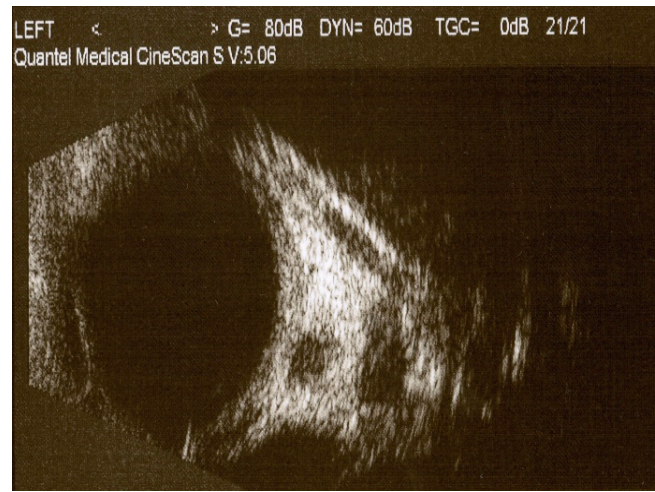
### Discussion

The association between congenital PFV diagnosed before ROP development has been described in the past [1]. However, a delayed presentation of PFV not seen at birth, complicated with opacification of the lens in a preterm infant after being diagnosed with ROP, has not been reported in the English literature to date.

A



B



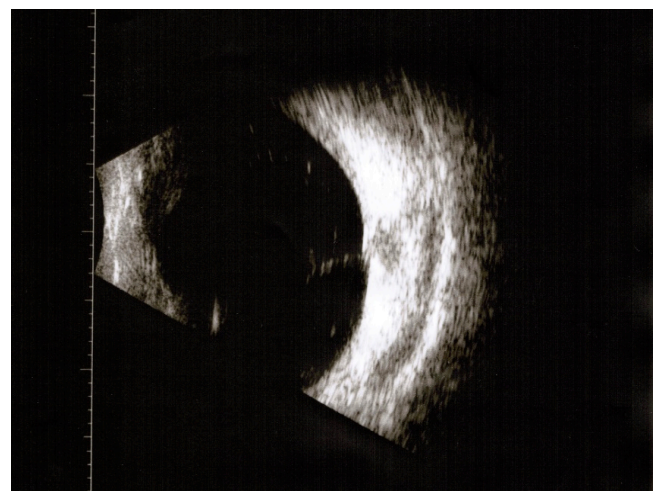
**Figure 1.** Ultrasound A scan mode demonstrating no persistent fetal vasculature at six weeks biological age (A) and ultrasound B scan mode demonstrating no persistent fetal vasculature at six weeks biological age (B)

Ocular vascularization occurs during embryonal development. The primary vitreous is a vascular structure within the developing globe, which contains the hyaloid vessels supplying the globe. It reaches peak development at 10 weeks of gestation [1], and may be visualized as anteriorly coursing from the retina to form the tunica vasculosa lentis that supplies the developing lens and anterior segment structures. It regresses by apoptosis at five to six months of gestation and completes atrophy at eight months of gestation [1]. Failure of regression of the primary vitreous results in subsequent fibrosis and is referred to as PFV. Persistent hyperplastic primary vitreous was the original term coined by Reese in 1955 [2]. In 1997, Goldberg suggested the term PFV, since it better represented the anatomy and pathology of the disorder [2, 3].

In PFV the fibrovascular stalk emanates from the optic disc to join the posterior lens capsule, where it fans out to form a white vascularized retrolental tissue often accompanied by the persistent hyaloid artery [3]. The pathology can be classified as anterior, posterior or combined with regards to anatomical location, and can be graded from mild to severe depending on the extent of the remaining persistent hyaloid system [3]. The white vascularized fibrous tissue may cause a break in the posterior or anterior

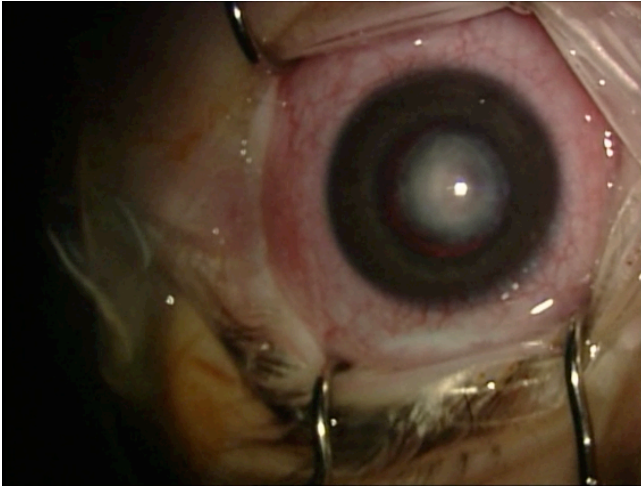
lens capsule, which leads to swelling and opacification of the lens, as occurred in our case [3].

The etiology of PFV is being continuously studied. Most cases are sporadic, and some autosomal dominant or recessive inheritance patterns have been described with linkage to the 10q11-q21 chromosomal region [4].

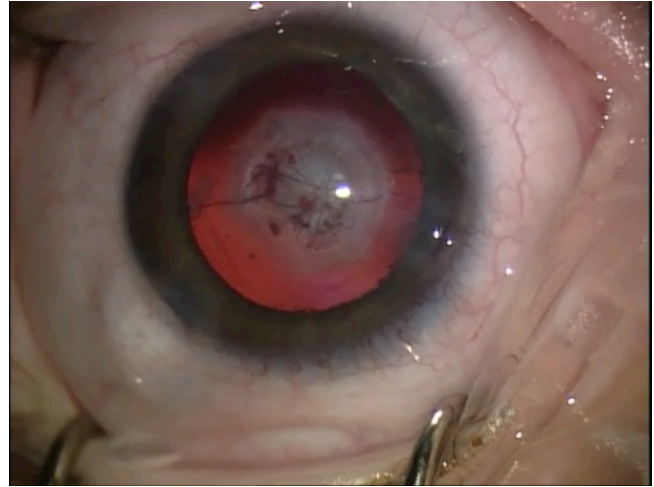


**Figure 2.** Ultrasound B scan mode demonstrating persistent fetal vasculature at eleven weeks biological age, not seen previously

A



B



**Figure 3.** Dense cataract prior to surgical extraction (A) and persistent fetal vasculature strands visible following cataract extraction (B)

Suspected iatrogenic causes of PFV include maternal protein C deficiency and clomiphene use [1]. Cocaine use has been reported in association with PFV, but is probably not related to its development [5].

Abnormalities in normal apoptosis lead to PFV [1], and past studies have established that normal arf, p53 tumor suppressor, Norrie disease pseudoglioma, and LRP5 genes are needed for typical hyaloid vascular regression; mutations in these genes are considered a part of the pathophysiology of the disease [4].

ROP is a condition in which incomplete vascularization of the retina results in relative peripheral retinal ischemia. Resultant overexpression of VEGF leads to neovascularization, and to severe ocular complications. Major risk factors for the development of ROP include low birth weight and low gestational age. Blood oxygen tension is an important factor in the development of ROP, yet its exact pathophysiological mechanism is not completely understood [1]. When comparing the risk factors for PFV and ROP, no overlap can be seen.

The interplay between ROP and PFV is being continuously studied in animal models. It has been shown that the hyaloid and iris vasculature is often dilated and engorged in ROP in animal models, and that PFV may persist in cases of severe ROP [6]. Based on animal models, some researchers

hypothesize that the failure of the hyaloid system to regress from its attachment at the retinal equator and demarcation line contributes to the development of ROP, since the retinal vessels cannot grow anteriorly and complete retinal vascularization occurs in preterm infants. In infants born to term, the hyaloid system completes its apoptosis and regresses, allowing the retinal vasculature to complete its anterior growth [1].

Animal model studies demonstrating failure of hyaloid vasculature regression show profound abnormalities in retinal vasculature [4]. Favazza et al. performed additional studies in rat models of ROP. They established an association between anterior segment vasculature abnormalities, such as persistent tunica vasculosa lentis, and ROP retinal abnormalities. The study demonstrated the extent of the anterior segment vascular changes with relation to the severity of the ROP [6].

Diagnosis of PFV is based on clinical and imaging findings. The presence of an opaque vascularized retrolental tissue is considered proof of PFV [3], and supportive ocular ultrasonic demonstration of the fibrovascular stalk can be confirmatory.

A differential diagnosis should be considered in all cases of PFV, and includes familial exudative vitreoretinopathy, Norrie disease pseudoglioma,

Coats' disease, incontinentia pigmenti, and retinoblastoma [4]. In our patient, ultrasound scans were performed after the clinical diagnosis was made, confirming the presence of the residual hyaloid vascular system.

The diagnosis of PFV in the presented case is atypical. The infant had undergone regular screening for ROP and no retrolental fibrovascular tissue was evident despite multiple examinations. Delayed development of the abnormality was found along with gradual opacification of the lens. To the best of our knowledge this is the first description in the English literature of such a delayed development of PFV after ROP.

Treatment of PFV requires surgical intervention in order to prevent its numerous complications, including lens opacification and obstruction of the visual axis [4]. Removal of the lens clears the visual axis and decreases the tendency for a shallow anterior chamber and secondary glaucoma [7]. Intraocular lens implantation in unilateral PFV cases can be utilized to prevent progressive pathological changes associated with the condition [4]. Vitrectomy and removal of the hyaloid stalk releases traction on the retina, which might restrict eye growth or cause traction on the ciliary body, and in turn might lead to hypotony and phthisis bulbi [7]. On the other hand, vitrectomy performed in ongoing ROP may cause severe complications, leading to severe proliferative vitreoretinopathy and retinal detachment [8].

Our case presented a complicated combination of ocular pathologies, which required a tailored treatment approach. Although it is customary to perform cataract extraction at a postmenstrual age of 44 to 46 weeks, the presence of ROP at 44 weeks in the non-cataractous eye presented a dilemma because the fellow retina was obscured by lens opacification. We assumed that ROP was also present in the cataractous eye, and therefore surgical intervention would exacerbate the condition.

Studies have shown that in 90% of patients, ROP already begins to involute at 44 postmenstrual weeks. We therefore postponed surgery to a postmenstrual age of 50 weeks when the ROP was expected to no longer be present.

## Conclusions

We describe a preterm infant with delayed development of PFV and cataract not seen on routine ROP screening examinations, and later diagnosed after ROP development. The unique timing of presentation of these ocular pathologies required a customized therapeutic approach to enable adequate visual rehabilitation. This may be a rare example supporting the finding presented in animal models.

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