



Clinical and pathological characterization of persistent fetal vasculature associated with vitreous hemorrhage

Waleed Alsarhani^{a,*}, Hind Alkatan^a, Azza Maktabi^b, Deepak P. Edward^{b,c}, Igor Kozak^{b,d}

^a College of Medicine, King Saud University, Riyadh, Saudi Arabia

^b King Khaled Eye Specialist Hospital, Riyadh, Saudi Arabia

^c Illinois Eye and Ear Infirmary, The University of Illinois at Chicago, Chicago, IL, USA

^d Moorfields Eye Hospital Centre, Abu Dhabi, United Arab Emirates

ARTICLE INFO

Keywords:

Persistent fetal vasculature
Persistent hyperplastic primary vitreous
Ocular pathology
Leukocoria

ABSTRACT

Purpose: To provide clinical and pathological features of posterior persistent fetal vasculature (PFV) presenting with vitreous hemorrhage.

Observations: Case 1 was a one-year old male with PFV reaching up to the posterior lens capsule. Case 2 and 3 both had history of blunt trauma. B-scans in cases 2 and 3 revealed vitreous hemorrhage and an intravitreal tissue attached to the optic disc. Pre-operative visual acuity in cases 1, 2 and 3 was undetermined due to age, hand motion and light perception, respectively. During vitrectomy, a fibrotic stalk attached to the optic nerve was removed, which consisted of fibrovascular tissue enveloping pockets of hemorrhage histopathologically. The fibrovascular tissue contained smooth muscle actin (SMA) positive spindle-shaped myofibroblasts in one case and hemosiderin-laden macrophages in another case. Glial fibrillary acidic protein (GFAP) stain was focally positive in two specimens. The proliferation index was low using Ki-67 stain in all cases. Post-operative visual acuity in case 3 remained unchanged, while improved in case 2 from hand motion to 20/70. There was no recurrence of the vitreous hemorrhage.

Conclusion and Importance: Vitreous hemorrhage may occur in cases of PFV with or without history of blunt trauma. Hemorrhage within the persistent fetal vasculature may become organized with reactive process in the hyaloid stalk. The fibrovascular stalk contained astrocytes and myofibroblasts which contribute to the formation and contractile function of PFV, respectively. The outcomes following vitrectomy seemed to be satisfactory.

1. Introduction

Persistent Fetal Vasculature (PFV), previously known as persistent hyperplastic primary vitreous (PHPV), is a congenital developmental disease caused by failure of regression of the hyaloid vasculature.¹ It is almost always a unilateral disease (90%) without any systemic manifestations.¹ Bilateral cases are associated with Mendelian mutations such as trisomy 13 (Patau syndrome).¹

In posterior PFV, a fibrous stalk is seen arising from the optic disc and extending anteriorly with one or more of the following features; retinal detachment, retinal folds, dysplasia, or optic nerve hypoplasia.^{1,2} Also, patients may develop leukocoria, strabismus, amblyopia and nystagmus.³ Retinal detachment is a complication of posterior PFV caused by tractional contractions of the fibrous stalk.¹ In most cases visual acuity is 20/200 or worse.⁴ Ultrasound and computed tomography are considered the best diagnostic methods to confirm posterior

PFV.⁵

This article shows the clinical and histopathological analysis of 3 consecutive pediatric case series with PFV who underwent pars plana vitrectomy with tissue excision. The hyaloid stalk was carefully separated from the optic nerve using bimanual technique in all cases. The tissue was examined by light microscopy, and the tissue components were examined using routine histopathological stains and immunohistochemical (IHC) stains. IHC stains used included smooth muscle actin (SMA), glial fibrillary acidic protein (GFAP) and Ki-67. To the best of our knowledge, this is the first to describe clinical and histopathological features of posterior PFV presenting with vitreous hemorrhage.

* Corresponding author. Department of Ophthalmology, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia
E-mail address: WAlsarhani@gmail.com (W. Alsarhani).

<https://doi.org/10.1016/j.ajoc.2020.100743>

Received 11 September 2019; Received in revised form 6 May 2020; Accepted 11 May 2020

Available online 18 May 2020

2451-9936/ © 2020 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

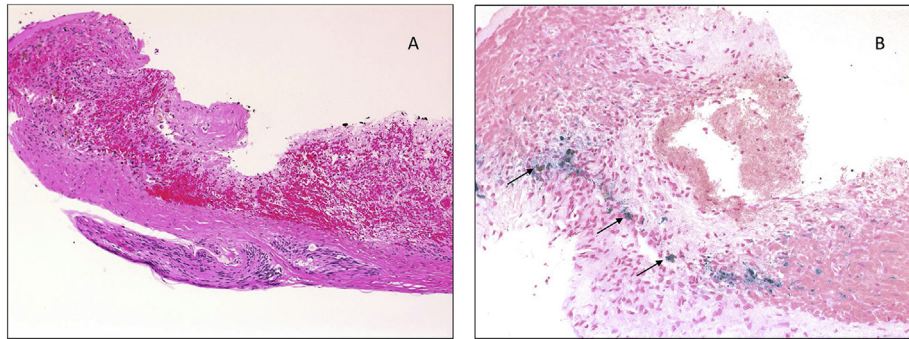


Fig. 1. (A) Persistent fetal vasculature with fibrous tissue and evidence of hemorrhage (x100 Hematoxylin & Eosin). (B) The same PFV showing hemosiderin deposits indicating previous hemorrhage (arrows) (x200 Iron).

2. Findings

2.1. Case 1

This was a one-year-old male with PFV reaching up to the posterior lens capsule with mildly opaque lens. Vitrectomy was performed and a fibrotic stalk attached to the optic nerve was identified and removed. Pathologically, the specimen consisted of fibrovascular tissue and enveloping pockets of hemorrhage (Fig. 1A). The fibrovascular tissue contained hemosiderin deposits with a low KI-67 index (Fig. 1B). Pre-operative and post-operative visual acuity were undetermined due to age. On subsequent follow ups, there was no recurrence of the vitreous hemorrhage.

2.2. Case 2

This was a four-year-old male who had history of blunt trauma. Pre-operative visual acuity was hand motion (HM). B-scans revealed vitreous hemorrhage and an intravitreal tissue attached to the optic disc (Fig. 2A). During vitrectomy, a fibrotic stalk attached to the optic disc was removed. Pathologically, the specimen consisted of fibrovascular tissue and enveloping pockets of hemorrhage. The fibrovascular tissue was positive for SMA and GFAP stains but had a low KI-67 index

(Fig. 2B and C). Post-operative visual acuity improved to 20/70. There was no recurrence of the vitreous hemorrhage.

2.3. Case 3

A nine-year-old male had history of blunt trauma four months prior to his presentation to the clinic. Pre-operative visual acuity was light perception. B-scans revealed growth of tissue attached to the optic disc in addition to vitreous hemorrhage (Fig. 3A). Pathologically, the specimen consisted of fibrovascular tissue and enveloping pockets of hemorrhage (Fig. 3B). The fibrovascular tissue contained hemosiderin deposits with a low KI-67 index (Fig. 3C and D). GFAP was focally positive (Fig. 3E). Post op visual acuity remained unchanged. There was no recurrence of vitreous hemorrhage.

3. Discussion

Vitreous hemorrhage may occur due to fragility of the hyaloid vasculature.⁶ It may be triggered by ocular trauma, posterior vitreous detachment or during rapid eye movement (REM) phase of sleep cycle.⁶⁻⁸ In cases 2 and 3, ocular trauma was presumably the triggering event of vitreous hemorrhage.

The vascular and glial components of the hyaloid vasculature

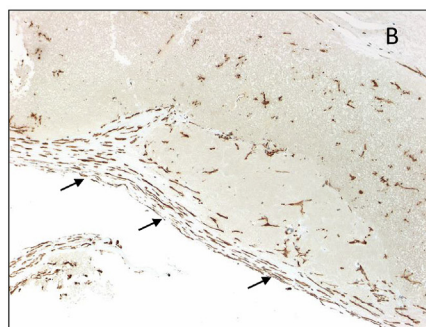
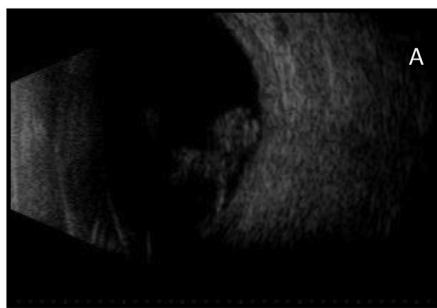
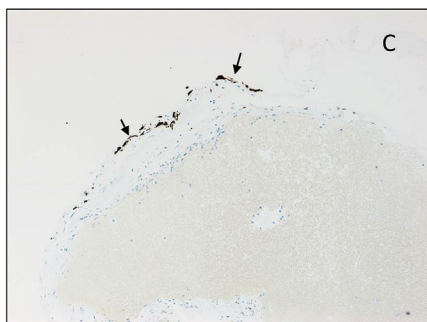


Fig. 2. (A) B-scans revealed a fibrotic stalk attached and extending from the optic disc. (B) Higher power photo of the persistent fetal vasculature which is outlined by smooth muscle like fibers (arrows) (Original magnification x200 SMA). (C) PFV showing few glial cells along the outer border of the proliferation (arrows) (Original magnification x100 GFAP).



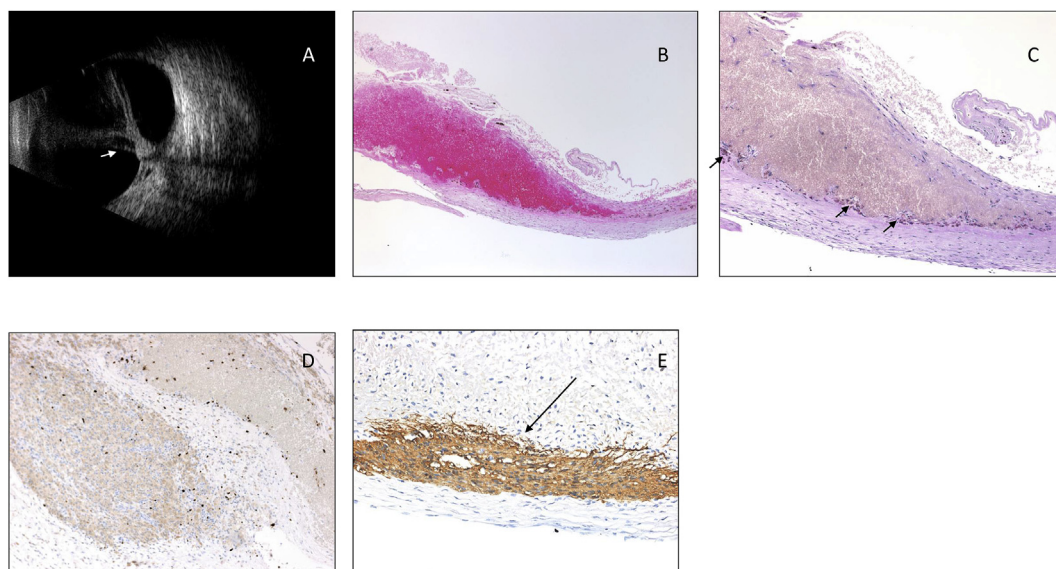


Fig. 3. (A) B scan showing a fibrovascular tissue attached by a stalk to the area of optic disc (arrow) (B) The histopathological appearance of fibrovascular tissue enclosing the hemorrhage (x40 Hematoxylin & Eosin). (C) Persistent fetal vasculature with hemosiderin deposits near the pockets of hemorrhage (arrows) (x100 Periodic Acid Schiff). (D) PFV showing low proliferative index (x100 Ki 67). (E) PFV associated focal area of glial tissue (arrow) (x200 GFAP).

accounts for the symptoms and signs of PFV.^{1,4} The pre-operative visual acuity was severely affected in cases 2 and 3 (hand motion and light perception respectively) due to pathological changes of PFV affecting the optic nerve and macula in addition to the superimposing vitreous hemorrhage. In our cases, fibrovascular tissue and hemorrhage were repeatedly identified. Two cases showed focal glial tissue, one of which was seen within the stalk of the fibrovascular tissue and the other as a rim of glial tissue around the fibrovascular tissue. GFAP indicates the presence of astrocytes which provide endothelial support. Consequently, astrocytes inhibit regression of fetal vasculature and contribute to the formation of PFV.⁹ The presence of myofibroblasts explains the tractional property of the stalk, which may cause retinal detachment.¹⁰ Lambert and his group reported two cases of congenital fibrovascular pupillary membrane where the fibrovascular membrane was SMA positive.¹¹ They also described similar IHC findings in a PFV patient.¹¹ Robb stated that congenital pupillary fibrovascular membrane is a variant of PFV with similar findings.¹² Hemosiderin-laden macrophages found in case 3 represented a chronic response to vitreous hemorrhage, which occurred four months prior to the patient's presentation.

Case 2 showed marked improvement in visual acuity from HM to 20/70. Visual acuity did not improve in case 3 due to late presentation and intervention. Age of presentation is an important predictor of post-operative visual acuity.^{2,13} Karr and Scott showed patients with the mean age of only 72 days who had a visual acuity of 20/200 or better.¹⁴ Posterior PFV has always been associated with a worse visual acuity than anterior PFV.¹ Indeed, prognosis after vitrectomy depends on the age of presentation, extent of PFV, and the presence of other complications.¹³ Goldberg stated the primary goal of surgery should be prevention of recurrence of vitreous hemorrhage and secondary complications rather than improving visual acuity.¹ There was no recurrence of vitreous hemorrhage in all our three case.

4. Conclusion

Vitreous hemorrhage may occur in cases of PFV with or without history of blunt trauma. Hemorrhage within the persistent fetal vasculature may become organized with reactive process in the hyaloid stalk. The fibrovascular stalk contained astrocytes and myofibroblasts which contribute to the formation and contractile function of PFV respectively. The outcomes following vitrectomy seemed to be satisfactory.

Patient consent

Patient consent was not obtained. The information in the article doesn't contain any personal information that could lead to the identification of the patients presented. The paper was approved by the IRB committee at King Khaled Eye Specialist Hospital (KKESH).

Funding

No funding or grant support.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The authors don't have any financial disclosures. No conflicts of interest to be reported by any author.

Acknowledgements

None.

References

- Goldberg MF. Persistent fetal vasculature (PFV): an integration of signs and symptoms associated with persistent hyperplastic primary vitreous (PHPV). LIV Edward Jackson Memorial Lecture. *Am J Ophthalmol.* 1997;124:587–626.
- Pollard ZF. Persistent hyperplastic primary vitreous: diagnosis, treatment, and results. *Trans Am Ophthalmol Soc.* 1997;95:487–549.
- Silbert M, Gurwood AS. Persistent hyperplastic primary vitreous. *Clin Eye Vis Care.* 2000;12(3-4):131–137.
- Pruett RC. The pleomorphism and complications of posterior hyperplastic primary vitreous. *Am J Ophthalmol.* 1975;80:625–629.
- Kaste SC, Jenkins 3rd JJ, Meyer D, Fontanesi J, Pratt CB. Persistent hyperplastic primary vitreous of the eye: imaging findings with pathologic correlation. *AJR Am J Roentgenol.* 1994;162(2):437–440.
- Goncalves A, Cruysberg JRM, Draaijer RW, et al. Vitreous haemorrhage and other complications of a persistent hyaloid artery. *Doc Ophthalmol.* 1996;92:55–59.
- Cekic O, Totan Y, Batman C. Traumatic vitreous hemorrhage from a persistent hyaloid artery. *J Pediatr Ophthalmol Strabismus.* 2000;37:117–118.
- Chen TL, Yang SS. Vitreous hemorrhage from a persistent hyaloid artery. *Retina.*

- 1993;13:148–151.
9. Edwards MM, McLeod DS, Grebe R, Heng C, Lefebvre O, Luty GA. Lama1 mutations lead to vitreoretinal blood vessel formation, persistence of fetal vasculature, and epiretinal membrane formation in mice. *BMC Dev Biol.* 2011;11:60.
 10. Kesarwani S, Murthy R, Vemuganti GK. Surgical technique for removing congenital fibrovascular pupillary membrane, with clinicopathological correlation. *J AAPOS.* 2009;13(6):618–620.
 11. Lambert SR, Buckley EG, Lenhart PD, Zhang Q, Grossniklaus HE. Congenital fibrovascular pupillary membranes: clinical and histopathologic findings. *Ophthalmology.* 2012;119(3):634–641.
 12. Robb RM. Fibrous congenital iris membranes with pupillary distortion. *Trans Am Ophthalmol Soc.* 2001;99:45–51.
 13. Hunt A, Rowe N, Lam A, Martin F. Outcomes in persistent hyperplastic primary vitreous. *Br J Ophthalmol.* 2005;89:859–863.
 14. Karr DJ, Scott WE. Visual acuity results following treatment of persistent hyperplastic primary vitreous. *Arch Ophthalmol.* 1986;104:662–667.