American Journal of Ophthalmology Case Reports 25 (2022) 101395

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Vitreous hemorrhage in X-linked retinoschisis

M. Margarita Parra *, M. Elizabeth Hartnett

Department of Ophthalmology and Visual Sciences, Moran Eye Center, University of Utah, Salt Lake City, UT, 84132, USA

ARTICLE INFO

Keywords:
X-linked retinoschisis
Ischemia
Neovascularization
Vitreous hemorrhage
Optical coherence tomography

ABSTRACT

Purpose: To report a case of preretinal hemorrhage from extraretinal neovascularization related to capillary non-perfused retina within a large schisis in a pediatric patient with X-linked retinoschisis (XLRS).
Observations: A 4-year old male with an *RS1* mutation and XLRS presented with preretinal and vitreous hemorrhage in the right eye. Retinal imaging, including wide angle fluorescein angiography (FA) and optical coherence tomography (OCT), showed vitreoretinal traction on extraretinal neovascularization and capillary non-perfused retina in the schisis cavity. Laser treatment to the non-perfused retina within the schisis was successful in reducing extraretinal neovascularization.
Conclusions: Vitreous hemorrhage is a well-known occurrence in XLRS. Imaging using wide angle FA and OCT were helpful to determine the causes of hemorrhage in order to develop a management plan.

1. Introduction

X-linked retinoschisis (XLRS) is a congenital vitreoretinal dystrophy with an estimated prevalence of 1:5,000 and 1:30,000.[1] Vitreous hemorrhage is a well-recognized occurrence[1–7] and is believed to arise from vitreous traction on retinal blood vessels in the elevated schisis[2–4,7] or on extraretinal neovascularization,[2] and in association with full-thickness retinal breaks.[1,8] We describe a patient with XLRS who presented with preretinal and vitreous hemorrhage from several causes. Imaging with wide angle fluorescein angiography (FA) and optical coherence tomography (OCT) helped in developing a management plan.

2. Case report

A 4-year-old male with XLRS was referred to pediatric retina for vitreous hemorrhage in the right eye (OD). Visual acuity was 20/80 OD and 20/125 left eye (OS). There was a preretinal and vitreous hemorrhage along the inferotemporal arcade abutting an inferotemporal retinoschisis.

An examination under anesthesia with wide angle FA revealed capillary non-perfusion within the schisis cavity and fluorescein leakage from extraretinal neovascularization at the edge of the schisis. OCT demonstrated a vitreous tractional membrane on a retinal vessel superior to the schisis leaflet with underlying hyporreflective intraretinal spaces (Fig. 1). The OS had vitreous veils without traction or capillary non-perfusion (Fig. 1).

It was believed that capillary non-perfusion in the schisis cavity presented a hypoxic stimulus for the formation of extraretinal neovascularization that then bled into the vitreous. Therefore, several sessions of FA-guided laser photocoagulation were performed to the outer retina of the schisis cavity in scatter fashion to treat the non-perfused retina. The extraretinal neovascularization partly resolved. At last follow-up 7 years later, corrected visual acuity was 20/40 OD and 20/250 OS and there was no vitreous hemorrhage (Fig. 2).

3. Discussion

Vitreous hemorrhage has been reported in 3%–21% of these patients with XLRS[1,6,9,10] and proposed to be secondary to retinal tears or vitreous traction on retinal blood vessels[2–4,7] or extraretinal neovascularization.[2] This report describes a patient with XLRS and vitreous hemorrhage due to several factors identified by FA and OCT. FA and OCT were important in determining a treatment plan.

In this case, a number of factors likely contributed to extraretinal neovascularization. On FA, there was an area of obvious nonperfused retina within the schisis cavity and leakage for extraretinal neovascularization occurred at the junction of the avascular retina and vascular retina. One cause of neovascularization may be from hypoxia that triggers the expression of multiple angiogenic factors (e.g., VEGF, angiopoietins, erythropoietin) through the stabilization of hypoxia-inducible factors. The separation of the retinal layers may have disrupted retinal perfusion within the schisis cavity and caused hypoxia to

* Corresponding author. 65 Mario Capecchi Dr, Salt Lake City, UT, 84132, USA.
E-mail addresses: mariamargaritaparrac@gmail.com (M.M. Parra), me.hartnett@hsc.utah.edu (M.E. Hartnett).

https://doi.org/10.1016/j.ajoc.2022.101395
Received 12 October 2021; Received in revised form 31 January 2022; Accepted 1 February 2022
Available online 3 February 2022

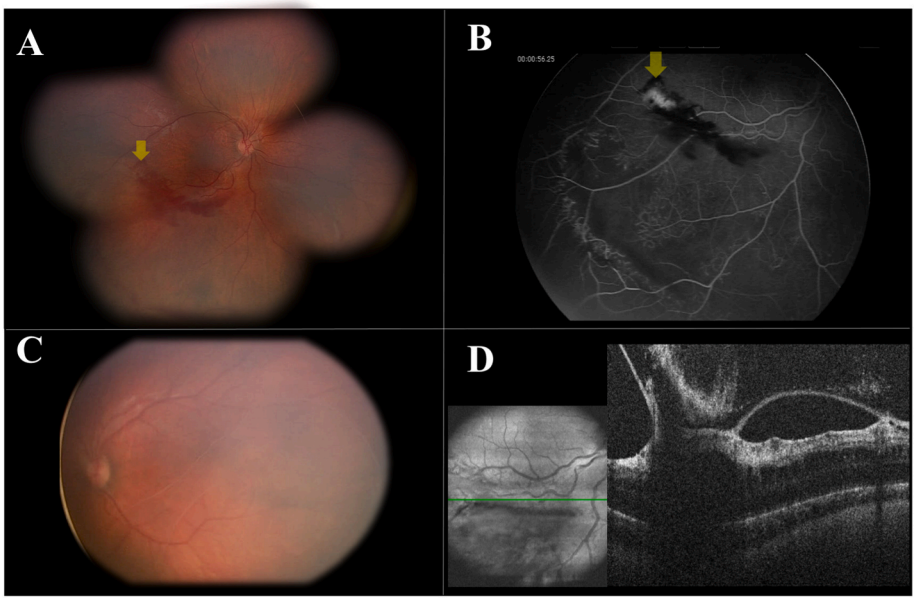

Fig. 1. Fundus imaging, fluorescein angiography and OCT in patient with X-linked retinoschisis and vitreous hemorrhage
A. Mosaic Retcam imaging: color showing preretinal hemorrhage along the inferotemporal arcade, and B. Fluorescein angiography of inferotemporal capillary non-perfused retina in the schisis cavity with fluorescein leakage from extraretinal neovascularization (yellow arrow). C. Left eye: attached retina and vitreous veils overlying the macula. D. Vitreous membrane exerts traction on retina superior to schisis cavity seen on infrared image at right. Cystic spaces in OCT to left. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

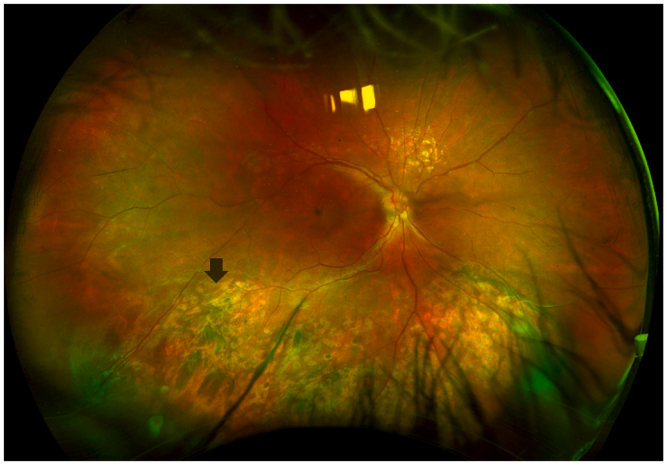

Fig. 2. Fundus imaging of the right eye after laser photocoagulation
Ultrawide field color imaging showing resolution of hemorrhage after laser treatment (black arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

cells within layers of the retina that express angiogenic factors,[2] including the RPE, glia and ganglion cells, as examples.[11] Extraretinal neovascularization has been identified using wide angle FA in XLRS[12] and in areas of overlying primary retinoschisis by OCT.

Traction may also contribute to extraretinal neovascular growth onto a vitreous scaffold since the layers of the retina are less adherent to one another than to the vitreous in XLRS due to a defect in the expression of *RS1* and retinoschisin.[1] In our case, vitreoretinal traction was appreciated by OCT. Besides vitreous traction disrupting capillaries within the schisis and causing capillary non-perfusion, the neovascularization may then grow onto the surface of the vitreous. What is unknown is if the separation of different retinal layers is more likely to be associated with extraretinal neovascularization.

Our rationale for using laser photocoagulation to ablate the RPE was to reduce the hypoxic drive from oxygen demand of retina lacking vascular perfusion where the schisis disrupted retinal vasculature. The RPE is perfused largely by the choroid and expresses angiogenic factors in diseases known to affect the inner retina.[13,14] We propose that laser ablation of the RPE reduced the angiogenic factors from the RPE and may have allowed choroidal oxygen no longer used by the RPE to diffuse to the retina and reduce hypoxic demand.

4. Conclusion

In this patient with XLRS, vitreous traction caused retinoschisis, capillary disruption and capillary non-perfusion within the schisis that contributed to hypoxia induced extraretinal neovascularization. FA and OCT helped to identify the causes of vitreous hemorrhage and develop a management plan. FA-guided laser to capillary non-perfusion in the outer retina of the schisis reduced extraretinal neovascularization and allowed spontaneous clearing of vitreous hemorrhage.

Financial

None.

Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

Declaration of competing interest

None.

References

1. Hartnett ME. *Pediatric Retina*. 3er edition. Philadelphia: Lippincott Williams & Wilkins; 2021:468–477. Section IV. Genetics and developmental disorders in pediatric retina.
2. Pearson R, Jagger J. Sex linked juvenile retinoschisis with optic disc and peripheral retinal neovascularisation. *Br J Ophthalmol*. 1989;73(4):311–313.
3. Lee JJ, Kim JH, Kim SY, Park SS, Yu YS. Infantile vitreous hemorrhage as the initial presentation of X-linked juvenile retinoschisis. *Kor J Ophthalmol*. 2009;23(2):118–120.
4. Ibad S, Wilkins CS, Pinhas A, Sun V, Wieder MS, Deobhakta A. Acute vitreous and intraretinal hemorrhage with multifocal subretinal fluid in juvenile X-linked retinoschisis. *Case Rep Ophthalmol Med*. 2020;2020:6638553.
5. Prasad A, Wagner R, Bhagat N. Vitreous hemorrhage as the initial manifestation of X-linked retinoschisis in a 9-month-old infant. *J Pediatr Ophthalmol Strabismus*. 2006;43(1):56–58.
6. Huang L, Sun L, Wang Z, et al. Clinical manifestation and genetic analysis in Chinese early onset X-linked retinoschisis. *Mol Genet Genomic Med*. 2020;8(10), e1421.

7. Lembo A, Bacci GM, Serafino M, et al. Unusual presentation of early-onset X-linked retinoschisis: report after 1yearof multimodal follow -up. *Eur J Ophthalmol*. 2021;31(3):NP60–NP64.
8. Fahim AT, Ali N, Blachley T, Michaelides M. Peripheral fundus findings in X-linked retinoschisis. *Br J Ophthalmol*. 2017;101(11):1555–1559.
9. Rosenfeld PJ, Flynn Jr HW, McDonald HR, et al. Outcomes of vitreoretinal surgery in patients with X-linked retinoschisis. *Ophthalmic Surg Laser*. 1998;29(3):190–197.
10. Sen P, Agarwal A, Bhende P, et al. Outcome of vitreoretinal surgery for rhegmatogenous retinal detachment in X-linked juvenile retinoschisis. *Indian J Ophthalmol*. 2018;66(12):1825–1831.
11. Le YZ. VEGF production and signaling in Müller glia are critical to modulating vascular function and neuronal integrity in diabetic retinopathy and hypoxic retinal vascular diseases. *Vision Res*. 2017;139:108–114.
12. Berenberg TL, Van Tassel SH, Patel SN, Chan RV. Juvenile X-linked retinoschisis: a comparison of imaging modalities and review of angiographic findings. *Retina*. 2016;36(12):e117–e119.
13. Stone J, Itin A, Alon T, et al. Development of retinal vasculature is mediated by hypoxia-induced vascular endothelial growth factor (VEGF) expression by neuroglia. *J Neurosci*. 1995;15(7 Pt 1):4738–4747.
14. Baker QB, Podgorski GJ, Vargis E, Flann NS. A computational study of VEGF production by patterned retinal epithelial cell colonies as a model for neovascular macular degeneration. *J Biol Eng*. 2017;11:26.