CASE REPORT PEER REVIEWED | OPEN ACCESS

Ophthalmic artery ischemia in hemophagocytic lymphohistiocytosis: A case report and review of current literature

Ayushi Gupta, Neal Shah, Zine ElHousseini, Fion Bremner, Riaz Asaria

ABSTRACT

Introduction: This case report describes the ocular manifestations of hemophagocytic lymphohistiocytosis in a 35-year-old male with suspected Adult-onset Still's Disease. Documented ocular presentations of hemophagocytic lymphohistiocytosis are variable, and the pathophysiology remains unclear. A complete review of the current literature suggests that posterior segment findings, including retinal and vitreous hemorrhage, are most common.

Case Report: Here we describe the first published case of bilateral combined choroidal and retinal ischemia in a patient with ocular hemophagocytic lymphohistiocytosis. This is suggestive of complete ophthalmic artery occlusion driving proliferative retinopathy. Mechanistic hypotheses include anemia, thrombocytopenia, coagulopathy, and histiocytic infiltration.

Conclusion: In this case, pre-retinal hemorrhage, retinal hemorrhage, and vitreous hemorrhage were treated with panretinal photocoagulation, pars plana vitrectomy, and bevacizumab at different stages in each eye. Unusually for ocular hemophagocytic lymphohistiocytosis, the patient developed a unilateral tractional retinal detachment, later thought to be due to early administration bevacizumab prior to vitrectomy in the left eye. Final visual acuity in this patient remains poor, and worse in the left eye. We therefore suggest early vitrectomy to maintain adequate views of the fundus before bevacizumab or panretinal photocoagulation in this patient cohort.

Keywords: Choroidal ischemia, Ocular hemophagocytic lymphohistiocytosis, Ophthalmic artery occlusion, Retinal ischemia

Ayushi Gupta[1], Neal Shah[2], Zine ElHousseini[3], Fion Bremner[4], Riaz Asaria[5]

Affiliations: [1]MBBS, Junior Doctor, Whittington Hospital, London, United Kingdom; [2]MBBS, Junior Doctor, University College Hospital, London, United Kingdom; [3]MD, Consultant Ophthalmic Surgeon and Vitreoretinal Surgeon, Ophthalmology Department, Royal Free Hospital, London, United Kingdom; [4]PhD, Consultant Ophthalmic Surgeon and Neuro-ophthalmologist, National Hospital for Neurology & Neurosurgery, Neuro-ophthalmology Department, Queen Square, London, United Kingdom; [5]BM, MD, Associate Professor and Consultant Ophthalmologist and Vitreoretinal Specialist, Ophthalmology Department, Royal Free Hospital, London, United Kingdom.

Corresponding Author: Ayushi Gupta, Whittington Hospital, Magdala Avenue, London N19 5NF, United Kingdom; Email: ayushi.gupta2@nhs.net

Received: 12 February 2024
Accepted: 29 March 2024
Published: 03 May 2024

How to cite this article

Gupta A, Shah N, ElHousseini Z, Bremner F, Asaria R. Ophthalmic artery ischemia in hemophagocytic lymphohistiocytosis: A case report and review of current literature. J Case Rep Images Opthalmol 2024;7(1):5–13.

Article ID: 100040Z17AG2024

****

doi: 10.5348/100040Z17AG2024CR

INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a rare immune disease, mediated by uncontrolled macrophage, natural killer cell and cytotoxic T-lymphocyte activation, and resulting in disseminated intravascular coagulation and multi-organ dysfunction [1, 2]. Hemophagocytic lymphohistiocytosis is classified into primary (genetic) or secondary (acquired or reactive), and the mortality rate is as high as 57.8% [2, 3]. Previously, ocular involvement

was considered rare; however, the latest evidence suggests that as many as 39% of HLH patients have some degree of ocular sequelae [4]. Several case reports of HLH with various types of ocular involvement have been published to date, with one retrospective study performed. We report the first case of combined retinal and choroidal ischemia in ocular HLH.

CASE REPORT

A previously healthy 35-year-old man developed arthralgia, fever, rash, and malaise. He presented to Accident and Emergency (A&E) with a seizure and reduced Glasgow Coma Scale (GCS), requiring intubation. During his hospital stay he was extensively investigated with blood tests, brain imaging, lumbar puncture, and liver, spleen, skin and bone marrow biopsies, and genetic testing (Tables 1 and 2). Investigations were in-keeping with a diagnosis of secondary HLH (H score 217), with previously undiagnosed Adult-onset Still's Disease thought to be the driver. He was transferred to a tertiary center for ongoing management with anakinra, high-dose intravenous (IV) methylprednisolone, and etoposide.

Once extubated, he reported bilateral visual symptoms including dry eye and reduced visual acuity (VA) at the level of counting fingers (CF). Bedside fundoscopy found severe bilateral four quadrant retinal hemorrhages and peripapillary cotton-wool spots. There was no uveitis and the optic discs were normal. Appearances were in-keeping with an ischemic retinal vasculopathy with differentials including intravascular lymphoma.

Following a 5-month hospital stay he was followed up in the Ophthalmology clinic where he was found to have bilateral macular ischemia, 4-quadrant preretinal and retinal hemorrhages (RH), and right vitreous hemorrhage (VH) (Figure 1A and B). Fundus fluorescein angiography (FFA) demonstrated poor retinal and choroidal filling (Figure 2A and B). Visual acuity at this time was hand movements (HM) in the right eye (RE) and 6/60 in the left eye (LE). He was managed with panretinal photocoagulation (PRP) in the RE as the view of the fundus was preserved, and VA temporarily improved to CF.

However, two months after presentation to the eye clinic, the VH worsened in his RE and a dense VH developed in his LE (Figure 3A and B) reducing VA to CF RE and HM LE. He underwent right pars plana vitrectomy with EndoLaser and received bevacizumab bilaterally. Five months later, the patient developed a LE tractional retinal detachment (TRD) with VA worsened to no perception of light (NPL). He underwent left pars plana vitrectomy with EndoLaser retinopexy, but there was no recovery of sight. Following these interventions, his VA is now stable at CF RE and NPL LE.

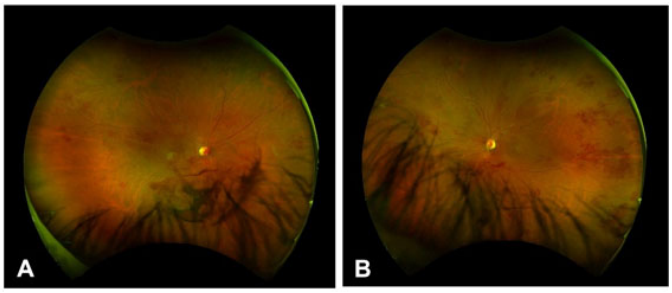

Figure 1: (A) Fundus imaging of the right eye five months after presentation with hemophagocytic lymphohistiocytosis shows an ischemic macula, 4-quadrant preretinal hemorrhage, and retinal hemorrhage with inferior vitreous hemorrhage. (B) Fundus imaging of left eye at the same time identifies macular ischemia and 4-quadrant preretinal hemorrhage and retinal hemorrhage.

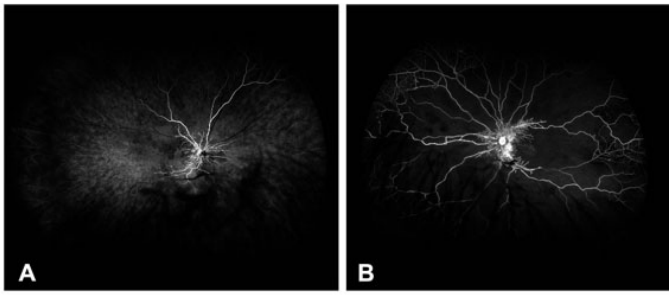

Figure 2: Fundus fluorescein angiography five months after presentation with hemophagocytic lymphohistiocytosis reveals poor retinal filling and patchy choroidal filling, worse in the right eye (A) than the left (B), suggestive of retinal and choroidal ischemia.

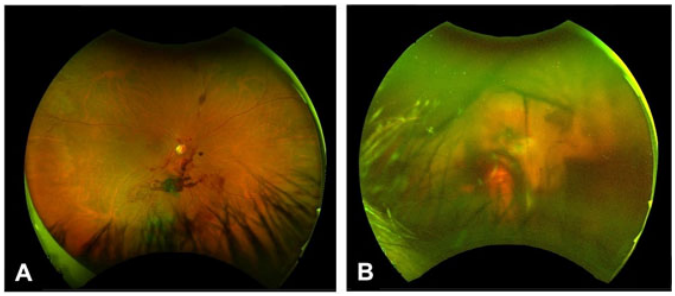

Figure 3: (A) Fundus imaging of the right eye seven months after presentation with hemophagocytic lymphohistiocytosis shows worsening preretinal, retinal, and vitreous hemorrhages. (B) The view of the left fundus at this time is completely obscured by dense vitreous hemorrhage.

DISCUSSION

Currently, there are 19 case reports (Table 3), 3 case series (Table 4), and 1 retrospective study regarding ophthalmic manifestations of HLH [4]. Posterior segment findings are well documented in the literature. Retinal hemorrhages and VH are some of the most common manifestations of HLH, and these are in keeping with the fundus examination in our case [4–14] (Figures 1A, B and 3A, B). However, our FFA images reveal reduced retinal filling and poor choroidal filling (Figure 2A and B), not

previously identified in the literature. These findings are suggestive of complete ophthalmic artery involvement.

Ischemia of the ophthalmic artery is thought to have driven proliferative retinopathy, resulting in RH and eventually VH in both eyes in our patient. The pathophysiology of ocular findings in HLH has been hypothesized to be due to lymphohistiocytic infiltration and inflammation, coagulopathy leading to ischemic vasculopathy, exacerbated by anemia [6–10, 12, 13, 15–22]. These are all plausible hypotheses causing bilateral ophthalmic artery ischemia in our case.

Serous retinal detachment has been documented in ocular HLH and pathophysiology is in keeping with an inflammatory or infiltrative process [4, 19, 23]. However, the TRD seen in our patient is not explained by our ischemic hypothesis. Although commonly used as an adjunct to TRD repair in proliferative retinopathy, bevacizumab has been shown in some cases to result in development or progression of TRD [24, 25]. Therefore, it is possible that bevacizumab contributed to the LE TRD in our case.

Visual acuity outcomes are not always reported in the literature as many cases occur in children or patients are systemically very unwell (Tables 3 and 4). However, reported VA is generally poor. In our case, outcomes were better in the RE, which received vitrectomy prior to treatment with bevacizumab. Therefore, we advocate for early vitrectomy in cases of ocular HLH with VH to enable visualization, assessment, and prompt treatment of retinal pathology with PRP or intravitreal bevacizumab.

Table 1: Patient investigations—hematinics, biochemistry, immunology, and genetic results

Investigations	Result
Hematinics and biochemistry	
Hb	66 g/dL
Platelets	96 × 10^9/L
White cell count	30.6 × 10^9/L
Neutrophils	27 × 10^9/L
Ferritin	21,363 ng/mL
Fibrinogen	6.3 g/L
Triglycerides	9.5 mmol/L
CRP	62 mg/dL
Autoimmune	
C3, C4, complement	Negative
Anti-DNA	Negative
Anti-GBM	Negative
Anti-MPO	Negative
ANCA	Negative
Rheumatoid factor	15 units/mL
Anti-Hu	Negative
Anti-Ri	Negative
Anti-Yo	Negative
Viral/Bacterial	
Hepatitis C	Negative
Hepatitis B	Negative
HIV	Negative
HTLV1/2	Negative
CMV	Negative
Enterovirus	Negative
EBV	Negative
Legionella/pneumococcal antigen	Negative
Leishmania	Negative
Rotavirus	Negative
Rickettsia	Negative
Salmonella	Negative

Table 1: *(Continued)*

Investigations	Result
Shigella	Negative
Sandfly fever	Negative
Tick borne encephalitis	Negative
West Nile virus	Negative
Trophyrema whipplei	Negative
Toxoplasma	Negative
Treponema	Negative
Beta D glucan	Negative
Galactomannan	Negative
Immunology	
Soluble CD25	<312 u/mL
CD3 (CD8+CD107+)	0.5%
Perforin (CD56+)	75.9%
Genetics	
SAP (XLP1)	95.4%
XIAP (XLP2)	93.1%

Table 2: Patient investigations—radio-imaging and tissue biopsy results

Investigations	Result
Imaging	
CT head	No abnormality detected
Whole body PET	FDG avid lymphadenopathy in the left supraclavicular region. Only low-grade uptake within a few small volume nodes elsewhere above and below the diaphragm, non-specific. Bilateral lower lobe areas of consolidation with some mild increased tracer uptake. Diffuse increased FDG uptake within the spleen and bone marrow, likely reactive. Non-specific uptake within the prostate gland.
Transthoracic echo	No significant abnormality
Transoesophageal echo	No significant abnormality
Tissue	
CSF	Glucose 3.7 mg/dL, protein 1.8 mg/dL, lactate 2 mmol/L, LDH 31 units/L, no white cells, no organisms
Bone marrow biopsy	Macrophage activation with phagocytosis, no evidence hematological malignancy/infiltration, consistent with HLH
Liver biopsy	Lymphohistiocytic inflammatory cell infiltrate, histiocytes, iron deposition, consistent with HLH
Skin biopsy	Minimal superficial perivascular lymphocytic inflammation, thrombotic findings. CD79a, CD20 negative.
Spleen biopsy	Numerous acute inflammatory Cells (macrophages, neutrophils), platelets, and scattered lymphocytes Numerous acute inflammatory cells, platelets, and scattered lymphocytes. CD61, CD34, CD117, and EBER negative.

Table 3: Literature summary of published case reports [5–23]

Author	Patient age	Gender	Trigger for HLH	Ocular examination findings	Intervention(s)—systemic and ocular	Visual outcomes	Hypothesis
Finn, et al. [15]	34 weeks	Male	Secondary, viral	Bilateral peripheral retinal ischemia, bilateral vascular proliferation and neovascularisation, unilateral macular dragging	Bone marrow transplant, laser photocoagulation	Fix and follow bilaterally	Severe anemia, disseminated intravascular coagulation (DIC), dysfibrinogenemia
Guilcher, et al. [5]	7 years	Female	Secondary, viral—EBV	Bilateral multiple subhyaloid hemorrhages with macular involvement	Vitrectomy, membrane peel, hyaloid stripping, EndoLaser	20/400 > 20/20 RE, 20/200 > 20/25 LE	Not discussed
Liao and Thompson [6]	14 years	Male	Secondary, viral	Bilateral flame shaped hemorrhages at the macula, unilateral subconjunctival hemorrhages	Nil	20/20 bilaterally	Severe anemia, histiocytic infiltration
Suzuki, et al. [7]	55 years	Male	Secondary, unknown	Bilateral dot-like hemorrhages, cotton-wool spots around optic disc	Prednisolone, ciclosporin	20/25 > 20/25 RE, 20/15 > 20/20 LE	Histiocytic infiltration
Matsubara, et al. [16]	7 years	Female	Secondary, unknown	Bilateral cotton-wool spots, extensive retinal edema, normal large vessels	Dexamethasone, etoposide, ciclosporin	22/50 RE, 20/200 LE	Arterial obstruction, dysfibrinogenemia
Li, et al. [23]	53 years	Male	Secondary, unknown	Unilateral keratic precipitates, flare, vitreous haziness, multiple serous pigment epithelial detachment, macular edema	Methylprednisolone, immunoglobulins, meropenem	20/200 RE (died)	Not discussed
Sebrow, et al. [8]	52 years	Female	Secondary, viral—EBV/CMV	Bilateral retinal whitening and edema, flame shaped hemorrhages, subretinal fluid, sparing of macular arterioles	Prednisolone, etoposide, rituximab	Hand movements	Occlusion of peripapillary capillaries, DIC
Cai, et al. [26]	10 month	Female	Primary (STXBP2)	Downbeat nystagmus	Etoposide , dexamethasone	Fully resolved	Not discussed
Engelbert, et al. [27]	1 month	Female	Primary, unknown	Bilateral white dots at posterior pole	Nil	No acuity recorded	Not discussed
Chiang, et al. [28]	2 year	Male	Primary (PRF1)	Unilateral 6th nerve palsy	Etoposide , dexamethasone, emapalumab, bone marrow transplant	Not recorded, nerve palsy resolved	Not discussed

Table 3: *(Continued)*

Author	Patient age	Gender	Trigger for HLH	Ocular examination findings	Intervention(s)—systemic and ocular	Visual outcomes	Hypothesis
Lee, et al. [9]	33 years	Male	Secondary, viral—CMV/EBV/HIV	Bilateral roth spots, unilateral large macular subinternal limiting hemorrhage and dome elevation, contralateral small subinternal limiting hemorrhage	Highly active antiretroviral therapy, etoposide, dexamethasone, immunoglobulins	20/400RE, 20/70 LE (died)	Anemia, thrombocytopoenia
Shekarchian, et al. [10]	9 years	Male	Unknown	Unilateral relative afferent pupillary defect, optic disc swelling and peripapillary hemorrhage, contralateral mild optic nerve margin blurring, splinter hemorrhage, macular epiretinal hemorrhage	Systemic chemoradiotherapy	20/40 > light perception RE, 20/20 > 10/20 LE	Tumoral infiltration
Suhr, et al. [17]	1 month	Female	Primary, unknown	Bilateral small white spots throughout the macula and beyond the arcades	Ciclosporin, dexamethasone, etoposide, stem cell transplant	No acuity recorded (died)	Histiocytic infiltration
Barreiro-González, et al. [11]	11 years	Female	Secondary, dermatomyositis	Bilateral venous tortuosity, flame like hemorrhage, cotton-wool spots, subcapsular cataract	Corticosteroids	20/20 RE stable, 20/20 LE stable	Not discussed
Chuang, et al. [12]	72 years	Female	Secondary, unknown	Bilateral keratic precipitates, moderate anterior chamber cells, posterior synechiae, vitritis, retinal hemorrhage and cotton-wool spots, cataracts	Oral and topical prednisolone	20/100 > 20/70 RE, 20/200 > 20/70 LE. Retinopathy and panuveitis resolved	Cytokine/interferon mediated
Chong, et al. [18]	8 months	Female	Primary (PRF1)	Left facial nerve palsy	Dexamethasone, etoposide, cyclosporin, ceftriaxone, aciclovir, gentamicin, chemotherapy (unspecifed), stem cell transplant	Normal pupillary responses, roving eye movements with poor tracking bilaterally	Histiocytic infiltration of optic nerve
Lee and Mieler, [19]	31 years	Female	Secondary, unknown	Bilateral diffuse macular edema, multiple serous pigment epithelial detachments in posterior pole and nasal retina	Nil	20/60 RE, 20/40 LE (died)	Uveal inflammation, histiocytic infiltration

Table 3: *(Continued)*

Author	Patient age	Gender	Trigger for HLH	Ocular examination findings	Intervention(s)—systemic and ocular	Visual outcomes	Hypothesis
Kawamura, et al. [20]	10 years	Male	Unknown	Unilateral upper eyelid swelling, optic disc edema and peripapillary retinal hemorrhages, contralateral multiple retinal white patches with perivenous distribution, bilateral optic nerve enlargement	Intrathecal methotrexate, etoposide, bone marrow transplant	20/130 > 20/25 > 20/20 RE, 6/200 > 20/50 > 20/25 LE	Histiocytic infiltration
Yao, et al. [21]	51 years	Male	Secondary, viral	Unilateral and eventually bilateral uveitis, irregular patchy of fluorescence of the choroid, multiple pinpoint areas of leakage and blocked fluorescence in the posterior pole	Gancyclovir, ofloxacin, prednisolone	20/200>20/40 LE	Uveal inflammation

Abbreviations: LE: left eye, RE: right eye, EBV: Epstein–Barr virus, CMV: cytomegalovirus, HIV: Human immunodeficiency virus.

Table 4: Literature summary of published case series [24–26]

Author	Patient age	Gender	Trigger for HLH	Ocular examination findings	Intervention(s)	Visual outcomes	Hypothesis
Kim, et al. [22]	8 weeks	Male	Primary (XIAP)	Bilateral uveitis progressing to retinal fibrosis, choroidal thickening and recurrent intraocular hemorrhage; cataract and band keratopathy	Methotrexate, mycophenolate, and adalimumab, canakinumab, bone marrow allograft, vitrectomy with silicone oil	Perception of light LE	Not discussed
	53 years	Female	Secondary, viral—EBV	Chemosis and proptosis, multiple retinal nerve fiber layer microinfarcts	Steroid, intravenous immunoglobulin, rituximab, ciclosporin, tarsorrhaphy	No acuity recorded (died)	Diffuse orbital infiltration
Vizcaino, et al. [13]	20 years	Male	Secondary, viral—EBV	Retinal hemorrhages	Methylprednisolone	No acuity recorded (died)	DIC
	70 years	Male	Secondary, acquired immunodeficiency syndrome	Grossly normal (ocular involvement identified on autopsy)	Prednisolone	No acuity recorded, reporting left visual loss (died)	Inflammatory infiltration
	49 years	Male	Secondary, unknown	Grossly normal (ocular involvement identified on autopsy)	Dexamethasone, etoposide	No acuity recorded (died)	Inflammatory infiltration
Rooms, et al. [14]	11 days	Male	Unknown	Peripheral perivascular retinal hemorrhages with peripheral retinal necrosis	Dexamethasone, cyclosporin	No acuity recorded	Not discussed

Table 4: *(Continued)*

Author	Patient age	Gender	Trigger for HLH	Ocular examination findings	Intervention(s)	Visual outcomes	Hypothesis
	4 months	Male	Unknown	Bilateral retinal hemorrhages	Craniotomy to evacuate subdural bleed, transfused red cells, platelets, fresh-frozen plasma, ventilatory assistance	No acuity recorded	Not discussed

Abbreviations: LE: left eye, EBV: Epstein–Barr virus.

CONCLUSION

Ocular manifestations of HLH are more common than previously believed. Emerging evidence suggests that the posterior segment is most commonly affected. To our knowledge, this is the first documented case of combined retinal and choroidal ischemia in a single individual with ocular HLH, suggestive of complete ophthalmic artery involvement in this patient. Visual acuity is often poor; however, early vitrectomy in cases of VH may improve longer term visual outcomes.

REFERENCES

1. Griffin G, Shenoi S, Hughes GC. Hemophagocytic lymphohistiocytosis: An update on pathogenesis, diagnosis, and therapy. Best Pract Res Clin Rheumatol 2020;34(4):101515.
2. Morimoto A, Nakazawa Y, Ishii E. Hemophagocytic lymphohistiocytosis: Pathogenesis, diagnosis, and management. Pediatr Int 2016;58(9):817–25.
3. Knaak C, Schuster FS, Nyvlt P, et al. Treatment and mortality of hemophagocytic lymphohistiocytosis in adult critically ill patients: A systematic review with pooled analysis. Crit Care Med 2020;48(11):e1137–46.
4. Wang L, Suo L, Kou F, et al. Ocular phenotypes in patients with hemophagocytic lymphohistiocytosis: A retrospective analysis in a single center over 7 years. Am J Ophthalmol 2023;253:119–31.
5. Guilcher GM, Gardiner JA, Wadsworth LD, Dix DB. Retinal hemorrhages requiring vitrectomy in a patient with hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer 2008;51(1):145.
6. Liao PM, Thompson JT. Ophthalmic manifestations of virus-associated hemophagocytic syndrome. Arch Ophthalmol 1991;109(6):777.
7. Suzuki S, Mizota A, Adachi-Usami E. A case of hemophagocytic syndrome with retinal changes resembling acute posterior multifocal placoid pigment epitheliopathy. Retina 2002;22(2):219–22.
8. Sebrow DB, Dhrami-Gavazi E, Horowitz JD, Yannuzzi LA. Purtscher retinopathy as a manifestation of hemophagocytic lymphohistiocytosis. Retin Cases Brief Rep 2017;11(4):335–8.
9. Lee AG, Kini TA, Igbinoba R, Al Othman BA, Li H. Roth spots may be ocular sign of hemophagocytic lymphohistiocytosis. Ophthalmology Times 2019. [Available at: https://www.ophthalmologytimes.com/view/roth-spots-may-be-ocular-sign-hemophagocytic-lymphohistiocytosis]
10. Shekarchian F, Abadi MKA, Shariati MM. Clinical approach to a child with hemophagocytic lymphohistiocytosis and bilateral optic nerve head infiltration: A case report and brief literature review. Clin Case Rep 2023;11(10):e7999.
11. Barreiro-González A, Cerdà-Ibáñez M, Barranco González H, et al. Purtscher-like retinopathy associated with dermatomyositis and hemophagocytic lymphohistiocytosis. Arch Soc Esp Oftalmol (Engl Ed) 2018;93(4):202–5.
12. Chuang CC, Hsiao CH, Lin KK, Chen KJ, Lai CC, Hwang YS. Bilateral panuveitis associated with hemophagocytic lymphohistiocytosis: A case report. Journal of the Ophthalmological Association of the Republic of China 2009;48(3):353–7.
13. Vizcaino MA, Eberhart CG, Rodriguez FJ. Hemophagocytic lymphohistiocytosis in adults with intraocular involvement: Clinicopathologic features of 3 cases. Ocul Oncol Pathol 2017;4(1):1–11.
14. Rooms L, Fitzgerald N, McClain KL. Hemophagocytic lymphohistiocytosis masquerading as child abuse: Presentation of three cases and review of central nervous system findings in hemophagocytic lymphohistiocytosis. Pediatrics 2003;111(5 Pt 1):e636–40.
15. Finn AP, Roehrs P, Grace SF, Vajzovic L. Ischemic retinal vascular disease in an infant with hemophagocytic lymphohistiocytosis. JAMA Ophthalmol 2017;135(11):1277–9.
16. Matsubara K, Nigami H, Harigaya H, et al. Ocular involvement and visual sequelae in hemophagocytic lymphohistiocytosis in association with congenital dyfsfibrinogenemia. Pediatr Hematol Oncol 1998;15(4):365–70.
17. Suhr KS, Chiang MF, Flynn JT, Engelbert M. Ocular involvement in hemophagocytic syndrome: A novel funduscopic manifestation and review of the literature. Retin Cases Brief Rep 2016;10(4):345–8.
18. Chong KW, Lee JH, Choong CT, et al. Hemophagocytic lymphohistiocytosis with isolated central nervous system reactivation and optic nerve involvement. J Child Neurol 2012;27(10):1336–9.
19. Lee EW, Mieler WF. Ocular findings in a patient with hemophagocytic syndrome. Arch Ophthalmol 2006;124(11):1656–8.
20. Kawamura H, Hatsukawa Y, Furukawa A, Inoue M, Kawa K. Ophthalmic findings in a case of hemophagocytic syndrome. Am J Ophthalmol 1997;124(2):261–3.

21. Yao H, Liu Y, Ding W, Xu Y, Cheng Y. Ocular findings in a patient with virus-associated hemophagocytic syndrome. Ocul Immunol Inflamm 2012;20(3):233–4.
22. Kim J, Steeples LR, Jones NP. Ocular involvement in the histiocytoses: A literature review with an illustrative case series. Ocul Immunol Inflamm 2022;30(3):600–14.
23. Li X, Ma Y, Tang J, Chen T, Ma X. A hemophagocytic lymphohistiocytosis patient that presented with unilateral panuveitis. Ocul Immunol Inflamm 2017;25(2):275–7.
24. Arevalo JF, Sanchez JG, Saldarriaga L, et al. Retinal detachment after bevacizumab. Ophthalmology 2011;118(11):2304.e3–7.
25. Saldarriaga L, Arevalo J, Sanchez JG, et al. Risk factors for the development or progression of tractional retinal detachment (TRD) after intravitreal Bevacizumab (Avastin) used as an adjuvant to vitrectomy for the management of severe proliferative diabetic retinopathy (PDR). Invest Ophthalmol Vis Sci 2010;17;51(13):4239.
26. Cai CX, Siringo FS, Odel JG, et al. Downbeat nystagmus secondary to familial hemophagocytic lymphohistiocytosis. J Neuroophthalmol 2014;34(1):57–60.
27. Engelbert M, Chiang MF, Flynn JT. Is eye involvement in hemophagocytic lymphohistiocytosis (HLH) an ominous prognostic sign? Presentation of a novel funduscopic picture and review of the literature. Invest Ophthalmol Vis Sci 2007 10;48(13):5168.
28. Chiang HH, Fernandez-Pol S, Bae GH, Rieger KE, Dahmoush HM, Beres SJ. Isolated sixth nerve palsies in a child with familial hemophagocytic lymphohistiocytosis type 2. J Neuroophthalmol 2023;43(1):137–40.

****

Author Contributions

Ayushi Gupta – Conception of the work, Design of the work, Acquisition of data, Interpretation of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Neal Shah – Interpretation of data, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Zine ElHousseini – Interpretation of data, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Fion Bremner – Interpretation of data, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Riaz Asaria – Interpretation of data, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Consent Statement

Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.