Bilateral Primary Vitreoretinal Lymphoma.

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Abstract

Title: Bilateral primary vitreoretinal lymphoma.

Objective: To report a rare case of bilateral primary vitreoretinal lymphoma (PVRL).

Method: Retrospective review of the patient's clinical assessment, vitreous biopsy, and response to treatment.

A 64-year-old female presented with gradual painless blurring of vision, associated with floaters in both eyes for 5 months duration. Her best corrected visual acuity (BCVA) was counting finger 1 foot in the RE and 6/24 in the LE. Anterior segment examination was unremarkable. RE fundus showed severe vitritis with large vitreous clumps and hazy fundus view. Whereas LE fundus showed mild vitritis with minimal vitreous clumps inferiorly with no retinitis, vasculitis, retinal haemorrhage, or sub-retinal infiltrate. All blood investigations including infective screening and tumour markers were unremarkable. A vitreous biopsy was performed in the RE and vitreous cytology showed atypical lymphoid cells highly suspicious for malignancy. As the vitreous sample was scanty, a cell block reading could not be carried out for immunohistochemistry. Magnetic resonance imaging (MRI) of brain and orbits were normal. Patient was diagnosed with presumed bilateral PVRL and intravitreal injection of methotrexate was initiated. MRI brain surveillance was planned for every 6 months. Her BCVA improved to 6/12 in the RE and 6/9 in the LE after completed 15 courses of intravitreal methotrexate.

Conclusion: PVRL is a rare disease in older patients with features of severe vitritis and absence of macular oedema that mimics chronic uveitis and poses diagnostic challenge. Intravitreal methotrexate is an effective and minimal-invasive treatment with good visual outcome if early recognition and prompt treatment.

Conflicts of Interest: The author reports no conflicts of interest.

Keywords: Primary vitreoretinal lymphoma, vitreous biopsy, vitritis, intravitreal methotrexate

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Introduction

Primary vitreoretinal lymphoma (PVRL) is a rare ocular condition, and its diagnosis remains a challenge as it can mimic chronic posterior uveitis1. PVRL is a variant of primary central nervous system lymphoma (PCNSL), which is an aggressive, diffuse

large B-cell malignancy associated with poor prognosis[2]. The commonest symptoms reported by Kimura et al[3] and Fardeau et al[4] were floaters and painless moderate loss of vision. The commonest clinical signs reported included moderate vitritis, retinal pigment epithelium (RPE) pigmentary changes and sub-retinal infiltrate, which was found in 50% of the cases[1]. The estimated annual incidence is 0.46 per 100,000 persons.[5]

Vitreous biopsy is the gold standard for diagnosis of the disease. Once the diagnosis is confirmed, without central nervous system (CNS) involvement, the treatment of choice includes intravitreal injections of methotrexate or rituximab[6]. However, the prognosis is poor, and 42-92% will develop primary CNS lymphoma within 8-29 months[7]. We report a patient with bilateral PVRL that presented with vitritis.

Case Report

A 64-year-old female with underlying dyslipidemia, presented with gradual worsening and painless blurring of vision in both eyes for 5 months. This was associated with floaters. She was being treated initially for bilateral posterior uveitis and was referred to our centre for vitreous biopsy in view of poor response to oral steroid. There was no previous history of ocular disease, trauma, or surgery.

The patient's BCVA worsened bilaterally, from 6/9 to counting finger 1 foot in the RE and 6/9 to 6/24 in the LE over the course of 5 months with the treatment of systemic steroid. There was no proptosis and the extraocular muscle movements were full in all directions with no diplopia. Anterior segment examination was unremarkable. RE fundus showed severe vitritis with large vitreous clumps and limited fundus view (Figure 1A), whereas LE fundus showed minimal vitreous clumps inferiorly with absence of retinitis, vasculitis, retinal haemorrhage, sub-retinal infiltrate or macular thickening (Figure 1B). Optical coherence tomography (OCT) of the macular revealed absence of macular oedema bilaterally. There was no palpable lymph nodes, hepatomegaly, splenomegaly, or central nervous system involvement on systemic examination.

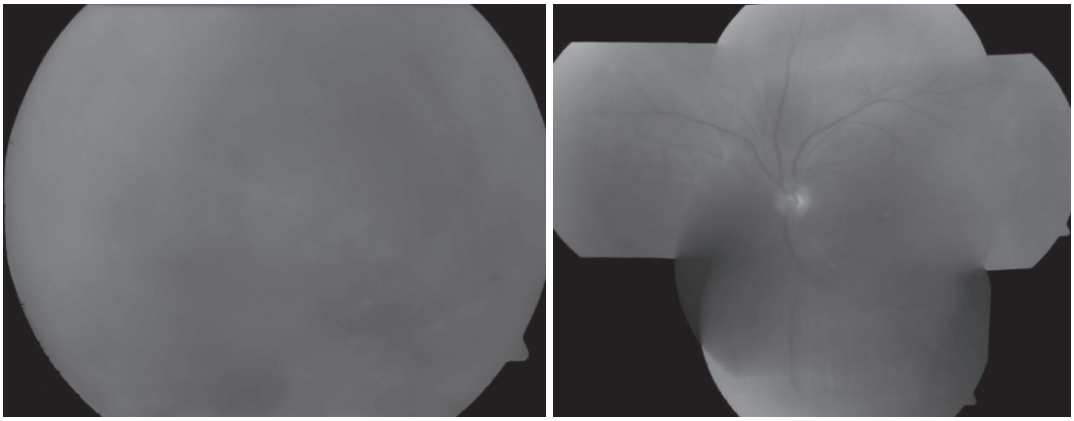

Figure 1: Fundus photo of both eyes before treatment. Right eye showed severe vitritis with large vitreous clumps and poor fundus view (A). Left eye showed minimal vitreous clumps inferiorly (B).

All blood investigations including full blood count, full blood picture, serology for toxoplasmosis, toxocara and syphilis were negative. Chest X-ray showed no signs of tuberculosis, sarcoidosis or malignancy. Mantoux test and tumour markers assessments were also negative.

RE vitreous biopsy was obtained by pars plana vitrectomy procedure. The intra-operative findings during vitrectomy procedure of the RE showed dense vitritis, snowballs inferiorly, retinitis infero-nasally, but there was no retinal haemorrhages or vasculitis seen and the macula was flat. The vitreous sample was

sent for Tuberculosis polymerase chain reaction (TB-PCR), cytology, culture and sensitivity (C&S), Gram stain and potassium hydroxide (KOH) test. All of the results came back negative except for cytology. The vitreous cytology result showed single atypical lymphoid cells with few histiocytes. The atypical cells showed enlarged, hyperchromatic nuclei and prominent nucleoli with high nuclear cytoplasmic ratio, that was highly suspicious for malignancy, suggestive of lymphoma. As the vitreous sample was scanty, a cell block reading could not be carried out for immunohistochemistry.

Patient was diagnosed as bilateral presumed PVRL based on the vitreous cytology findings. Magnetic resonance imaging (MRI) of brain and orbits showed no evidence of orbital or intracranial lesion suggestive of infiltration. The patient was co-managed with an oncologist for the treatment plan. Both eyes were treated with intravitreal injection of methotrexate 400 microgram/0.1ml. Injections were given biweekly for one month, followed by weekly for one month, fortnightly for one month and monthly. She received a total of 15 injections. Following treatment, her BCVA improved to 6/12 in the RE and 6/9 in the LE. Fundus examination showed resolution of vitritis and vitreous clump (Figure 2). MRI brain surveillance was planned for every 6 months and being monitored by both ophthalmologist and oncologist. Subsequent follow-up at one year showed no neurological symptoms with no ocular side-effect of intravitreal methotrexate or any abnormality of the brain on MRI.

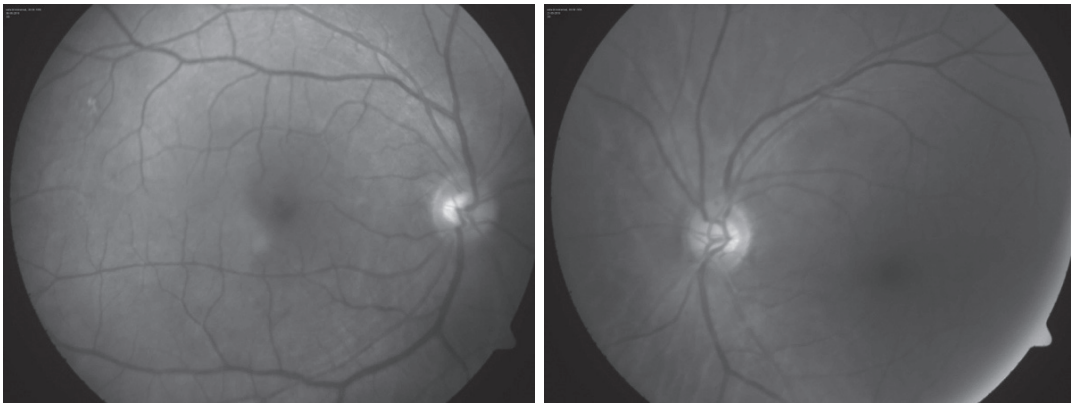

Figure 2: Fundus photo of both eyes after completed intravitreal injection of Methotrexate. Right eye showed clear media and resolved vitritis and vitreous clumps (A). Left eye showed clear media with resolved vitritis and vitreous clumps (B).

Discussion

PVRL commonly presents as a masquerade syndrome making its diagnosis extremely challenging and complicated8. In many cases, PVRL also masquerades as chronic posterior uveitis. The vitreous floaters are frequently thought to occur in vitritis or degenerative changes. Clinically, PVRL typically occurs in older patients with median age range of 60s with almost equal distribution between both genders[9,10.] Phillips et al[11] reported higher incidence in male than in female. No racial or regional variations have been documented[12]. Risk factors for the development of PVRL are immunodeficiency and immunosuppression as reported by Mochizuki et al[13] Our patient was a 64-year-old presented with blurring of vision and associated with floaters. According to Chan et al[19], about 80% of PVRL patients will eventually develop PCNSL.

The differential diagnosis of PVRL includes a wide spectrum of infectious and non-infectious conditions such as toxoplasmosis, syphilis, tuberculosis, viral retinitis, sarcoidosis, Adamantiades-Behcet's disease, idiopathic uveitis, endophthalmitis, amelanotic melanoma and metastasis[2,8].

Vitreous biopsy remains the gold-standard in diagnosing PVRL[3]. The biopsy specimen can be sent for performing a wide range of laboratory examinations including cytological and histopathological examination, immunocytochemistry, flow cytometry, molecular investigations and exploration of cytokine profile[8,14,15]. However, only 40% of the patients, the initial diagnosis of intraocular lymphoma is established with a single biopsy[16]. Therefore, the clinical presentation and progression is important to support the diagnosis. In our patient, the diagnosis was established by cytology from vitreous biopsy. However, due to limited vitreous sample, immunohistochemistry was not performed.

A multidisciplinary assessment of patients with PVRL and/or PCNSL is required and the collaboration between ophthalmologists, pathologists and oncologists (either hemato-oncologists or neuro-oncologists) is essential in optimizing management in these patients5,17,18. Treatment with intravitreal methotrexate is extremely successful in achieving clinical remission of ocular involvement in PVRL with sustainable morbidity[8]. There were no reports of intraocular recurrences in PVRL patients that were treated with intravitreal methotrexate as a first line therapy[12]. The most commonly reported complications were transient elevation of intraocular pressure and corneal epitheliopathy. Increasing the intervals between consecutive injections[7]. Our patient responded with intravitreal injections of methotrexate. Her ocular findings resolved with improvement of BCVA.

Conclusion

PVRL is a rare disease in older patients with features of severe vitritis and absence of macular oedema that mimics chronic uveitis and poses diagnostic challenge. Steroid-resistant chronic uveitis supported by presence of atypical lymphoid cells on cytology suggestive of PVRL. Intravitreal methotrexate is an effective and minimal-invasive treatment with good visual outcome if early recognition and prompt treatment.

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References

1. Tan SZ, Steeples LR, Chhabra R, Jones NP. An unusual case report of primary vitreoretinal lymphoma. BMC Ophthalmol [Internet]. 2018 Sep 14;18(Suppl 1):223. Available from: http://dx.doi.org/10.1186/s12886-018-0860-9
2. Pe'er J, Hochberg FH, Foster CS. Clinical review: treatment of vitreoretinal lymphoma. Ocul Immunol Inflamm [Internet]. 2009 Sep;17(5):299-306. Available from: http://dx.doi.org/10.3109/09273940903370755
3. Kimura K, Usui Y, Goto H, Japanese Intraocular Lymphoma Study Group. Clinical features and diagnostic significance of the intraocular fluid of 217 patients with intraocular lymphoma. Jpn J Ophthalmol [Internet]. 2012 Jul;56(4):383-9. Available from: http://dx.doi.org/10.1007/s10384-012-0150-7
4. Fardeau C, Lee CPL, Merle-Béral H, Cassoux N, Bodaghi B, Davi F, et al. Retinal fluorescein, indocyanine green angiography, and optic coherence tomography in non-Hodgkin primary intraocular lymphoma. Am J Ophthalmol [Internet]. 2009 May;147(5):886-94, 894.e1. Available from: http://dx.doi.org/10.1016/j.ajo.2008.12.025
5. Aziz HA, Peereboom DM, Singh AD. Primary central nervous system lymphoma. Int Ophthalmol Clin [Internet]. 2015 Winter;55(1):111-21. Available from: http://dx.doi.org/10.1097/IIO.0000000000000055
6. Char DH, Kemlitz AE, Miller T. Intraocular biopsy. Ophthalmol Clin North Am [Internet]. 2005 Mar;18(1):177-85, x. Available from: http://dx.doi.org/10.1016/j.ohc.2004.08.007
7. Chan C-C, Sen HN. Current concepts in diagnosing and managing primary vitreoretinal (intraocular) lymphoma.

Discov Med [Internet]. 2013 Feb;15 (81):93-100. Available from: https://www.ncbi.nlm.nih.gov/pubmed/23449111
8. Sagoo MS, Mehta H, Swampillai AJ, Cohen VML, Amin SZ, Plowman PN, et al. Primary intraocular lymphoma. Surv Ophthalmol [Internet]. 2014 Sep;59(5):503-16. Available from: http://dx.doi.org/10.1016/j.survophthal.2013.12.001
9. Chan C-C, Rubenstein JL, Coupland SE, Davis JL, Harbour JW, Johnston PB, et al. Primary vitreoretinal lymphoma: a report from an International Primary Central Nervous System Lymphoma Collaborative Group symposium. Oncologist [Internet]. 2011 Nov 1;16(11):1589-99. Available from: http://dx.doi.org/10.1634/theoncologist.2011-0210
10. Hah YY, Ho SL, Beng SC, Agrawal R. Epidemiology and clinical features of intraocular lymphoma in Singapore. Nepal J Ophthalmol [Internet]. 2019 Jul;11(22):158-66. Available from: http://dx.doi.org/10.3126/nepjoph.v11i2.27822
11. Phillips EH, Fox CP, Cwynarski K. Primary CNS lymphoma. Curr Hematol Malig Rep [Internet]. 2014 Sep;9(3):243-53. Available from: http://dx.doi.org/10.1007/s11899-014-0217-2
12. Kalogeropoulos D, Vartholomatos G, Mitra A, Elaraoud I, Ch'ng SW, Zikou A, et al. Primary vitreoretinal lymphoma. Saudi J Ophthalmol [Internet]. 2019 Jan;33(1):66-80. Available from: http://dx.doi.org/10.1016/j.sjopt.2018.12.008
13. Mochizuki M, Singh AD. Epidemiology and clinical features of intraocular lymphoma. Ocul Immunol Inflamm [Internet]. 2009 Mar;17(2):69-72. Available from: http://dx.doi.org/10.1080/09273940902957305
14. Zhou M, Xu G. Recent progress in the diagnosis and treatment of primary vitreoretinal lymphoma. Taiwan J Ophthalmol [Internet]. 2016 Oct;6(4):170-6. Available from: http://dx.doi.org/10.1016/j.tjo.2016.05.002
15. Araujo I, Coupland SE. Primary Vitreoretinal Lymphoma -- A Review. Asia Pac J Ophthalmol (Phila) [Internet]. 2017 May;6(3):283-9. Available from: http://dx.doi.org/10.22608/APO.2017150
16. Lobo A, Lightman S. Vitreous aspiration needle tap in the diagnosis of intraocular inflammation. Ophthalmology [Internet]. 2003 Mar;110(3):595-9. Available from: http://dx.doi.org/10.1016/S0161-6420(02)01895-X
17. Hoang-Xuan K, Bessell E, Bromberg J, Hottinger AF, Preusser M, Rudà R, et al. Diagnosis and treatment of primary CNS lymphoma in immunocompetent patients: guidelines from the European Association for Neuro-Oncology. Lancet Oncol [Internet]. 2015 Jul;16(7):e322-32. Available from: http://dx.doi.org/10.1016/S1470-2045(15)00076-5
18. Nguyen D-T, Houillier C, Choquet S, Cassoux N, Soussain C, Le Cossec C, et al. Primary Oculocerebral Lymphoma: MTX Polychemotherapy Alone on Intraocular Disease Control. Ophthalmology [Internet]. 2016 Sep;123(9):2047-50. Available from: http://dx.doi.org/10.1016/j.ophtha.2016.03.043