Contents lists available at ScienceDirect

Journal of Acute Disease

journal homepage: www.jadweb.org

Document heading doi: 10.1016/S2221-6189(13)60102-X

A masquerader: A report of rapid progressive primary intraocular lymphoma

Siti Hajar Mat Abu[1,2*], Hanizasurana Hashim[1], Roslin Azni Aziz[1], Norfariza Ngah[1], Adil Hussein[2], Noriah Othman[3]

[1]*Department of Ophthalmology, Selayang Hospital, Selangor, Lebuhraya Selayang-Kepong, 68100, Batu Caves, Selangor, Malaysia*
[2]*Department of Ophthalmology, School of Medical Science, Universiti Sains Malaysia, 16150, Kubang Kerian, Kelantan, Malaysia*
[3]*Department of Pathology, Selayang Hospital, Selangor, Lebuhraya Selayang-Kepong, 68100, Batu Caves, Selangor, Malaysia*

ARTICLE INFO

Article history:
Received 30 March 2012
Received in revised form 24 May 2012
Accepted 20 July 2012
Available online 20 March 2013

Keywords:
Primary intraocular lymphoma
Panuveitis
Vitrectomy
Methotrexate

ABSTRACT

Primary intraocular lymphoma (PIOL) is an uncommon subset of primary central nervous system lymphoma (PCNSL). We report a rapid progressive of this disease in a 73 years old lady who presented with one year history of left eye floaters, associated with deterioration of left vision. Examination revealed left eye vitritis and typical vitreous clumps. Left vitrectomy and vitreous biopsy was performed with result showed few singly dispersed atypical lymphoid cells. She was diagnosed to have Primary Intraocular lymphoma and was started on intravitreal methotrexate. Initially she responded well but later the tumour spread to liver, breast and brain within a year. She finally succumbed to the disease. High index of suspicion of PIOL is mandatory in all elderly patients presenting with panuveitis. Co-management with the Neurologist is vital in the continuous management of these patients in view of the high rate of mortality.

1. Introduction

Primary intraocular lymphoma (PIOL) is a subset of primary central nervous system lymphoma (PCNSL). It is uncommon, but no central database exists for this disease. The Central Brain Tumor Registry of the U.S. recorded an incidence of 0.46 (95% confidence interval (*CI*), 0.45-0.47) per 100 000 person-years in 2004-2007[1]. The principal risk factors for development of primary intraocular lymphoma appear to be older patient age, female gender, and immunosuppression (primary or acquired)[2]. The lymphoma cells are usually aggressive diffuse large, pleomorphic B lymphocytes. Between 65%-90% of patient who initially present with PIOL alone will develop CNS lymphoma[1]. About 30% of patient present with unilateral involvement and 85% of patient had delayed involvement of second eye[3]. We report this rare case of rapid deterioration of progression in Primary intraocular lymphoma.

2. Case report

A 73 years old Chinese lady with no medical illness complained of seeing floaters in the left eye for one year. It was associated with deterioration in the left eye vision. There was no eye pain, redness or prior trauma. She had no history of fever or unwell. No history of cough, night sweat, loss of appetite or weight and no history of contact with PTB patient. She also had no history of joint pain or skin changes, and was not on any medications before. She denied any neurological symptoms such as headache, nausea, vomiting or fits. She had no family history of malignancies. Examination revealed a right eye vision of 6/24 correctable to 6/15 with pin-hole and a left visual acuity of 6/45 not correctable with pin hole. Left eye anterior segment showed mild uveitis with keratic precipitates (Figure 1). Both eye intraocular pressures were normal. Funduscopy on presentation revealed left vitreous clumps with vitritis (Figure 2) and right eye showed drusen at macula area and

*Corresponding author: Siti Hajar Mat Abu, Department of Ophthalmology, School Of Medical Sciences, Universiti Sains Malaysia, 16150, Kubang Kerian, Kelantan, Malaysia.
Tel: +6016 9152172
E-mail: drsitihajar_76@yahoo.com

peripherally. Optical Coherence Tomography showed no macular oedema. Baseline investigations including FBC, RP, LFT, RBS and ESR were normal. Mantoux test was negative. VDRL was non reactive. Chest X-ray was normal. Tumour markers showed normal level of Alpha Fetoprotein and CEA. Initial MRI brain and Orbit showed no evidence of brain or orbital lesions. Ultrasound abdomen finding was unremarkable. Left vitrectomy and vitreous biopsy were performed. The result of the biopsy showed few singly dispersed atypical lymphoid cells, having large nuclei, prominent nucleoli and scanty of cytoplasm. There are few small mature lymphocytes in the background (Figure 3).

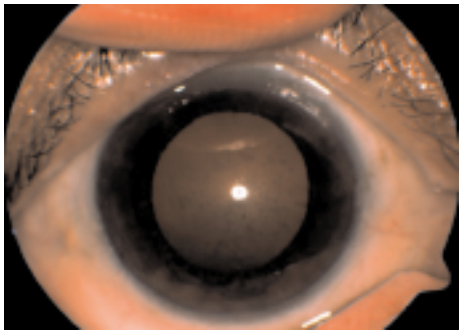

Figure 1. Pigments on anterior capsule indicate previous incidence of anterior uveitis.

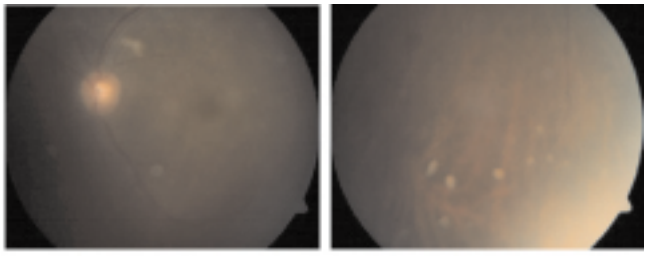

Figure 2. Left eye vitritis with yellowish clumps on initial presentation.

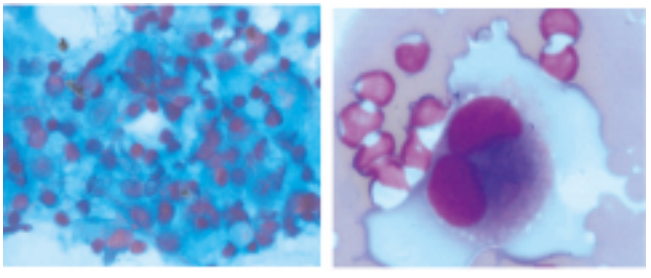

Figure 3. (Left) Arrows showed atypical lymphoid cells display large round nuclei with prominent nucleoli (PAP stain×400). (Right) Atypical lymphoid cell, binucleated (MGG stain×400).

Subsequently the clinical finding worsened and she developed bilateral pan uveitis. There was vitritis with yellowish choroidal lesions at the posterior pole. No vasculitic or retinitis changes noted. A diagnosis of bilateral primary intraocular lymphoma was made. Patient was co-managed with Haematologist and Neurologist team. However, they did not find any significant features to suggest CNS or haematological involvement. Therefore she was managed locally and received ten courses of Intravitreal Methotrexate of 400 μg in 0.1 mL. Initially, she responded. But later she developed few episodes of recurrences. There were numerous new lesions with worsening of vitritis and multifocal choroidal lesions (Figure 4). She was not started on chemotherapy or radiotherapy in view of the absence of neurological or systemic involvement at that point. Patient refused for lumbar puncture for cerebral spinal fluid analysis. Unfortunately, five months after the diagnosis her general condition started to deteriorate with symptoms of lethargy, confusion and forgetfulness. Her vision also deteriorated to hand movements in both eyes. A whole body MRI performed which showed liver and left breast metastasis. She was planned for tissue biopsy. However, patient default her follow up. Three months later she became generally weak and subsequently presented to Emergency Department with unresponsive. A CT brain showed subdural bleed, white matter edema and gross midline shift which was suggestive of brain metastasis (Figure 5). She eventually succumbed to the disease.

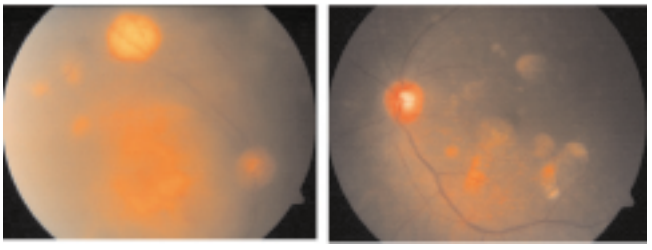

Figure 4. Right eyes fundus photo showed large choroidal lesion and left eye multiple choroiditis.

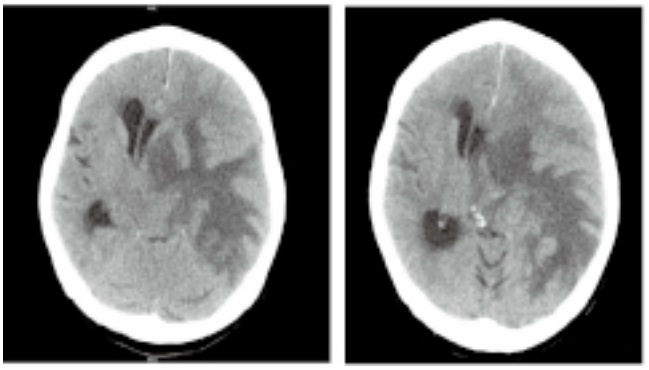

Figure 5. CT brain showed extensive white matter edema and gross midline shift.

3. Discussion

Primary intraocular lymphoma (PIOL) is a variant of extra nodal non-Hodgkin lymphoma[4]. It has been divided

anatomically into vitreoretinal and uveal forms. Intraocular lymphoma can infiltrate any part of the eye, including the vitreous, retina, sub-RPE space, subretinal space and uveal tract. Primary vitreoretinal lymphoma is one of the subtypes, characterized by diffuse cellular infiltration of the vitreous and accumulations of lymphomatous cells in the subpigment epithelial space of the retina[2]. It is generally an aggressive, diffuse large B-cell malignancy (intermediate-grade lymphoma) associated with poor prognosis[4,5]. Our patient showed signs of this subtype of intraocular lymphoma. Other features include retinal vasculitis, vascular occlusion, exudative retinal detachment and optic atrophy. Lack of cystoids macular oedema (CMO) is an important diagnostic clue, since in true uveitis significant vitritis is almost always accompanied by CMO[3].

On the other hand the uveal form is associated with systemic non-Hodgkin lymphoma and also with involvement of orbital structures. It is typically small B-cell proliferation (low-grade lymphoma) and usually occurs with advanced systemic disease. Rare cases of T-cell lymphoma with ocular involvement have been reported[4,5]. Mild anterior uveitis with cells, flare, keratic precipitates, multifocal, large, yellowish and solid sub-RPE infiltrates that progress to involve the choroid, are common signs in this subtype of intraocular lymphoma. Our patient also had developed signs of this subtype of intraocular lymphoma. Therefore, she had a combination of two subtypes; vitreoretinal and uveal forms. Diagnosis of PIOL requires pathologic identification of atypical lymphoma cells from the vitreous or retina. However, the cytopathologic diagnosis is challenging because of the fragility and paucity of the atypical lymphoma cells in the vitreous. Furthermore, atypical lymphoma cells in the vitreous often admix with reactive lymphocytes, necrotic cells and debris, adding to the difficulty of diagnosis[5]. We manage to diagnose our patient by cytological analysis from vitreous sample. This is a sensitive and specific test to confirm the diagnosis despite of clinical suspicious. The correct diagnosis of intraocular lymphoma is often not established until late in the disease course. Most patients are initially misdiagnosed as having an idiopathic diffuse uveitis, posterior uveitis, or vitritis. Even with present of yellowish white chorioretinal lesions and vitritis, an almost pathognomonic presentation, diagnosis is usually delayed. As in this patient the PIOL is masquerading as panuveitis for a year before she presented to us. In term of management, this patient was treated by intraocular injection to avoid systemic toxicity of chemotherapy and risk of complication with radiotherapy as well as risk of partial failure. Smith and associates reported a series of 26 eyes of 16 patients with vitreoretinal lymphoma from two centres using intravitreal injections of 400 μg methotrexate in 0.1 mL. They used a protocol of two injections per week for a month as the induction phase, weekly consolidation injection for a month in one centre and two months in the other centre, and subsequently a maintenance phase of monthly injection to complete one year. All eyes were cleared clinically of lymphoma cells after a maximum of 12 methotrexate injections. Three patients from one centre who had relapse in the eye were treated again using the same protocol, with complete remission[6].

The long term prognosis for patients with PCNSL remains poor. Multiple factors have been found to be of significance in predicting outcomes and survival in patients with PCNSL, including age, performance status, and neurological function, single versus multiple lesions, and superficial cerebral and cerebellar hemisphere lesions versus deep nuclei and periventricular region lesions. The median survival time after detection of infiltrative intraocular lesions in most series is three to five months. Patients with primary central nervous system lymphoma with ocular involvement (PCNSLO) have a poor prognosis even with chemoradiation, and many succumb to central nervous system (CNS) disease within two years[3].

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgements

The authors would like to acknowledge Datin Dr Kalavathy Ramachandram and Dr. Norazlah Bahari for their assistance in preparing this manuscript.

References

[1] Chi-Chao Chana, James L. Rubensteinb, Sarah E. Couplandc, Janet L. Davisd, J. William Harbourg, Patrick B. Johnstone, et al. Primary vitreoretinal lymphoma: A report from an international primary central nervous system lymphoma collaborative group symposium. *Oncologist Express* 2011; **16**(11): 1589-1599.

[2] James J. Augsburger, William G. Tsiras. Lymphoma and leukaemia, section 1 malignant intraocular lymphoma, part 8 intraocular tumors. *Yanoff Duker Ophthalmol* 2009; 911-912.

[3] Russell W. Read. 'Masquerade syndromes: neoplasms', section 9 masquerade syndromes, part 7 uveitis and other intraocular inflammations. *Yanoff Duker Ophthalmol* 2009: 882-886.

[4] Pe'er J, Hochberg FH, Foster CS. Clinical review: Treatment of vitreoretinal lymphoma. *Ocul Immunol Inflam* 2009; **17**(5): 299-306.

[5] Yujuan Wang, Defen Shen, Vinson M. Wang, H. Nida Sen, Chi-Chao Chan. Molecular biomarkers for the diagnosis of primary vitreoretinal lymphoma. *Int J Mol Sci* 2011; **12**: 5684-5697.

[6] Jacob Pe'er. Current approach toward treating vitreoretinal lymphoma. www.oncologynews.biz/pdf/nov_dec_10.