Published in final edited form as:

Clin Experiment Ophthalmol. 2007 July ; 35(5): 468–472.

Primary diffuse large B-cell lymphoma of the spleen with coincident serous retinal detachments responsive to corticosteroids

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Abstract

Non-Hodgkin's lymphoma is the sixth leading cause of cancer death in the USA. Herein, a patient is presented with primary diffuse large B-cell lymphoma whose initial complaint was blurred vision and who presented with corticosteroid-responsive serous retinal detachments mimicking Vogt–Koynagi–Harada. Extensive clinical examination including imaging and blood testing was negative. Splenectomy led to a diagnosis of splenic lymphoma

Keywords

corticosteroids; malignancy; serous retinal detachment

Introduction

Non-Hodgkin's lymphoma is the sixth leading cause of cancer death in the USA. Herein we present a patient with primary diffuse large B-cell lymphoma whose initial complaint was blurred vision and who presented with corticosteroid-responsive serous retinal detachments mimicking Vogt–Koynagi–Harada syndrome (VKH).

Case report

A 58-year-old white man was referred to the National Eye Institute for evaluation of fluctuating blurry vision for evaluation carrying a provisional diagnosis of VKH.¹ He had hyperlipidaemia, mild inactive eczema and bilaterally well-controlled primary open angle glaucoma on timolol 0.5% eye drops. The patient was doing well up to a year ago when he had persistent tinnitus that resolved with a therapeutic trial of oral prednisone. He had then an inconclusive medical work-up; normal central nervous system imaging and evident mild sensorineural hearing loss. He was symptom free until he developed blurry vision with vague malaise 10 months later. He was evaluated by an ophthalmologist who suspected VKH based on the malaise, history of tinnitus and serous retinal detachments (Fig. 1). Both the retinal fluorescein angiography (Fig. 2) and optical coherence tomography (OCT) were abnormal in both eyes (OU), demonstrating serous and pigment epithelial detachments. Ocular B-scan was reportedly normal OU. He was mildly anaemic (Table 1), attributed to bleeding haemorrhoids.

A purified protein derivative skin test for tuberculosis was negative. Oral prednisone was prescribed at a dose of 60 mg daily and tapered off by 10 mg weekly for 6 weeks. There was prompt improvement in the symptoms and coincident decrease in serous detachments over a few weeks (Fig. 3). However, a week after termination of prednisone he experienced chills, fever (38.5°C) and night sweats, accompanied by a non-productive cough. Infectious disease consultation yielded no conclusive results. Chest X-ray and electrocardiogram were normal. Oral prednisone was reinstated (Fig. 4a) and he was on 20 mg daily on the day of referral to the National Eye Institute.

On physical examination the patient was alert, orientated and pale. His vital signs were normal. The vision was 6/7.5 OU. The pupils and anterior segments were unremarkable OU. The vitreous was normal OU. The right fundus appeared normal now, and the left fundus demonstrated a small central retinal pigment epithelial detachment. Fluorescein angiography was unremarkable now, but the OCT scan (on presentation) was abnormal (Fig. 4b) and the height of the serous detachment was less than in the prior OCT image. Indocyanine angiography was non-contributory. Based on his clinical presentation VKH was considered unlikely.¹

He underwent a comprehensive physical examination, which revealed a palpable spleen without enlarged lymph nodes (chronology of symptoms, signs and tests: Table 1). The chest X-ray was normal. On the basis of progressive anaemia and thrombocytopaenia (Table 1), and provocative history of sustained response to corticosteroids, a haematology consultation was sought. Coombs direct and indirect, cold agglutinin, lupus coagulant by Russell viper venom, and prothrombin time, partial thromboplastin time were unremarkable. A taper of oral prednisone was begun. Computed tomography scan abdomen confirmed splenic enlargement.

The peripheral blood smear appeared unremarkable and blood flow cytometry was inconclusive. Of the lymphocytes, 62% were T-cells, 33% were B-cells and 5% were natural killer cells. However, 0.1% of B-cells expressed cluster of differentiation (CD) 19, bright CD 20, bright CD 22 and bright CD 11c suspicious for a minor population of abnormal B-cells (Table 1). Molecular analysis of the B-cells did not demonstrate a clonal band to define a lymphoid malignancy. The brain magnetic resonance imaging was normal and cerebrospinal fluid did not reveal malignant cells by cytology and flow cytometry. Flow cytometry of bone marrow aspirates revealed 72% T-cells, 20% B-cells and 8% natural killer cells. Interestingly, similar to studies of the peripheral blood, a minor (0.08%) population of mononuclear cells appeared to be monoclonal B-cells expressing CD 19, bright CD 20, bright CD 22, bright CD 11c, bright CD 25, CD 103, CD 79b. Kappa surface light chain was positive but lambda was negative. CD 5, CD 10 and CD 23 were detected in the bone marrow and raised the spectre of hairy cell leukaemia or mantle cell lymphoma. Splenectomy was proposed as a possible diagnostic and therapeutic measure after confirmation of significant splenomegaly on computed tomography scan. The patient received standard immunization before splenectomy and being off oral prednisone for 3 days, Splenectomy was performed.

Histopathological examination of the spleen revealed splenomegaly (1030 g; normal being 130–150 g) and a diffuse lymphomatous infiltration of the red pulp leading to a diagnosis of diffuse large B-cell lymphoma (DLBCL) (Fig. 5). Immunopathology is listed in Table 1. The cervical spine magnetic resonance imaging demonstrated osseous metastases to the spine leading to a classification of the DLBCL as Stage IV B. A week post Splenectomy, the retina was flat OU (Fig. 4c) with resolution of the serous detachments 12 days off prednisone. Therapy was instituted using the EPOCH-R regimen (etoposide, prednisone [60 mg] Oncovin, cyclophosphamide, halotensin with rituximab).² There were no ocular symptoms or signs on serial comprehensive evaluations over 8 months.

Discussion

The incidence of DLBCL is steadily increasing worldwide.³ The initial presentation of DLBCL with ocular symptoms in the absence of central nervous system disease is relatively uncommon.⁴ VKH was ruled out because of the absence of the diagnostic criteria that would generally include optic nerve abnormalities on angiography.^{5,6} There have been illuminating reports describing varied intraocular presentations of non-Hodgkin's lymphoma, and even linking VKH with non-Hodgkin's lymphoma.⁶ Even so, ocular involvement is present in less than 10% of patients with systemic lymphoma.⁷ Ocular metastasis of systemic lymphoma usually are orbital⁸ and uveal. The retina and vitreous are rarely involved.

The serous detachments promptly resolved after splenectomy, even in the face of the discontinued corticosteroids. The clinical history and response to corticosteroids in all likelihood ruled out central serous chorioretinopathy. Indocyanine green angiography and OCT did not demonstrate retinal or uveal tumour. This sequence was intriguing and we speculate that the retinal detachments may be related to cytokine production by the lymphoma or be an immune-mediated effect. Interleukins associated with lymphoid tumours have been reported prior to being associated with serous detachments in non-Hodgkin's lymphoma.⁷ Metastases to the choroids could be an explanation for the dramatic response to corticosteroids.

A diagnosis of malignancy may have to be considered in the evaluation of vague qualitative visual complaints with serous retinal detachments that may masquerade as autoimmune disease.^{9,10}

References

1. Read RW, Rao NA, Cunningham ET. Vogt-Koyanagi-Harada disease. *Curr Opin Ophthalmol* 2000;11:437-42. [PubMed: 11141638]
2. Wilson WH, Gutierrez M, O'Connor P, et al. The role of rituximab and chemotherapy in aggressive B-cell lymphoma: a preliminary report of dose-adjusted EPOCH-R. *Semin Oncol* 2002;29:41-7. [PubMed: 11842388]
3. Clarke CA, Glaser SL. Changing incidence of non-Hodgkin lymphomas in the United States. *Cancer* 2002;94:2015-23. [PubMed: 11932904]
4. Hormigo A, Abrey L, Heinemann MH, DeAngelis LM. Ocular presentation of primary central nervous system lymphoma: diagnosis and treatment. *Br J Haematol* 2004;126:202-8. [PubMed: 15238140]
5. Gass, JDM. *Stereoscopic Atlas of Macular Diseases: Diagnosis and Treatment*. 4. St. Louis: Mosby; 1997.
6. Hunyor AP, Harper CA, O'Day J, McKelvie PA. Ocular-central nervous system lymphoma mimicking posterior scleritis with exudative retinal detachment. *Ophthalmology* 2000;107:1955-9. [PubMed: 11013206]
7. Hashida N, Kanayama S, Kawasaki A, Ogawa K. A case of Vogt-Koyanagi-Harada disease associated with malignant lymphoma. *Jpn J Ophthalmol* 2005;49:253-6. [PubMed: 15944834]
8. Tovilla-Canales JL, Tovilla y Pomar JL, Ceron JR. Lymphoproliferative disorders of the ocular adnexa. *Curr Opin Ophthalmol* 2004;15:401-5. [PubMed: 15625900]
9. Kumar H, Garg SP, Kumar A, Gupta P. Serous macular detachment in lymphoproliferative disorders. *Can J Ophthalmol* 1991;26:280-2. [PubMed: 1933668]
10. Mathai A, Lall A, Jain R, Pathengay A. Systemic non-Hodgkin's lymphoma masquerading as Vogt-Koyanagi-Harada disease in an HIV-positive patient. *Clin Experiment Ophthalmol* 2006;34:280-2. [PubMed: 16671912]

Figure 1.
(a) Right eye and (b) left eye: bilateral serous detachments, left eye prominent.

Figure 2.
(a) Right eye and (b) left eye: fluorescein angiogram of bilateral serous detachments with hyperfluorescent spots at the retinal pigment epithelial level, left eye prominent, oral prednisone initiated.

Figure 3.
(a) Right eye and (b) left eye: no serous detachments evident in both eyes after a course of oral prednisone.

Figure 4.
(a) Oral prednisone restarted for serous detachment left eye. (b) Decreased serous fluid left eye after 5 weeks of prednisone (after presentation). (c) Post-splenectomy left eye.

Figure 5. Microphotographs of the spleen showing (a) diffuse infiltration of lymphoma cells in the red pulp and (b) numerous large atypical lymphoma cells with mitosis and prominent nucleus. Haematoxylin and eosin, original magnification $\times 200$ (a) or $\times 400$ (b).

Table 1
Chronology of significant events (dates have been formatted to read day/month/year)

	Timeline of clinical progression					Normal values
	Presentation: serous retinal detachments ↓ 15/10/2004	B symptoms ↓ 5/12/2004	Thrombocytopenia ↓ 6/1/2005	Splenectomy 9/2/2005 ↓ 14/1/2005	Resolution of serous retinal detachments ↓ 17/2/2005	
WBC	5.4		5.1		6.44	3.8–10.8 × 10 ³ /μL
RBC	3.92		3.27		3.3	4.20–5.80 × 10 ⁶ /μL
HGB	13.4		10.3		10.6	13.2–17.1 g/dL
HCT	38.2		31		32.7	38.5–50%
MCV			95		99.1	
Platelet	197	157	NT		205	
% Lymphs	40				56	15–51%
% Grans	43				36	52–75%
% Monos	12				47.5	0–11%
ANC					13.9	1500–7800 cells/μL
ESR			2448		3207	0–20 mm/h
LDH			85			113–229 U/L
Prednisone	None	Tapered	None	535 Tapered		

Histopathology and immunophenotype of tumour in the spleen: diffuse large B-cell lymphoma, splenomegaly (1060 g), CD 20+, CD 19+, CD 22+, Bcl-6 weakly+, surface Kappa+, CD 5 weakly+, Mum-1–, p53–, CD 10–, *In situ* hybridization for Epstein Barr Virus negative. ANC, absolute neutrophil count; ESR, erythrocyte sedimentation rate; HCT, hematocrit; HGB, hemoglobin; LDH, lactate dehydrogenase; MCV, mean corpuscular volume; NT, not tested; RBC, red blood cells; WBC, white blood cells.