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CASE SERIES

Bilateral simultaneous central retinal vein occlusion secondary to hyperviscosity in Waldenstrom's macroglobulinaemia

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Abstract

Purpose **Central retinal vein occlusions (CRVOs) are rarely treatable; most therapy is directed towards prevention or treatment of complications. Bilateral CRVO can be due to serum hyperviscosity, which affects 15% of all patients with Waldenstrom's macroglobulinaemia (WM). Although previously reported in a handful of cases, bilateral CRVO is a rare presenting feature.**
Patients and methods **Illustrated case reports of three patients presenting with bilateral CRVO due to undiagnosed WM.**
Results **Plasma exchange, which successfully restored vision in two patients, was followed by long-term cytotoxic therapy.**
Conclusions **Plasma electrophoresis should be performed in all patients with retinal vein occlusions to exclude a paraproteinaemia. In patients with bilateral venous changes, there should be a very high level of suspicion of hyperviscosity, with the possibility of effective early therapy.**
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Keywords: retinal vein occlusion; hyperviscosity; Waldenstrom's macroglobulinaemia; paraproteinaemia

Introduction

Central retinal vein occlusion (CRVO) is a common cause of visual loss for which there is usually no treatment. Most interventions are aimed at the prevention or treatment of complications. Waldenstrom's macroglobulinaemia (WM) is a malignant monoclonal lymphoproliferative disorder. Bilateral simultaneous CRVO is a rare presenting feature of WM. We present three cases.

Case 1

A 40-year-old gentleman presented with sudden right visual disturbance. Visual acuities were 6/24 OD, 6/9 OS with bilateral non-ischaemic CRVO on fundoscopy (Figure 1). Fluorescein angiography demonstrated bilateral delayed venous filling, right macular oedema, and mild right optic disc congestion.

Laboratory investigations showed a reduced haemoglobin (Hb) (8.3 g/dl (13–18 g/dl), raised ESR (109 mm/h (1–10 mm/h)), serum viscosity (3.24 (1.5–1.7)), and total protein (122 g/l (61–79 g/l)), and monoclonal IgM paraproteinaemia with suppression of heterogenous gammaglobulins on plasma electrophoresis. Cardiovascular risk-factor screening was normal.

The blood film showed marked rouleaux formation, and bone marrow trephine biopsy was consistent with lymphoplasmacytoid lymphoma/WM.

The patient underwent plasma exchange twice. Ten days later, acuities were 6/6 bilaterally, with resolution of retinal haemorrhages and normal venous calibre (Figure 1), and the patient was maintained on oral fludarabine and cyclophosphamide therapy.

Case 2

A 61-year-old lady presented with right visual disturbance. Acuities were 6/18 OD, 6/6 OS;

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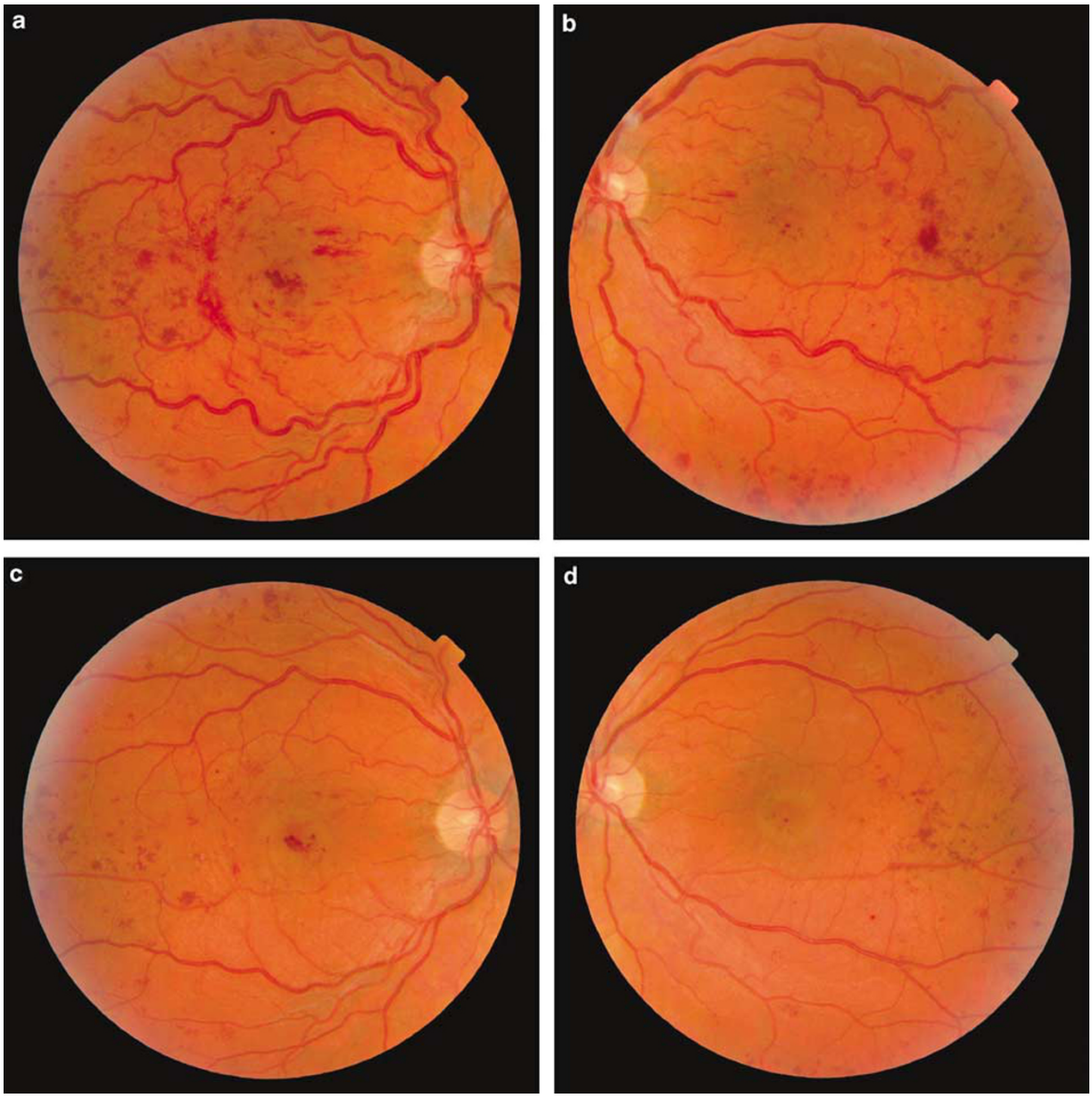

Figure 1 (a and b) Dilated fundal examination of patient no. 1 showed tortuous dilated veins, preretinal and intraretinal haemorrhages in all quadrants of both eyes, and mild optic disc swelling in the right eye. Visual acuities were 6/24, right eye; 6/9 left eye. (c and d) Dilated fundal examination of patient no. 1 following two plasma exchanges showed almost normal venous calibre, with resolution of most haemorrhages. The patient's visual acuities had returned to 6/6 in both eyes.

fundoscopy revealed bilateral non-ischaemic CRVO. Laboratory investigations showed Hb 8.3 g/dl, ESR 80 mm/h, viscosity 6.24, and extensive rouleaux on blood film (Figure 2a) with an IgM paraproteinaemia on plasma electrophoresis. Computed tomography scans of the chest, abdomen, and pelvis were normal but bone marrow trephine biopsy revealed plasmacytoid lymphocyte infiltration. Following three plasma exchanges, continuous oral chlorambucil 6 mg/day was commenced. Four months later, fundal appearances had improved but acuities were unchanged. Two years later, the patient's condition recurred, requiring plasma exchange, chlorambucil, fludarabine, rituximab, and monoclonal anti-CD20 therapy.

Case 3

A 66-year-old man with a history of hypertension, cardiac failure, and smoking complained of dazzling bright lights in both eyes, and was found to have bilateral

CRVO. He reported calf and thigh pain on exercise, which was relieved by rest, and appeared breathless; he was admitted urgently by the physicians. Blood tests revealed Hb 8.5, WBC 42, and ESR 81. The plasma viscosity was too high to be measured. Electrophoresis demonstrated an IgM-κ paraproteinaemia, and trephine bone marrow biopsy confirmed lymphoplasmacytoid lymphoma. Following plasma exchange, the patient's dyspnoea and visual symptoms completely resolved, and viscosity improved to 2.25. The patient was successfully treated with three courses of chlorambucil, followed by 1 year of fludarabine therapy, with 4-weekly plasma exchange. A disease relapse 3 years later was successfully treated with two courses of fludarabine and cyclophosphamide. The patient died from myocardial infarction a further 3 years later.

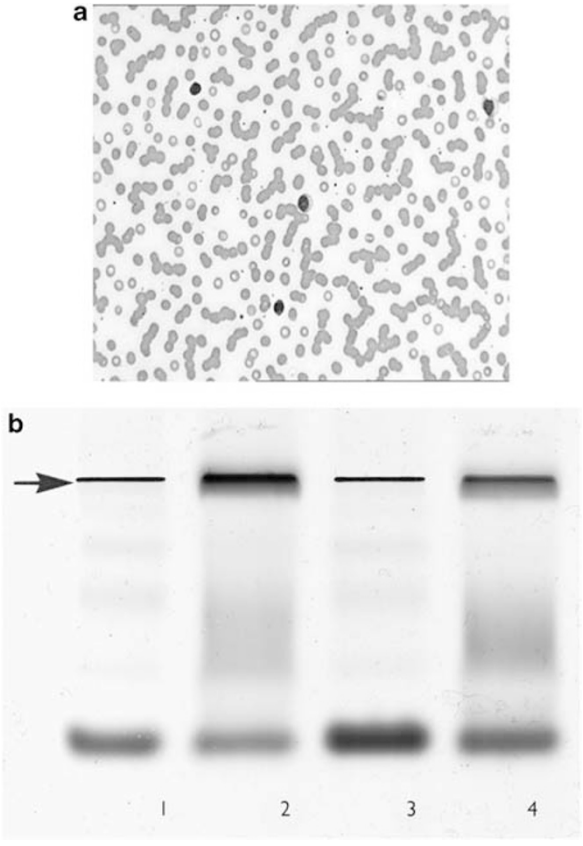

Figure 2 (a) Blood film in patients with WM typically show marked rouleaux formation, with a high background signal due to the paraprotein (patient no. 2). (b) Serum electrophoresis of patient no. 1 showing a strong monoclonal band (arrow). Lane 2 was performed before plasma exchange and lane 4 afterwards (lanes 1 and 3 are controls).

Comment

Waldenstrom's macroglobulinaemia is a monoclonal gammopathy-associated lymphoplasmacytic lymphoma, with an incidence of 4 per million per year,[1] first described by Jan Waldenstrom in 1944.[2]

Serum hyperviscosity affects 15% of patients at diagnosis and is related to the increasing concentrations of IgM pentamers causing erythrocyte aggregation.[3] Clinical manifestations of hyperviscosity are spontaneous mucosal bleeding, neurological symptoms for example, stroke, and visual disturbances. Nevertheless, bilateral CRVO is an uncommon presenting feature; to our knowledge, only five previous cases have been reported, making our series the largest in the literature.[4–8] Table 1 compares the clinical and haematological characteristics of these patients; they tend to be younger than patients with CRVO due to other risk factors. Although 64% of patients over 50 years with CRVO have uncontrolled hypertension,[9] none of the patients with WM had high blood pressure at presentation. It is also interesting to note that visual symptoms can begin at markedly varying plasma viscosity levels. Menke *et al*[10] have demonstrated that using indirect ophthalmoscopy and scleral depression, retinal manifestations of hyperviscosity can be present at viscosities as low as 2.1. Symptomatic hyperviscosity also occurs in 2–6% of patients with multiple myeloma, a high-grade lymphoproliferative disorder.[11] Plasma

Table 1 Comparison of age, gender, blood pressure, haemoglobin, plasma viscosity, and visual acuities of patients with bilateral CRVO secondary to Waldenstrom's macroglobulinaemia, as published in the English Language

	Age, sex	*Blood pressure*	*Haemoglobin*	*Plasma viscosity*	*VA*
Patient 1	40, M	Normal	8.3	3.24	6/18, 6/6
Patient 2	61, F	Normal	8.3	6.24	6/24, 6/9
Patient 3	66, M	Treated hypertension	8.5	Unrecordably high	6/9, 6/9
Feman and Stein[5]	68, M	Not mentioned	Not mentioned	11	6/24, 6/30
Lekhra *et al*[4]	48, F	Normal	7.1	Not mentioned	6/60, 6/60
Avashia and Fath[7]	55, M	Not mentioned	Not mentioned	Not mentioned	20/200, HM
Casares *et al*[6]	57, F	Not mentioned	11.0	>5.0	6/9, 6/6

CRVO = central retinal vein occlusion.

exchange can alleviate symptoms and may restore vision by reducing serum viscosity, but long-term management is directed at preventing paraprotein production.[11]

The Royal College of Ophthalmologists has recommended that plasma electrophoresis should be performed in all patients with retinal vein occlusion.[9] In patients with bilateral venous changes, there should be a very high level of suspicion of hyperviscosity, with the possibility of effective early therapy for restoring vision.

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