A Case with Bilateral Central Retinal Vein Occlusion as the Initial Finding of Multiple Myeloma: Documentation of Long-term Retinal Alterations and a Literature Review

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ABSTRACT

51-year-old male patient with no remarkable medical history presented with blurred vision in both eyes. Best corrected visual acuity (BCVA) was 1.0 OU. Fundus evaluation revealed bilateral central retinal vein occlusion with no ischemia on fluorescein angiography. Optical coherence tomography (OCT) showed irregularities on outer plexiform/outer nuclear layer and intraretinal cysts mainly in the outer nuclear layer. Blood tests revealed severe anemia and high sedimentation rate. Serum immunofixation electrophoresis and bone marrow biopsy results were consistent with multiple myeloma diagnosis. The patient was referred for chemotherapy. The patient was reevaluated 3.5 years after the diagnosis. BCVA was 1.0 OU, fundus evaluation showed the resolution of retinal hemorrhages, venous tortuosity and dilation except for irregularities in outer plexiform/outer nuclear layers on OCT. Retinopathy might be the initial finding in hyperviscosity syndrome. Timely diagnosis and management would be sight and life-saving, therefore ophthalmologists should determine hyperviscosity syndrome in the differential diagnosis of bilateral central retinal vein occlusion. Some structural retinal alterations might persist despite successful systemic treatment.

Keywords: bilateral central retinal vein occlusion, macular edema, multiple myeloma, retinal layer integrity.

INTRODUCTION

Hyperviscosity syndrome (HS) refers to the increase in blood viscosity due to an increase in the cellular/acellular elements or due to the defective cells such as in sickle cell anemia.[1] The classical triad of HS is mucosal bleeding, neurological and visual symptoms. The most commonly related diseases are Waldenstrom macroglobulinemia, multiple myeloma and leukemia.[1-10]

The most common ocular findings in HS are tortuosity and dilation of the retinal vessels, retinal hemorrhages, cotton wool spots, and optic disc edema. Bilateral central retinal vein occlusion (CRVO) is the most commonly encountered manifestation. [1-12] Ocular findings might be the initial findings of the underlying disease which can be life-threatening.[2,6] Furthermore, hyperviscosity retinopathy (HR) diagnosis can be challenging, particularly when it presents unilaterally or with a coexistent disease such as diabetes mellitus, leading a false diagnosis of diabetic maculopathy/retinopathy.[8,9] Therefore, it is crucial for the ophthalmologist to be aware of HR for timely management of systemic and ocular involvement. Here we report a case with bilateral CRVO as the first clinical finding of multiple myeloma and document long term retinal structural alterations as assessed by SD-OCT.

CASE REPORT

51-year-old male patient presented with blurred vision in both eyes for several weeks. His medical history was unremarkable. Best-corrected visual acuity (BCVA) was 1.0 (Snellen) in both eyes whereas the mean intraocular pressures were 15mmHg in the right eye and 18mmHg in the left eye. Anterior segment findings were unremarkable. Posterior segment evaluation revealed bilateral venous dilation, tortuosity, Roth spots, flame-shaped hemorrhages compatible with bilateral CRVO (Figure 1). Fluorescein angiography showed bilateral optic disc hyperfluorescence with no peripheral ischemia whereas optical coherence

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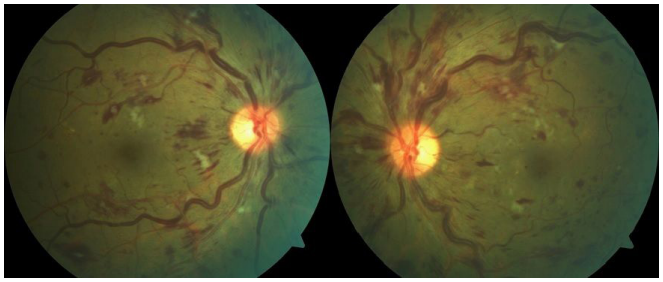

Figure 1: *Color fundus photo shows bilateral venous dilatation, tortuosity, Roth spots, flame shaped hemorrhages compatible with bilateral central retinal vein occlusion.*

tomography (OCT) showed irregularities on outer plexiform/outer nuclear layer and intraretinal cysts mainly in the outer nuclear layer (Figure 2,3).

Blood tests revealed severe anemia (hemoglobin, 7.5 mg/dl; MCV: 86 fL). Sedimentation rate was 132mm/hr. The patient was referred to the hematology clinic. Further work-up showed IgG lambda monoclonal gammopathy on serum immunofixation electrophoresis (IgG=8617mg/dl (N=700-1600), lambda light chain=558.7mg/dl (N=93-242)). Bone marrow biopsy documented lambda monoclonal plasma cell infiltration consistent with multiple myeloma diagnosis. After bortezomib-based chemotherapy, autologous stem cell transplantation was performed in the remission. After

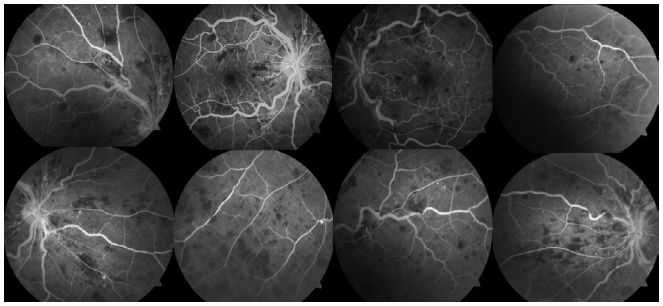

Figure 2: *Fluorescein angiography shows bilateral optic disc hyperfluorescence with no peripheral ischemia.*

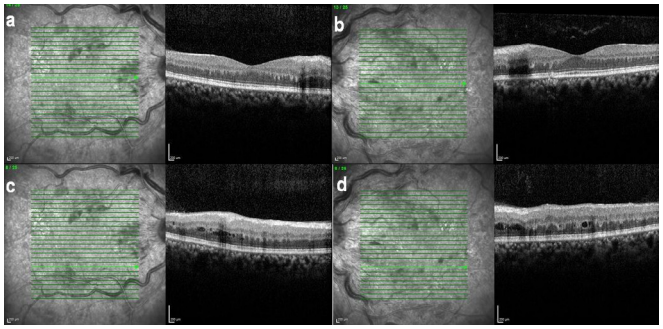

Figure 3: *Optical coherence tomography shows irregularities on outer plexiform/outer nuclear layer in the right (a) and left eye (b) and intraretinal cysts mainly in the outer nuclear layer in the right (c) and left eye (d).*

starting chemotherapy, the patient was lost to follow-up for further ophthalmic evaluation. After 3.5 years, his systemic illness was stable and he presented with BCVA of 1.0 (Snellen) in both eyes, fundus evaluation revealed total resolution of retinal hemorhages, venous tortuosity and dilation except for irregularities in outer plexiform/outer nuclear layers on OCT mainly in the left eye (Figure 4, 5).

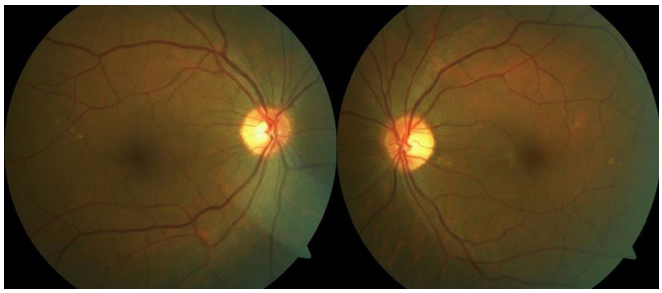

Figure 4: *Color fundus photo shows complete resolution of retinal findings.*

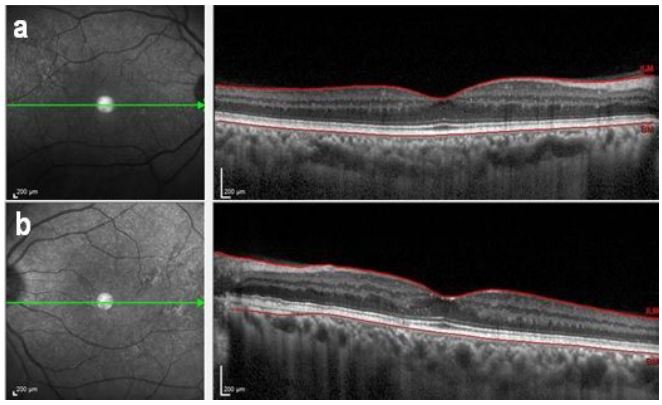

Figure 5: *Optical coherence tomography shows resolution of intraretinal cysts except for some irregularities in outer plexiform/outer nuclear layers which was less prominent in right eye (a) compared to the left eye (b).*

DISCUSSION

The most common HS related diseases are Waldenstrom macroglobulinemia, multiple myeloma and leukemia. [1-10] Retinal involvement is a major finding in HS, characterized with mostly bilateral venous dilatation, tortuosity, retinal hemorrhages, peripheric vascular occlusion, and peripheral microaneurysms. Bilateral CRVO is a particularly alarming finding. [1-11] Optic disc edema and a hyperpermeable disc on fluorescein angiography may also be seen. Optic disc findings might appear due to the increase in venous pressure, infiltration by the primary disease as in leukemia, or papilledema secondary to increased cerebrospinal fluid pressure.[12]

Our case had bilateral CRVO as the initial finding of multiple myeloma, similar to the previous literature. It

is also worth to note that the patient had a good visual acuity despite striking fundus findings, which emphasizes the importance of fundus evaluation in every patient. Besides CRVO, peripheral microaneurysms, capillary non-perfusion and neovascularization areas may be also seen in HR, particularly in chronic myeloid leukemia. [13,14] Despite venous system involvement is generally more prominent in HS, retinal artery occlusion might be the leading finding in primary polycythemia vera. [9,15] HS might also appear unilaterally and as a masquerading syndrome mimicking diabetic macular edema. [8,9,16]

Paraproteinemic maculopathy is an important feature related to HS, characterized by subretinal fluid, cystoid macular edema and silent macula on fluorescein angiography. [3,16,17] Silent macula is a major finding, indicating non-leakage on fluorescein angiography despite prominent submacular detachment on optical coherence tomography. Those features are especially important in discriminating paraproteinemic maculopathy from the other maculopathies, particularly central serous chorioretinopathy. In our case, there were some non-central intraretinal cysts, however, macular edema wasn't a major finding.

HR treatment should be planned according to the underlying disease causing hyperviscosity and the retinal findings might improve accordingly by the systemic treatment. [2,7,12,14,16,17] There are conflicting reports about the additive role for anti-vascular endothelial growth factor and steroid agents in maculopathy.[2,17] Timely diagnosis and management of HS is not only important for life-saving but also for the protection of visual acuity. In literature, there is very limited data regarding the long-term consequences of HR. Lin et al. reported that longer duration of HS might cause poor visual acuity and permanent impairment in retinal architecture.[5] In our case, despite the patient had very prompt treatment, good visual acuity and no clinically observable retinal alterations at the final visit, SD-OCT revealed retinal structural changes in long term. These findings suggest that, the delay in diagnosis might cause more prominent retinal impairment.

In summary, our case highlights the importance of determining the diagnosis of HS in bilateral CRVO cases. Ophthalmologist should be aware of HR, particularly in cases with bilateral CRVO or refractory macular edema with various etiology. Urgent systemic work-up and referral to an internist might be sight and life-saving. Despite prompt initiation of treatment, some subclinical retinal structural alterations might occur.

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