A 43-Year-Old Female with Vision Loss in Both Eyes

Abdallah M. Jeroudi, MD; Gaurav K. Shah, MD

Introduction:

A 43-year-old female presented to The Retina Institute for evaluation of painless vision loss in left eye of 2 weeks duration. She reported her vision had been blurry in both eyes for a number of months, but especially worsened in the left eye over the span of 2 weeks. The patient denied past ocular trauma, conditions, or surgery. The patient reported she was otherwise healthy. She denied oral contraceptive use or use of any medications. She denied a family history of blindness, glaucoma, or age related macular degeneration. She drank alcohol socially and denied smoking or illegal drug use.

Visual acuity measured 20/100 OD and 20/200 OS. Vision did not improve with pinhole testing. There was no relative afferent pupillary defect. Extraocular motions were intact. Intraocular pressure (IOP) measured 16 OD and 13 OS by applanation tonometry. The anterior segment exam was normal.

Dilated fundus examination revealed a cup to disc ratio of 0.1 with sharp disc margins. The vitreous was clear. Notable on examination were serous macular detachments with significant dilation and tortuousity of the venules (Figure 1). Intraretinal hemorrhages were seen in the periphery bilaterally.

Time-domain OCT confirmed the presence of bilateral serous macular detachments with associated cystoid macular edema (CME) (Figure 2). Fluorescein angiogram (FA) indicated delayed venous transit, but no leakage was noted in the area of subretinal fluid seen on color photography (Figure 3). The blood pressure reading in the office was 130/58 mmHg.

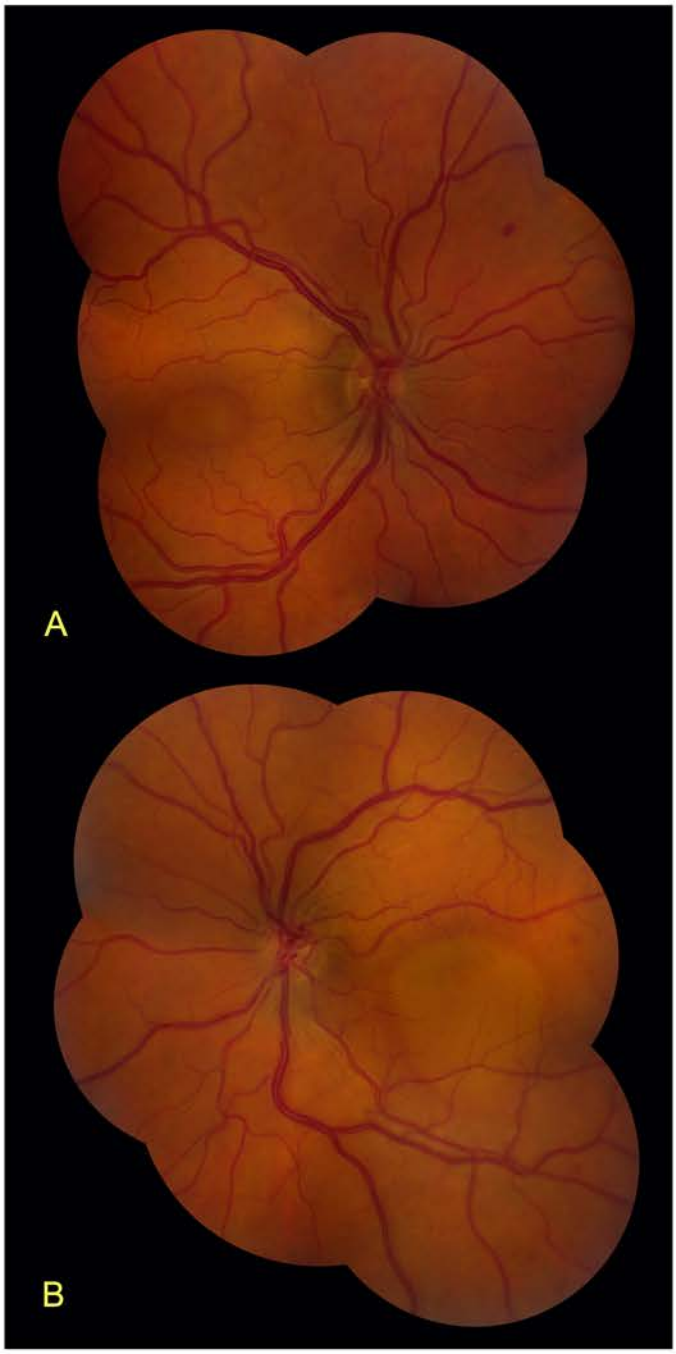

Figure 1 – Color Photograph of the right eye (A) and left eye (B) showing dilated venules and serous macular detachment.

Work Up:

The patient was referred for bilateral central retinal vein occlusion (CRVO) by her general ophthalmologist which would be unusual considering the patient's age, bilaterality of her presentation, and minimal leakage on

FA in the setting of CME and subretinal fluid. The differential diagnosis for her presentation included CRVO / Hypertensive Retinopathy, diabetic retinopathy, ocular ischemic syndrome, HIV retinopathy, central serous chorioretinopathy, and retinopathy secondary to blood dyscrasia.

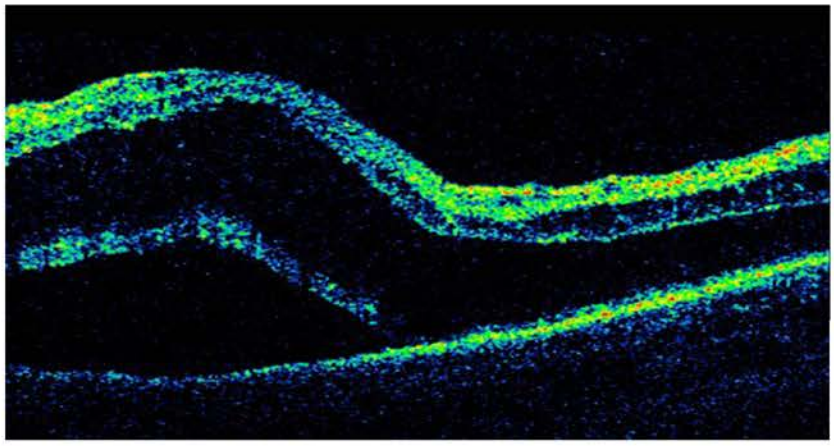

Figure 2 – Time-domain Ocular Coherence Tomography (TD-OCT) of the left eye at the initial visit showing cystoid macular edema and subretinal fluid.

Laboratory work up including Complete Blood Count (CBC), Rapid Plasma Reagin (RPR), Erythrocyte Sedimentation Rate (ESR), Hemoglobin A1c level, lipid panel, serum protein electrophoresis (SPEP), and serum viscosity was obtained. Her laboratory work up was notable for revealing macrocytic anemia (Hemoglobin 6, Mean Corpuscular Volume 105), thrombocytopenia (platelets 30), increased serum viscosity (9.1 centipoise (cP)), and a monoclonal M spike in the gamma region (IgM Kappa monoclonal band). Bone marrow biopsy performed by the Hematology / Oncology service confirmed a clonal CD 45 positive population of B cells. Skeletal survey was negative for lytic bone lesions. She was diagnosed with Waldenstrom Macroglobulinemia / Hyperviscosity Syndrome Retinopathy, underwent plasmapheresis, and started on chemotherapy after receiving a blood transfusion.

The patient's retinal findings were followed serially with improvement in her vision and OCT appearance paralleling the decline in the IgM and serum viscosity level with treatment (Figure 4). Her initial VA of 20/400 OD and 20/100 OS associated with serum viscosity of 9.1 cP improved to a final VA of 20/40-2 OD and 20/200 OS with a serum viscosity of 2.1 cP at 49 months of follow up. CME/SRF completely resolved at 6 months and 45 months for the right and left eyes respectively (Figure 4 and 5). Vision in the left eye was limited due to macular RPE/ellipsoid loss (Figure 5).

Discussion:

Waldenstrom Macroglobulinemia (WM) is a chronic lymphoproliferative condition characterized by a clonal population of B lymphocytes in the bone marrow which leads to an over production of Immunoglobulin M (IgM). There are 1,500 new cases of WM per year in the United States [1].

Symptoms from this indolent lymphoplasmacytic lymphoma occur from the elevated IgM levels as well as plasmacytic infiltration of the bone marrow and other organs. Elevated IgM may lead to a hyperviscosity syndrome in which neurovascular symptoms such as headache, seizures, vertigo, ataxia, and even coma may occur due to elevated blood/serum viscosity [1,2]. The incidence of hyperviscosity syndrome in series of patients with WM (17 to 90%) is higher as compared to other paraproteinemias like Multiple Myeloma (2 to 6%) due to the larger IgM pentamer preferentially staying intravascularly [1,2]. Anemia and thrombocytopenia are more common in these patients due to rouleaux formation of the red blood cells (RBCs) leading to RBC lysis as well as hypoproduction in the bone marrow. Patient may complain of easy fatigability and experience mucous membrane bleeding.

Hyperviscosity syndrome may also lead to a Hyperviscosity Syndrome Retinopathy (HVSR) that

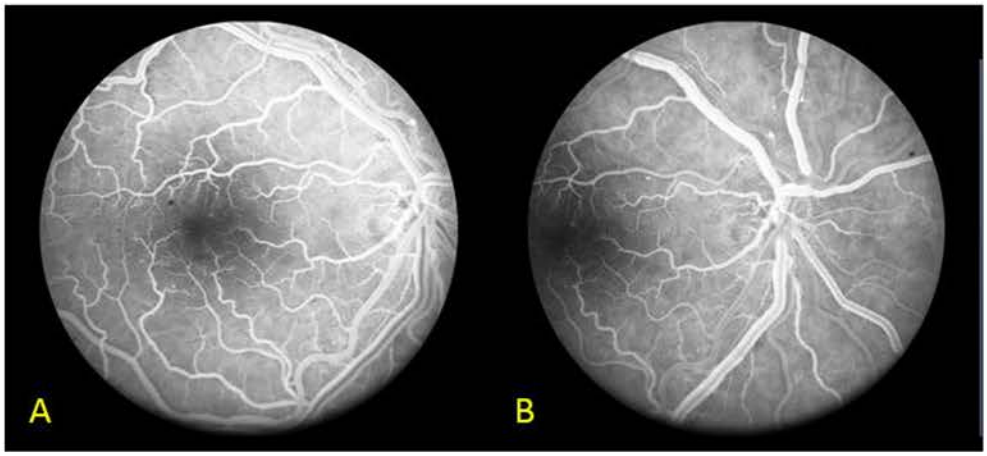

Figure 3 – Fluorescein angiography of the right eye showing delayed venous transit. There was a lack of dye leakage in the area of cystoid macular edema and subretinal fluid.

may mimic the appearance of CRVO. The clinical appearance is characterized by venous dilation (which compensates for increased viscosity), intraretinal hemorrhages (IRH), areas of perfusion abnormality, disc edema (may or may not be present), and subretinal fluid. The presence and severity of HVSR has been correlated to serum IgM levels as well as serum or blood viscosity in patients with WM [3-6].

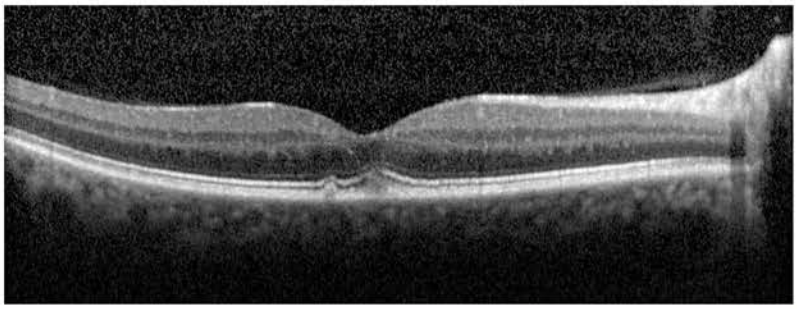

Figure 4 - Spectral-domain ocular coherence tomography (SD-OCT) of the right eye with resolution of subretinal fluid and CME. Final visual acuity was 20/40-2 in the right eye.

In a prospective study with age-matched controls of 46 patients with WM, serum viscosity levels were measured to identify the incidence of HVSR in this population as well as the threshold serum viscosity levels in which findings of HSVR become apparent [3]. In this series, of all patients with WM, 52% of patients exhibited no HVSR findings (mean serum viscosity 2.5 ± 0.7 cP), 39% exhibited dilated venules with peripheral IRH (mean serum viscosity 3.1 ± 0.7 cP, and 9% exhibited central IRH with or without disc edema (mean serum viscosity 5.6 ± 0.7 cP). In all, 48% of patients with WM in their series exhibited findings of HVSR with more severe findings associated with increased serum viscosity [3]. HVSR was asymptomatic until central involvement occurred. In a follow-up study in that series of patients, the mean threshold value of IgM level and serum viscosity to identify the presence of HVSR findings were 5442 mg/dL and 3.1 cP respectively [4]. In 9 patients for which pre and post-treatment retinal grading was performed, all patients experienced reduction in the IgM level, serum viscosity level, retinal venule diameter, degree of vascular tortuosity, amount of retinal hemorrhages, and disc edema (if initially present) [4].

In terms of patients with the presence of cystoid macular edema and subretinal fluid, a series of 8 eyes from 4 patients with WM associated HVSR further characterized this finding [5]. In their series, none of the eyes with CME or SRF experienced leakage during fluorescein angiography. It is postulated that the presence of SRF and CME in HVSR is due to a venous stasis choroidopathy that leads to a breakdown of the blood-RPE barrier and subsequent inability of the retinal pigment epithelium to absorb this presumably high oncotic pressure (from excess IgM) fluid accumulation [5,6]. Few histologic reports documented immunoglobulins in the subretinal space [6]. Although no specific IgM level or serum viscosity values were reported in that series, successful treatment of WM lead to resolution of the SRF/CME, but with poorer visual prognosis in these patients [5]. In a series and review of the literature of patients with paraproteinemic maculopathy, the study group found that maculopathy from hyperviscosity may present unilaterally as well as SRF/CME accumulation may occur at a lower threshold immunoglobulin level in diabetics (4115 mg/dL) as compared to non-diabetic patients (7306 mg/dL, p=0.10) [6]. Importantly, there was a positive correlation

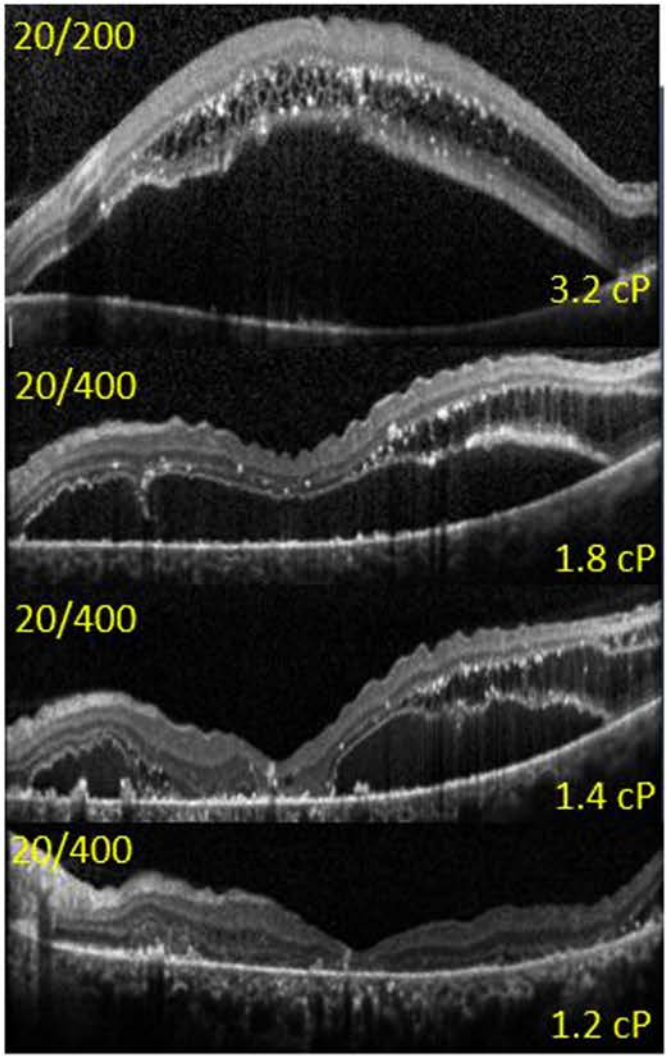

Figure 5 – Serial Spectral-domain ocular coherence tomography (SD-OCT) of the left eye with associated serum viscosity level at visit month 26, 31, 33, and 49 respectively. Subretinal fluid (which was more prominent initially in the left eye) was slower to resolve as compared to the right eye with treatment.

between the area of the macular detachment and serum viscosity (p=0.017), and immunoglobulin level was strongly positively correlated with serum viscosity (p=0.007) [6].

Early recognition and treatment, as in our patient's case, is key to prevent irreversible vision loss. Although the right eye regained vision, vision in the left eye was limited due to macular RPE/ellipsoid loss.

Conclusions:

Hyperviscosity Syndrome Retinopathy (HVSR) due to paraproteinemias such as Waldenstrom Macroglobulinemia may mimic the appearance of Central Retinal Vein Occlusion (CRVO). Approximately 48% of patients with WM may present with varying degrees of HVSR with central involvement (leading to symptoms of visual loss) in 9% in one series. As the serum viscosity and immunoglobulin level increases, HVSR findings are more likely to be apparent first peripherally then centrally. The threshold serum viscosity level to detect HVSR findings is roughly 3.1 cP with a lower immunoglobulin level threshold in diabetics as compared to non-diabetics. Visual morbidity occurs with central involvement with rare reports of central CME/SRF accumulation that characteristically does not leak on fluorescein angiography. Treatment in the form of plasmapheresis and chemotherapy that reduces immunoglobulin levels (and serum viscosity) improves the appearance of HVSR. Early recognition and treatment are important to prevent visual morbidity.

References:

1. Shaheen SP, Talwalkar SS, Lin P, et al. "Waldenstrom macroglobulinemia: a review of the entity and its differential diagnosis." Adv Anat Pathol. 2012; 19(1):11-27.
2. Mehta J, Singhal S. "Hyperviscosity syndrome in plasma cell dyscrasias." Semin Thromb Hemost. 2003; 29(5):467-71.
3. Menke MN, Feke GT, McMeel JW, et al. "Hyperviscosity-related retinopathy in waldenstrom macroglobulinemia." Arch Ophthalmol. 2006; 124(11):1601-6.
4. Menke MN, Feke GT, McMeel JW, et al. "Ophthalmologic techniques to assess the severity of hyperviscosity syndrome and the effect of plasmapheresis in patients with Waldenstrom's macroglobulinemia. "Clin Lymphoma Myeloma/ 2009; 9(1):100-3.
5. Baker PS, Garg SJ, Fineman MS, et al. "Serous macular detachment in Waldenstrom macroglobulinemia: a report of four cases." 2013; 155(3):448-55.
6. Mansour AM, Arevalo JF, Badal J, et al. "Paraproteinemic maculopathy." Ophthalmology. 2014; 121(10):1925-32.

UPCOMING EVENTS:

10th Annual RRDF Trivia Night
April 9, 2016

Spring Retina Update
May 14, 2016

OIC-WAVE
June 22-25, 2016

Midwest Ophthalmological Symposium
featuring the 33rd Annual Visiting Professor Lecture
September 10, 2016

Ocular Imaging Conference
October 16, 2016

Contact Kelly McKittrick for more information on any or all of these events

kelly.mckittrick@rc-stl.com
314-367-1181 x-2157