American Journal of Ophthalmology Case Reports 12 (2018) 49–51

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.elsevier.com/locate/ajoc

Case report

Bilateral simultaneous central retinal vein occlusion in hyperviscosity retinopathy treated with systemic immunosuppressive therapy only

Michal Blau-Most[a,b], Raz Gepstein[a,b], Alexander Rubowitz[a,b,*]

[a] Department of Ophthalmology, Meir Medical Center, Kfar Sava, Israel
[b] Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

ARTICLE INFO

Keywords:
Bilateral
CRVO
Hyperviscosity
Retinopathy
Waldenstrom's macroglobulinemia

ABSTRACT

Purpose: To describe the clinical presentation and imaging features of a patient presenting with bilateral central retinal vein occlusion (CRVO), who was subsequently diagnosed with hyperviscosity retinopathy due to B cell lymphoproliferative disease, and had a good response to systemic immunosuppressive therapy.

Observations: A clinical case report of an 87-year-old woman who presented with bilateral CRVO. Visual acuity, clinical examination, spectral domain optical coherence tomography (SD-OCT), color fundus photography and systemic evaluation were obtained. Ocular examination at presentation revealed bilateral CRVO, and OCT examination revealed significant central macular edema bilaterally. Six months after the diagnosis of hyperviscosity retinopathy and administration of systemic cyclophosphamide immunosuppressive therapy for B cell lymphoproliferative disease, most of the retinal hemorrhages resolved and partial resolution of the macular edema in the left eye was observed.

Conclusion and Importance: This case describes the association between bilateral simultaneous CRVO and hyperviscosity. Under unique circumstances our patient received systemic therapy alone, without plasmapheresis. Although only limited therapy was applied, she didn't have deterioration or recurrent events; she had a small improvement in her macular edema and a significant improvement in her systemic functional state as well as reduction in her monoclonal IGM level.

1. Introduction

Bilateral central retinal vein occlusion (CRVO) is a rare presentation of B cell lymphoproliferative diseases. Treatment of the underlying disease may facilitate reduced blood viscosity and reduce risk of ocular manifestations. We present a case of bilateral simultaneous CRVO in B cell lymphoproliferative disease that had good systemic response to systemic immunosuppressive therapy, but had only partial ocular response, as the retinal bleedings resolved but there was sustained macular edema in both eyes.

2. Case report

An 87-year-old woman with dementia and macrocytic anemia presented with bilateral decreased vision.

Her ocular history was significant for pseudophakia in both eyes and a YAG laser capsulotomy in the left eye.

Visual acuity was 6/20 in the right eye and 6/15 in the left eye. The anterior segment examination was normal. Fundus examination revealed bilateral, diffusely dilated tortuous retinal veins and intraretinal deep blot hemorrhages in all four quadrants of the retina in both eyes (Fig. 1). An OCT showed significant central macular edema in both eyes, more prominent in the left eye (Fig. 2). She (again with the support of her family and custodian) refused to have FA. The clinical picture was consistent with simultaneous bilateral perfused CRVO and cystoid macular edema (CME). We advised treatment with bilateral intravitreal bevacizumab (avastin) for macular edema. However, due to her systemic condition and dementia, it was decided (with support from her family and custodian) that she will not receive treatment for her ocular condition and continue follow-up only.

Systemic workup included hematologic assessment, blood count, serum protein electrophoresis and serum immunoglobulin analysis. The results revealed macrocytic anemia (hemoglobin 7.5 g/dL), thrombocytopenia (platelets 74,000/μL), monoclonal IGM on serum protein electrophoresis and elevated IgM of 6610 mg/dL. She was diagnosed with B cell lymphoproliferative disease, most probably Waldenström's macroglobulinemia. Bone marrow biopsy to confirm Waldenström's macroglobulinemia was not performed at her request (again with the

* Corresponding author. Department of Ophthalmology, Meir Medical Center, 59 Tschernihovsky St., Kfar Sava, 44410, Israel.
E-mail address: arubowi@smile.net.il (A. Rubowitz).

https://doi.org/10.1016/j.ajoc.2018.08.006
Received 29 January 2018; Received in revised form 9 July 2018; Accepted 28 August 2018
Available online 29 August 2018

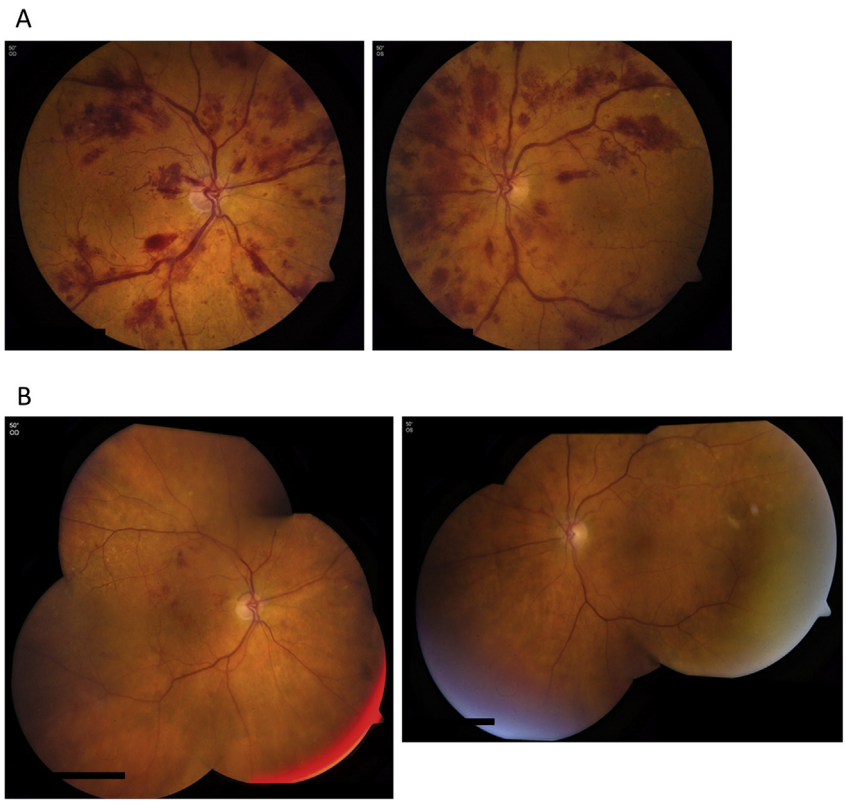

Fig. 1. Fundus photographs of bilateral simultaneous CRVO before and after administration of systemic immunosuppressive therapy.
A: Fundus photographs at presentation showing bilateral, diffusely dilated tortuous retinal veins and intraretinal blot hemorrhages in all four quadrants of both eyes.
B: Montage fundus photographs 6 months after administration of systemic immunosuppressive therapy shows resolution of most of the diffuse deep intraretinal blot hemorrhages and partial resolution of the macular edema.

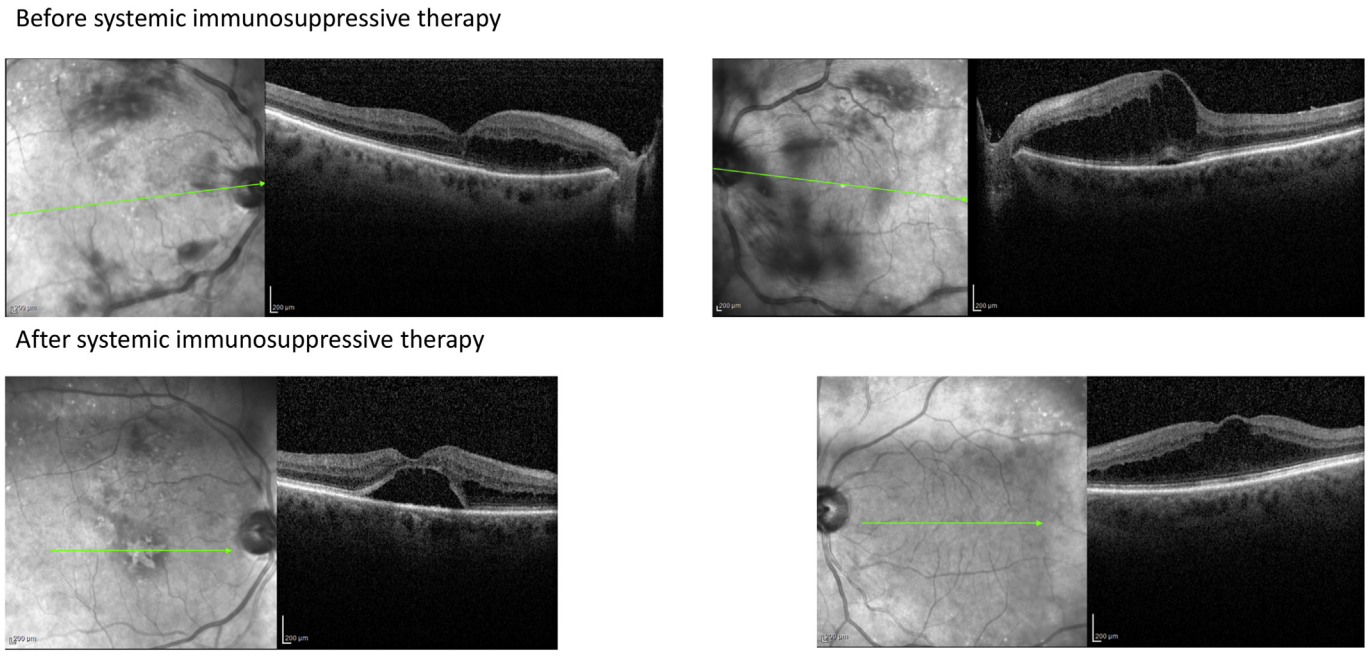

Fig. 2. Macular OCT before and after systemic immunosuppressive therapy. The right eye: Before therapy there is macular edema with subretinal fluid and preserved foveal contour (central thickness (CT) 296 μm). After therapy there is less subretinal fluid, but there is a new large pigment epithelial detachment (PED) in the fovea (CT 403 μm). The left eye: Before therapy there was significant macular edema with subretinal fluid and destructed foveal contour as well as small PED in the fovea (CT 700 μm). After therapy there was a decrease in the macular edema and the PED resolved as well (CT 668 μm).

support of her family and custodian). Systemic therapy included cyclophosphamide (600 mg monthly) and prednisone (30 mg) with tapering down (to a final maintenance dose of 5 mg). With this therapy she experienced improvement in her clinical and functional state, the hematologist described that she was more alert and less sleepy, the hemoglobin increased from 7.5 g/dL to 10.3 g/dL and the monoclonal IGM levels decreased from 6610 g/dL to 4850 g/dL.

Six months after administration of systemic immunosuppressive therapy she had a follow-up eye evaluation. She claimed to have better vision, but we could not perform a reliable visual acuity test because of poor cooperation, due to dementia. Fundus examination revealed resolution of most of the hemorrhages, (Fig. B), and an OCT examination showed partial resolution of macular edema in the left eye, and a new pigment epithelial detachment (PED) in the right eye (Fig. 2).

3. Discussion

Waldenström's macroglobulinemia is a lymphoproliferative B-cell disease, with high concentration of monoclonal IgM. It may cause hyperviscosity syndrome, which can manifest first with spontaneous bleeding from mucous membranes, visual changes, hyperviscosity retinopathy and neurologic symptoms[1]

IgM is a heavy, mainly intravascular antibody, which has direct effect on the viscosity and blood flow. As noted, our patient presented with a very high concentration of monoclonal IgM[2]

Retinal hyperviscosity is usually bilateral, and related to dysproteinemia, such as Waldenström's macroglobulinemia or multiple myeloma. Therefore, in any patient presenting with bilateral simultaneous CRVO, one should make a proper evaluation including serum protein electrophoresis and a hematological consultation.[3,4] Plasmapheresis was found to reverse hyperviscosity retinopathy and syndrome, and is considered by many as first line therapy.[2,5] In the largest case series in the literature of 3 cases of bilateral CRVO in Waldenström's macroglobulinemia, all patients were treated with plasmapheresis and systemic immunosuppressive therapy (different combinations of cyclophosphamide, fludarabine, chlorambucil and rituximab), two of them had better visual acuity following treatment and one was unchanged.[3] Another case report of patient with bilateral CRVO and Waldenström's macroglobulinemia, who was treated with plasmapheresis and systemic immunosuppressive therapy (prednisolone, cyclophosphamide and vincristine) showed improved visual acuity. There is no comparison of the different immunosuppressive regimens in patients with bilateral CRVO due to Waldenström's macroglobulinemia to date. Though Plasmaphersis is beneficial in hyperviscosity syndrome, it does not affect the underlying disease and concomitant chemotherapy is often initiated.[2,5,6] Additionally, this treatment carries risks for the patient (such as lowering blood pressure) and requires cooperation (which we didn't have due to her dementia disease). For these reasons and after consulting with her hematologist, we decided not to use it in our patient.

The retinal bleeding in CRVO can resolve spontaneously, and therefore we can't necessarily attribute their resolution to the systemic therapy. Moreover, the macular edema improved slightly in the left eye, but there was still significant macular edema in both eyes, and we would still recommend our patients anti VEGF therapy in such circumstances. We didn't have an objective visual acuity measurement in our 6 months follow-up, and we had only the subjective impression of improvement from the patient and her caregivers. Intravitreal Bevacizumb was found to be beneficial in serous macular detachment and significant macular edema in bilateral CRVO due to Waldenström's macroglobulinemia.[7]

To our knowledge, this is the first report of immunosuppressive treatment alone for hyperviscosity syndrome due to Waldenström's macroglobulinemia with bilateral CRVO. We didn't add plasmapheresis therapy and anti VEGF intravitreal injections because of the special circumstances we described above. Although the systemic condition improved under this therapy, and the monoclonal IGM level was reduced significantly, the improvement in the macular edema was minor and we would still recommend plasmapheresis and anti VEGF intravitreal injections for our next patients. At least there were no recurrent events and no deterioration in the ocular state under this therapy, and the risk for those was probably lower because of the reduced monoclonal IGM and the reduced viscosity of the blood respectively. We hope that by sharing those unsuccessful ocular results, we will help some other clinicians taking decisions in uncertain cases in the future.

4. Conclusions

The importance remains in high level of suspicion when one encounter bilateral CRVO, and any such case should prompt a proper evaluation including serum protein electrophoresis and a hematological consultation. Our patient didn't have recurrent events or deterioration in her ocular condition after initiating systemic therapy alone without plasmapheresis and without anti VEGF injections. However, we would recommend additional therapy with plasmapheresis and anti VEGF injections as those can improve the visual acuity and the macular edema in our next patients[34].

Patient consent

The patient and her legal guardian consented to publication of the case orally.

Funding

None.

Conflicts of interest

The authors have no financial disclosures.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ajoc.2018.08.006.

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