



Case Report

Hyperviscosity retinopathy as the initial presentation of aggressive multiple myeloma

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Submission : 17-Sep-2019
Revision : 15-Nov-2019
Acceptance : 30-Dec-2019
Web Publication : 11-Mar-2020

ABSTRACT

Multiple myeloma (MM) is a hematologic malignancy resulting from the uncontrolled proliferation of neoplastic plasma cells and the excessive production of monoclonal immunoglobulins, both of which may lead to hyperviscosity retinopathy. Here, we present a 56-year-old male who had progressive painless loss of vision for 1 month. Ophthalmic examination revealed hyperviscosity retinopathy with bilateral central retinal vein occlusion-like appearance. Hematologic assessment revealed immunoglobulin A MM. Although the patient was treated with chemotherapy and autologous stem cell transplantation soon after referral, he did not survive due to the aggressive course of the disease. We highlight the importance of the ophthalmic presentation of MM. Early recognition and referral to an oncologist can lead to timely diagnosis and appropriate management.

KEYWORDS: *Bilateral central retinal vein occlusion, Hyperviscosity retinopathy, Multiple myeloma*

INTRODUCTION

Multiple myeloma (MM) represents approximately 1% of all cancers and 13% of all hematologic malignancies [1]. It is a hematologic disease resulting from the uncontrolled proliferation of neoplastic plasma cells in the bone marrow and the excessive production of monoclonal immunoglobulins, both of which may lead to hyperviscosity syndrome (HVS) [2]. Common systemic symptoms include fatigue, bodyweight loss, bone pain, and loss of appetite. Although ophthalmic involvement is not uncommon in patients with HVS, MM cases initially manifesting with blurred vision due to hyperviscosity retinopathy have been scarcely reported [3]. Here, we report a case with the progressive painless loss of vision and bilateral central retinal vein occlusion (CRVO)-like appearance with Roth spots as an initial presentation of MM.

CASE REPORT

This is a retrospective case report approved by the Institutional Review Board of Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation (IRB# 08-CR-097), presenting data recorded on the patient's chart. Informed written consent was waived by IRB.

A 56-year-old male presented with progressive painless loss of vision in both eyes for 1 month and visited our ophthalmic clinic. After careful inquiry of past symptoms, the patient mentioned fatigue, dyspnea, and body weight loss occurring in the

past 3 months. Physical examination showed pale skin and conjunctiva. On initial ophthalmic examination, the best-corrected visual acuity (BCVA) was 0.6 in the right eye and 0.15 in the left eye. Findings of the anterior segment were unremarkable. Fundus photography showed hyperviscosity retinopathy with bilateral CRVO-like appearance. Dilation and tortuosity of the central retinal vein, extensive intraretinal hemorrhage, disc swelling, cotton wool spots (CWS), and multiple Roth's spots were seen in both eyes [Figure 1a and b]. Optical coherence tomography (OCT) revealed marked subretinal fluid (SRF) and intraretinal fluid [Figure 1c and d]. The average central retinal thickness (CRT) was 539 μ m in the right eye and 688 μ m in the left eye.

Initial laboratory investigation showed pancytopenia with white blood cell count: 3.74 K/ μ L, hemoglobin: 3.9 g/dL, and platelet counts: 97 K/ μ L. Chest X-ray and computed tomographic showed a well-defined mass over the left upper lung [Figure 2]. Considering the patient's clinical presentation, we immediately referred this patient to an oncologist for comprehensive evaluation. Further blood workup demonstrated immunoglobulin A (IgA) hypergammaglobulinemia

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Access this article online

Quick Response Code:



Website: www.tcmjmed.com

DOI: 10.4103/tcmj.tcmj_214_19

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How to cite this article: Kuo HH, Shen EP. Hyperviscosity retinopathy as the initial presentation of aggressive multiple myeloma. Tzu Chi Med J 2020; 32(4): 401-3.

(4480 mg/dL) and elevated β 2-microglobulin (5710 ng/mL). Serum protein electrophoresis showed an M-spike in the gamma region. Biopsy of the left upper lung mass and bone marrow revealed a positive reaction to the monoclonal κ light chain [Figure 3], proving the diagnosis of IgA MM.

The patient subsequently underwent chemotherapy with bortezomib, thalidomide, and prednisolone. Twenty-one days after chemotherapy treatment, his BCVA improved to 0.7 in both eyes. Fundus photography showed a decrease in the number of Roth spots and CWS in both eyes [Figure 4a and b]. OCT revealed decreased SRF, and CRT improved to 307 μ m in the

right eye and 495 μ m in the left eye [Figure 4c and d]. The patient's ophthalmic condition showed further improvement 50 days after chemotherapy; however, his systemic condition worsened. An autologous stem-cell transplant was done trying to control the disease. Nonetheless, the transplant procedure failed and the patient died due to the aggressive course of disease.

DISCUSSION

Diverse ocular manifestations of MM have been reported, including corneal deposition, scleritis, pars plan cysts,

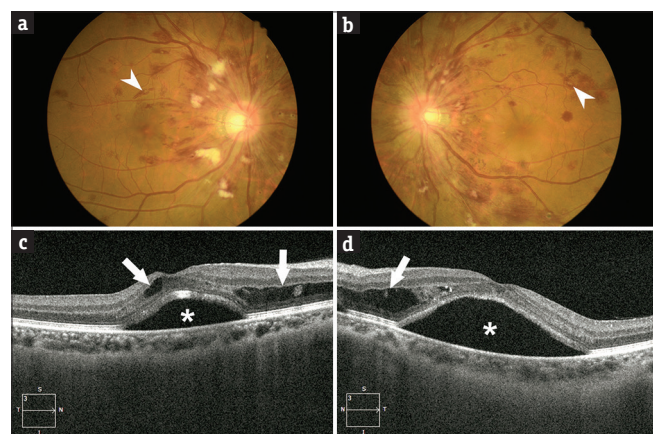


Figure 1: Fundus photography of the (a) right eye and (b) left eye showed dilation and tortuosity of the central retinal vein, extensive intraretinal hemorrhage, disc swelling, multiple cotton wool spots, Roth spots (arrowheads), and macular edema. Optical coherence tomography images of the right (c) and left (d) macula revealed marked subretinal fluid (asterisk) and intraretinal fluids (arrows)

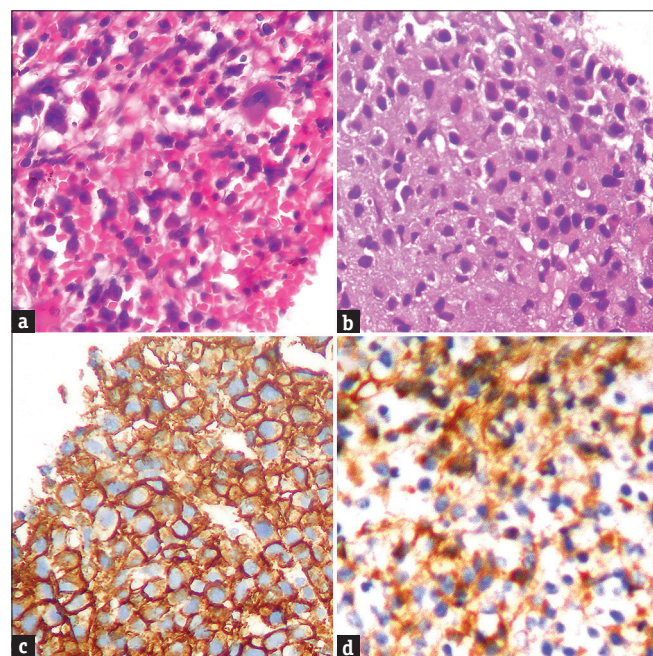


Figure 3: (a) Histopathology with H and E, $\times 400$ showed diffuse infiltration of plasmacytoid cells in the bone marrow. (b) Diffuse infiltration of plasmacytoid cells over the left upper lung (H and E, $\times 400$). (c) The tumor cells from the left upper lung mass were immunoreactive for CD138 (IHC, $\times 400$). (d) The tumor cells were immunoreactive for monoclonal kappa light chains but not to lambda light chains (IHC, $\times 400$)

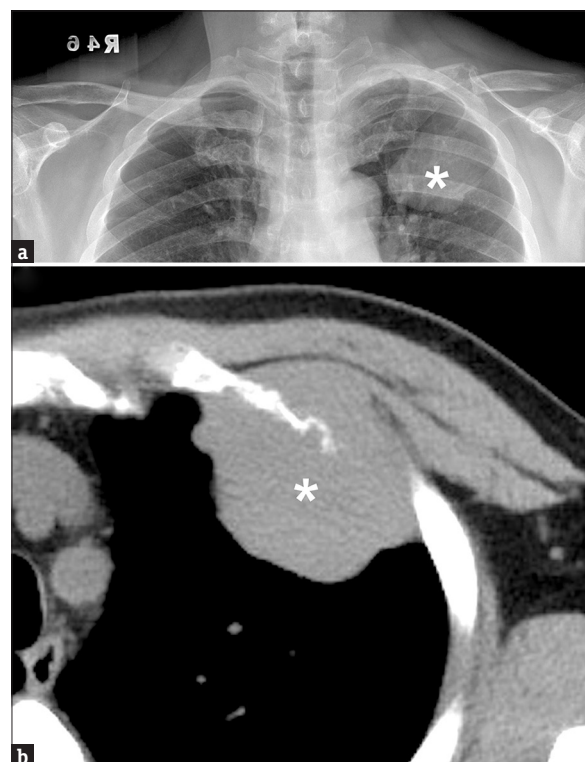


Figure 2: (a) Chest X-ray showed left upper lung mass (asterisk) with soft-tissue density. (b) Computed tomography of the chest noted a 6.5 cm left upper lung mass (asterisk) with rib destruction

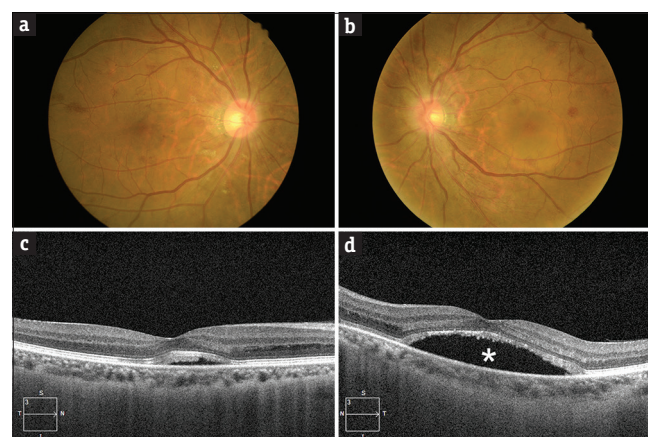


Figure 4: Fundus photography of (a) right and (b) left eyes 3 weeks after chemotherapy showed a few remaining blot retinal hemorrhages without Roth spots and cotton wool spots. Optical coherence tomography images of the right (c) and left (d) eyes revealed near total absorbance of subretinal fluid in the right eye and a notable decrease in subretinal fluid (asterisk) in the left eye

choroidal infiltrates, retinal capillary microaneurysm, ocular plasmacytoma, hyperviscosity retinopathy, and CRVO [4-6]. Due to the highly variable clinical presentation, a high index of suspicion must be regarded for the early diagnosis of MM.

Retinal vascular disorders are not uncommonly seen in MM patients; however, symptomatic HVS occurs only in about 5% of the cases [2]. Excessive production of monoclonal immunoglobulins due to abnormal plasma cells may lead to HVS [2]. The clinical presentation in HVS consists of the triad of mucosal bleeding, visual changes, and neurological symptoms, including headache, vertigo, seizures, and coma. In our case, visual change is the most prominent presentation. Hyperviscosity retinopathy was seen in both eyes of our patients. It mimics that of CRVO presenting as diffuse retinal hemorrhages in all four quadrants of the retina, with dilated and tortuous retinal veins, disc edema, CWS, and serous macular detachment. CRVO is usually a unilateral disease with common underlying diseases such as hypertension and/or diabetes mellitus [7]. However, when it occurs bilaterally, other causes must be considered. Differential diagnosis of bilaterally CRVO-like appearance includes MM, dysproteinemias, polycythemia, antiphospholipid syndrome, protein C and S deficiency, hyperhomocysteinemia, and other hematological disorders [3].

White-centered hemorrhages, also known as Roth spots, are not commonly seen with CRVO. However, Roth spots are noted in both eyes of our patients. Roth spots are usually associated with systemic conditions such as subacute bacterial endocarditis, leukemia, anemia, anoxia, carbon monoxide poisoning, prolonged intubation, hypertensive retinopathy, diabetic retinopathy, neonatal birth trauma, complicated delivery, and acute reduction of intraocular pressure following trabeculectomy [8]. The formation of Roth's spots has been thought to be related to ischemic insults to the capillary endothelium with elevated venous pressure leading to rupture of the retinal capillaries, and thus extravasation of the blood [8]. Subsequent coagulation cascade resulted in the formation of a fibrin-platelet thrombus, which appeared as a white-centered retinal

hemorrhage [8]. In MM, as in our case, severe anemia may have caused retinal ischemia which resulted in the unusual appearance of multiple Roth spots in both eyes of our patient.

CONCLUSION

Comprehensive ophthalmic and systemic examination should be performed in patients presenting with hyperviscosity retinopathy. Ocular manifestation may be the initial manifestation of a potentially life-threatening hematologic illness. Early recognition and referral can lead to timely diagnosis and appropriate management.

Financial support and sponsorship

This work was supported by a grant from the Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, TCRD-TPE-108-08.

Conflicts of interest

There are no conflicts of interest.

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