Bilateral Serous Macular Detachment and Unilateral Choroidal Neovascular Membrane in a Patient With Waldenström's Macroglobulinemia*

Waldenström Makroglobulinemi'li Bir Olguda Bilateral Seröz Makula Dekolmanı ve Unilateral Koroidal Neovasküler Membran Birlikteliği

Önder AYYILDIZ[1], A. Hakan DURUKAN[2], Gökhan ÖZGE[1], Murat KÜÇÜKEVCİLİOĞLU[1], Dorukcan AKINCIOĞLU[3], Seçkin AYKAŞ[1]

ABSTRACT

A 74-year-old male with hyperviscosity due to Waldenström's macroglobulinemia (WM) presented with bilateral decreased vision. Bilateral serous macular detachment (SMD) was observed in fundoscopy. Optical coherence tomography (OCT) confirmed bilateral SMD, which was associated with choroidal neovascular membrane (CNVM) in the left eye (LE). The patient received plasmapheresis due to hyperviscosity. He experienced visual improvement in the right eye (RE) shortly after the plasmapheresis. However, there was not any visual improvement in the LE three months after the plasmapheresis. Optical coherence tomography revealed the complete resolution of SMD, and also the presence of CNVM with a central foveal thickness of 308 micron. The patient recieved three doses of intravitreal ranibizumab (IVR) injections monthly to treat CNVM in the LE, which later showed no visual and anatomical improvement. We describe the first case of WM with bilateral SMD associated unilateral CNVM in our knowledge who was treated with plasmapheresis and IVR.

Keywords: Waldenström's Macroglobulinemia, serous macular detachment, choroidal neovascular membrane, optical cohorence tomography, intravitreal ranibizumab.

ÖZ

Waldenström makroglobulinemiye (WM) bağlı hiperviskozite bulunan 74 yaşında erkek bir hasta bilateral görme azlığı ile başvurdu. Fundoskopide bilateral seröz makula dekolmanı (SMD) gözlendi. Optik koherens tomografi (OKT), sol gözde koroidal neovasküler membran (KNVM) ile ilişkili olan bilateral SMD varlığını gösterdi. Hastaya hipervizkozite nedeniyle plazmaferez uygulandı. Plazmaferezden hemen sonra sağ gözde görme düzeyinde artış oldu. Fakat, plazmaferezden üç ay geçmesine rağmen sol gözde görme artışı olmadı. Optik koherens tomografi sol gözde SMD'nin tam rezolüsyonunu ve aynı zamanda KNVM ile birlikte merkezi foveal kalınlığın 308 mikron olduğunu gösterdi. Sol gözündeki KNVM'yi tedavi etmek amacıyla hastaya üç doz intravitreal ranibizumab (IVR) aylık uygulandı, fakat görsel ve anatomik düzelme sağlanamadı. Plazmaferez ve IVR ile tedavi edilmiş, unilateral KNVM ile ilişkili iki gözünde SMD tespit edilen bildiğimiz kadarıyla ilk WM'li vakayı tanımlıyoruz.

Anahtar Kelimeler: Waldenström Makroglobulinemi, seröz makula dekolmanı, koroidal neovasküler membran, optik kohorens tomografi, intravitreal ranibizumab.

This work was presented at the June 6-9, 2015 Congress (Vienna / Austria).

1- M.D. GATA Medical Faculty, Department of Ophthalmology, Ankara/TURKEY
AYYILDIZ O., dronderayyildiz@gmail.com
OZGE G., gozge.gata.edu.tr
KUCUKEVCILIOGLU M., mkucukevcilioglu.gata.edu.tr
AYKAS S., seckinaykas@hotmail.com
2- M.D. Professor, GATA Medical Faculty, Department of Ophthalmology, Ankara/TURKEY
DURUKAN H.A., ahakand@yahoo.com
3. M.D. Asistant GATA Medical Faculty, Department of Ophthalmology, Ankara/TURKEY
AKINCIOGLU D., dr.dorukcan@yahoo.com

Geliş Tarihi - Received: 18.11.2015
Kabul Tarihi - Accepted: 28.03.2016
Ret-Vit 2016;24:330-332

Yazışma Adresi / Correspondence Adress:
M.D. Onder AYYILDIZ
GATA Medical Faculty, Department of Ophthalmology, Ankara/TURKEY

Phone: +90 505 253 86 90
E-mail: dronderayyildiz@gmail.com

INTRODUCTION

Waldenström's Macroglobulinemia (WM) is a type of lymphoproliferative disease placed in subcategory of low-grade Non-Hodgkin lymphoma and characterized by overproduction of monoclonal IgM protein.[1] Increased protein load in the blood stream may cause hyperviscosity characterized by circulatory stasis. This progressive plasma cell dyscrasia has the capacity to induce devastating effects on many of the body's vital organ systems, including neurologic, cardiac, renal, gastrointestinal and pulmonary.[2] Among many systemic problems, 37% of patients exhibit ocular findings at diagnosis including venous obstruction, serous retinal detachment, macular edema and retinopathy.[3] We report a case of WM with bilateral serous macular detachment (SMD) and unilateral choroidal neovascular membrane (CNVM), which to the best of our knowledge has never been reported before.

CASE REPORT

A 74-year-old male with hyperviscosity due to WM presented with bilateral decreased vision. There was macroglobulinemia in blood, monoclonal gammopathy in electrophoresis and B-cell lymphoproliferation in bone marrow biopsy. His systemic medications included dexametasone, chlorambucil and allopurinol. Best corrected visual acuity (BCVA) was 20/80 in both eyes (BEs). Biomicroscopy revealed posterior chamber intraocular lens in BEs. Bilateral SMD was observed in fundoscopy. Optical coherence tomography (OCT) confirmed bilateral SMD, which was associated with CNVM in the left eye (LE) (Figure 1). We could not perform fluorescein angiography (FA) due to renal failure and hyperviscosity at admission. The patient received plasmapheresis due to hyperviscosity. He experienced visual improvement in right eye (RE) shortly after the plasmapheresis, three months later his BCVA improved to 20/40 with complete resolution of SMD (Figure 2). After one year of plasmapheresis, BCVA improved to full vision with no evidence of SMD in RE. However, there was not any visual improvement in LE (BCVA: 20/80) 3 months after the plasmapheresis. Optical coherence tomography revealed the complete resolution of SMD, and also the presence of CNVM related submacular intraretinal fluid with a central foveal thickness (CFT) of 308 micron (Figure 2). The patient recieved 3 doses intravitreal ranibizumab (IVR) injections monthly to treat CNVM in the LE, which later showed no visual and anatomical improvement. During the following 2 years his BCVA fluctuated depending on the presence of intraretinal fluid, and totally he received 6 IVR injections when needed. At the time of the last visit, there was a minimal subretinal fluid on OCT with a BCVA of 20/20 in the RE (Figure 3). In the LE, BCVA was 20/1250 with a central macular atrophy (CFT=169 microns) (Figure 3). We were able to perform FA at the last visit and dried CNVM was visualized without any flourescein leakage (Figure 3).

DISCUSSION

Waldenstrom's macroglobulinemia is common in elderly men who present with weakness, fatigue, recurrent infections, lymphadenopathy, and hepatosplenomegaly.[4] Ocular manifestations of WM typically result from an increased serum viscosity and include immunoprotein deposition in the cornea and conjunctiva, serous retinal detachment, retinal vascular occlusions, retinopaties, macular edema and other orbital invasions as well as immunoglobulin M (IgM) deposits in all layers of the retina.[1,5]

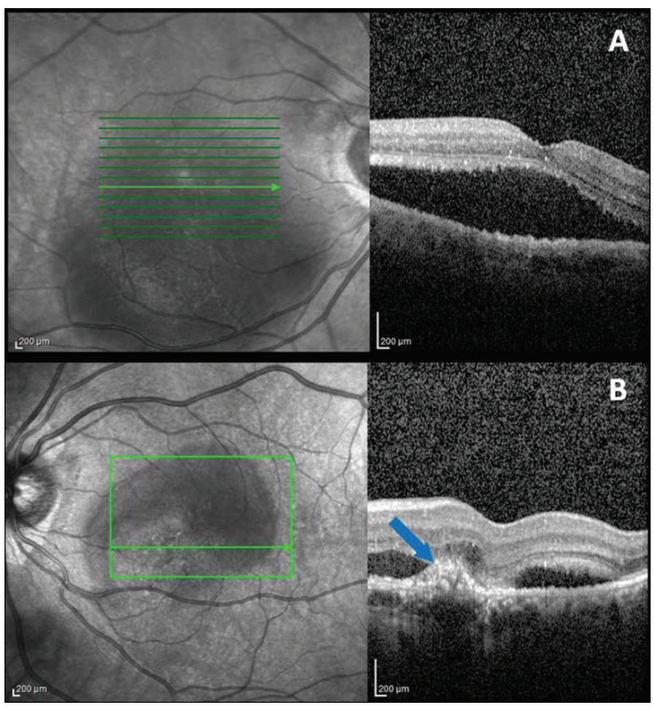

Figure 1A-B: *OCT images at admission.*
OCT shows (A) SMD in the right eye and (B) SMD associated with CNVM (blue arrow) in the left eye.

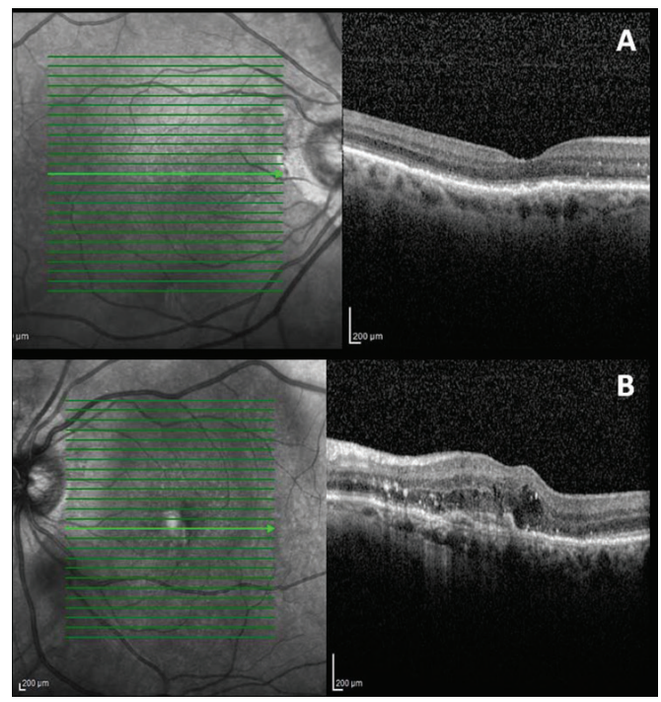

Figure 2A-B: *OCT images three months after the plasmapheresis.*
OCT revealed (A) complete resolution of SMD in the right eye and (B) resolution of SMD in the left eye with CNVM related intraretinal fluid (central foveal thickness was 308 micron).

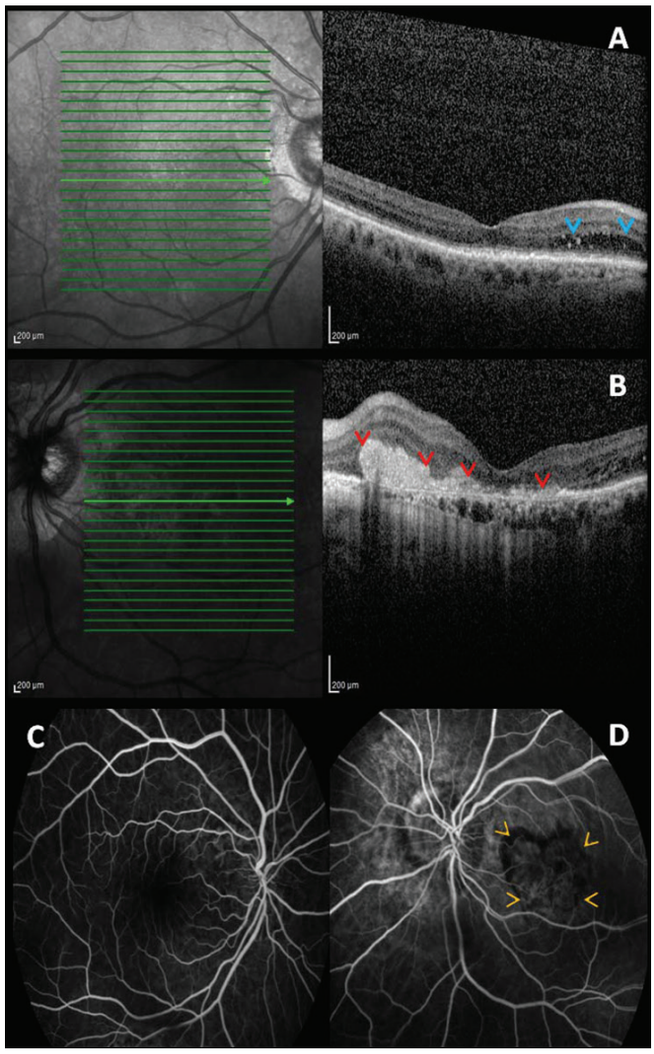

Figure 3A-D: *OCT and FA images at the time of the last visit. OCT revealed (A) no evidence of submacular fluid in the right eye, but there was minimal subretinal fluid (blue arrows) located between optic disc and macula. (B) In the left eye, OCT revealed a central macular atrophy (central foveal thickness was 169 microns) and scar formation of CNVM (red arrows). (C) FA was normal in the right eye and (D) CNVM (yellow arrows) was visualized without any flourescein leakage in the left eye.*

Serous macular detachment, which was bilateral in our case, has previously been reported. It has been suggested that IgM deposits were responsible for the occurence of SMD. It is considered to result from the presence of proteinaceous osmotic leakage into the subretinal space from the retina or the choriocapillaris.[6] Daicker et al, suggested that IgM deposition in the choroidea could lead to RPE dysfunction.[7] Immunoglobulin M is a large molecule to diffuse from vascular structures but the presence of Ig deposits were identified both in the superficial retina and subretinal fluid by immunofluorescence.[8,9] In retinal metabolism RPE transports ions, water and metabolic end products from subretinal space though osmotic gradients between retina and choroidea are also helpful.[9] So the IgM overproduction breaks down this balance by both toxicity to RPE and disrupting osmotic gradient. The striking decrease in height of subretinal fluid in our patient following plasmapheresis was supporting this theory. Plasmapheresis to reduce the high serum concentrations of IgM in patients with WM is quite successful in relieving the serum viscosity, together with an improvement of chorioretinal complications and visual dysfunction owing to macular detachment.[2,10,11] Concurrent systemic treatment may also limit the progression of the underlying plasma cell malignancy. The visual improvement in the RE of our patient just after the plasmapheresis, and complete resolution of SMD after three months may be attributable to the efficacy of plasmapheresis. Similar to the previous reports we suggest to reduce the high serum viscosity for ocular complications with systemic manifestations in WM. Despite the increase in BCVA to 20/20 in the RE and resolution of SMD in both eyes, there was not a significant visual improvement in the LE due to the refractory subfoveal intraretinal fluid related to CNVM. To our knowledge among the all the ocular manifestations in WM, no chorioretinal neovascularisation was reported before. There is a strong association of CNVM in various ocular disorders like age related macular degeneration (AMD), angioid streaks and myopia. Although our patient was in AMD, we did not detect drusen on examination and OCT. We argue that the occurence of CNVM may be related with pathophysiology of WM. It has been established that angiogenesis might be a basic pathophysiologic component for disease evolution and progression in WM.[12] It was also showed that vascularity of bone marrow (increased neovascularization) and serum levels of angiogenesis cytokines and growth factors (Vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), transforming growth factor beta (TGF-beta)) are increased in WM patients.[12] So we think that this was an unusual case because there was no sign of retinopathy as usual in WM, but only SMD associated with CNVM.

REFERENCES/KAYNAKLAR

1. Sen HN, Chan CC, Caruso RC, et al. Waldenström's macroglobulinemia–associated retinopathy. Ophthalmology 2004;111:535-9.
2. Pilon AF, Rhee PS, Messner LV. Bilateral, persistent serous macular detachments with Waldenström's macroglobulinemia. Optom Vis Sci 2005;82:573-8.
3. Baker PS, Garg SJ, Fineman MS, et al. Serous macular detachment in Waldenstrom macroglobulinemia: A report of four cases. Am J Ophthalmol 2013;155:448-455.
4. Knox CM, Wong IG, Howes EL, et al. Vitreitis and Waldenström's macroglobulinemia. J Ophthalmol 1998;126:314-5.
5. Şimşek HC, Akkoyun İ, Yılmaz G. Hematolojik Hastalıklarda Göz Bulguları. Ret-Vit 2014;22:85-92.
6. Brollya A, Janon C, Precaustac F, et al. Pseudovitelliform subfoveal deposit in Waldenström's macroglobulinemia. Case Rep Ophthalmol 2012;3:236-9.
7. Daicker BC, Mihatsch MJ, Strom EH, Fogazzi GB. Ocular pathology in light chain deposition disease. Eur J Ophthalmol 1995;5:75-81.
8. Friedman AH, Marchevsky A, Odel JG, et al. Immunofluorescent studies of the eye in Waldenström's macroglobulinemia. Arch Ophthalmol 1980;98:743-6.
9. Berta A, Beck P, Mikita J. IgM paraprotein in the subretinal fluid of a patient with recurrent retinal detachment and Waldenström's macroglobulinaemia. Acta Med Hung 1985;42:179-186.
10. Fenicia V, Balestrieri M, Perdicchi A, et al. Intravitreal injection of dexamethasone ımplant in serous macular detachment associated with Waldenström's disease. Case Rep Ophthalmol 2013;4:64-9.
11. Gedik Ş, Gür S, Yılmaz G, Akova YA. Multipl Myelom, Hiperviskozite Sendromu ve Santral Retinal Ven Tıkanıklığı İlişkisi. Ret-Vit 2005;13:147-151.
12. Terpos E, Tasidou A, Kastritis E, et al. Angiogenesis in Waldenström's macroglobulinemia. Clinical Lymphoma & Myeloma 2009;9:46-9.