

Bilateral central retinal vein occlusion in non-Hodgkin lymphoma and the effects of intravitreal bevacizumab injection

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ABSTRACT

The purpose of this study is to report bilateral central retinal vein occlusion in a patient with non-Hodgkin lymphoma and the effects of intravitreal bevacizumab injection. This is a case report of a patient seen and treated in the ophthalmology department of Ondokuz Mayıs University Medical Faculty. Bilateral central retinal vein occlusion was observed in the patient because of hyperviscosity due to non-Hodgkin lymphoma which resulted in decreased visual acuity and increased macular thickness. Bilateral intravitreal bevacizumab injection increased best corrected visual acuity and reduced intraretinal, subretinal edema markedly. A hyperviscosity syndrome or inflammatory condition should be suspected when a patient, less than 50 years, has bilateral and simultaneous central retinal vein occlusion. Intravitreal bevacizumab injection is as an effective treatment for intraretinal and subretinal edema in central retinal vein occlusion secondary to non-Hodgkin lymphoma.

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1. Introduction

After diabetes mellitus, central retinal vein occlusion (CRVO) is the most common disease causing visual loss (Central Vein Occlusion Study Group, 1997). Various risks have been identified, including hypertension, hyperlipidemia, diabetes mellitus and hyperviscosity syndrome caused by leukaemia or lymphoma. (Williamson, 1997; Cheung and Tsaloumas, 2002) CRVO commonly affects patients older than 65 years. Bilateral involvement can be seen in 7.7% to 19% of all patients with CRVO (Hayreh, 2003). A hyperviscosity syndrome or inflammatory condition should be suspected when a patient younger than 50 years has bilateral and simultaneous CRVO. Because bilateral ocular involvement can be the first sign of a severe systemic disease, timely diagnosis is very important.

Our patient had bilateral CRVO resulting from non-Hodgkin lymphoma. Ocular involvement can be observed in 7% of patients with non-Hodgkin lymphoma so it is important to prevent visual threatening complications. There is increasing evidence that vascular endothelial growth factor (VEGF) plays a key role in the pathogenesis of macular edema secondary to CRVO. Therefore, VEGF appears to be a promising therapeutic target in the treatment of CRVO (Rosenfeld et al., 2005; Iturralde et al., 2006; Jaissle et al., 2006; Kahook et al.,

2006). Intravitreal bevacizumab injection is a new and effective treatment in CRVO.

The purpose of this study is to report bilateral CRVO in a patient with non-Hodgkin lymphoma and the effect of intravitreal bevacizumab injection in the treatment of macular edema.

2. Case

A 48 years old man, diagnosed with non-Hodgkin lymphoma, presented when his right eye suffered a sudden visual loss. Ophthalmological examination revealed that, best corrected visual acuity (BCVA) was 20/30 in his right eye and 20/20 in his left eye. Anterior segment and angles were unremarkable on slit-lamp biomicroscopy and intraocular pressure measurements were normal in both eyes. Intraocular pressure was normal in both eyes. Fundus examination showed swollen optic discs, venous tortuosity and extensive retinal haemorrhages bilaterally, findings consistent with bilateral CRVO (Fig. 1).

The patient was re-evaluated two weeks later. BCVA was 20/30 in his right eye and had decreased to 20/25 in his left eye. The patient was examined with optical coherence tomography (OCT). Macular edema was diagnosed because

central macular thickness (CMT) was 348 μm in the right eye and 625 μm in the left eye (Fig. 2).

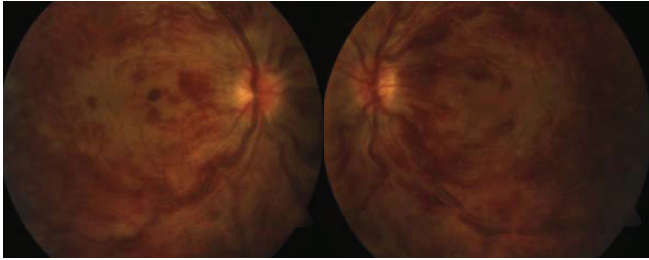


Fig. 1. Bilateral SRVO, swollen optic discs, venous tortuosity and extensive retinal haemorrhages

Intervention was not required because of bilateral good visual acuity. On examination after the first month, BCVA had decreased markedly to 20/400 in the right eye and counting fingers at one meter in the left eye. OCT revealed intraretinal and subretinal edema bilaterally (Fig. 3).

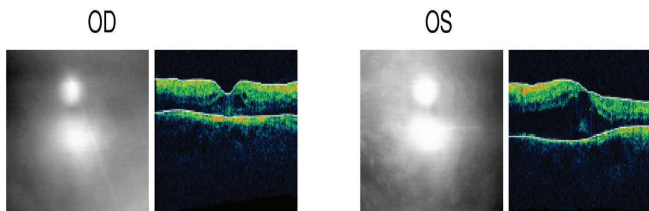


Fig. 2. At the week 2, bilateral intraretinal edema was evident

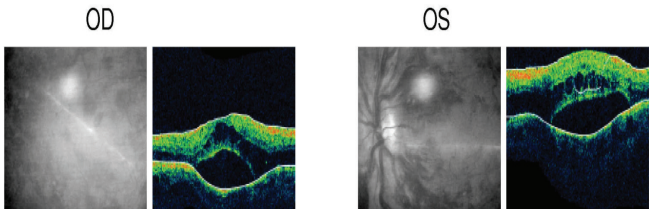


Fig. 3. At 1 month, there was increased intraretinal and subretinal edema bilaterally

CMT was 852 μm in the right eye and 649 μm in the left eye. As a result of increased macular edema and decreased visual acuity, it was decided to perform bilateral intravitreal bevacizumab injection. Firstly, for the left eye, the 2.5 mg of bevacizumab was prepared and placed in a tuberculin syringe using aseptic techniques. After the eye had been prepared using 5% povidoneiodine, an eyelid speculum was used to stabilize the eyelids and the injection of bevacizumab was performed 3.5 mm posterior to the limbus and through the inferotemporal pars plana with a 30-gauge needle under topical anaesthesia. The same procedure was performed for the right eye one week later. No complications were observed. At the week 3, after bevacizumab injection, BCVA was 20/50 in his right eye and 20/200 in his left eye. OCT showed that CMT had decreased to 453 μm in the right eye and 437 μm in the left eye while intraretinal and subretinal edema had decreased markedly in both eyes (Fig. 4). At the last visit, 9 months after bevacizumab injection, BCVA was 20/25 μm in the right eye, 20/25 μm in the left eye. Fundus examination showed normal optic discs and bilaterally, there were neither venous tortuosity nor retinal haemorrhages (Fig. 5).

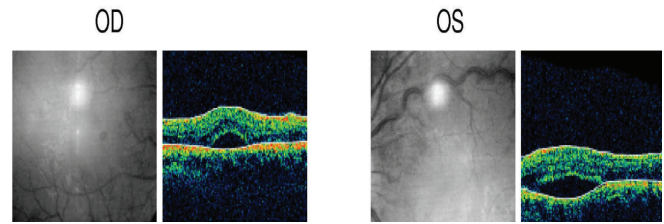


Fig. 4. At the week 3 after bilateral intravitreal bevacizumab injection, there was decreased intraretinal and subretinal edema

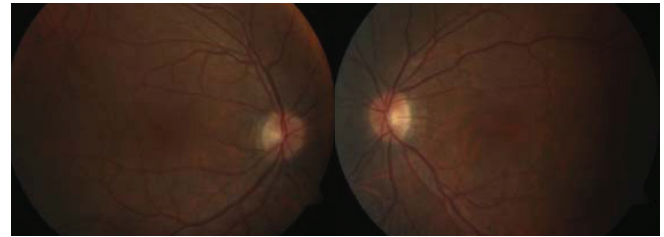


Fig. 5. At 9 month after treatment, fundus examination showed normal optic discs and bilaterally there were neither venous tortuosity nor retinal haemorrhages

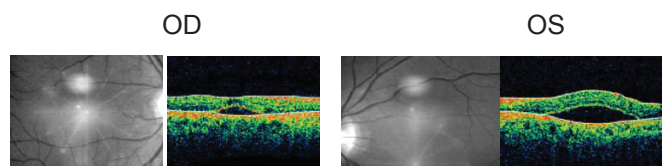


Fig. 6. At 9 month after treatment, there was subretinal fluid in both eyes at

CMT score was 314 and 521 in the right and left eye, respectively. There was subretinal fluid in both eyes at OCT (Fig. 6). Further injections were proposed but the patient declined and follow-up was discontinued.

3. Discussion

After diabetes mellitus, CRVO is the second most frequent disease causing visual loss. (The Central Vein Occlusion Study Group, 1997) The causes of CRVO are hypertension, cardiovascular disease, cerebrovascular disease, arteriosclerosis, diabetes mellitus, systemic lupus erythematosus, antiphospholipid antibody syndrome, dysproteinemias, hyperhomocysteinemia, leukaemia and lymphoma with thrombocytopenia (Williamson, 1997; Cheung and Tsaloumas, 2002). CRVO commonly affects patients older than 65 years. Bilateral involvement can be seen in 7.7% to 19% of all patients with CRVO (Hayreh, 2003). A hyperviscosity syndrome or inflammatory condition should be suspected when a patient younger than 50 years has bilateral and simultaneous CRVO. Because bilateral ocular involvement can be the first sign of a severe systemic disease, timely diagnosis is very important. Our patient had bilateral CRVO according to the disease of non-Hodgkin lymphoma.

Ocular involvement can be observed in 7% of patients with non-Hodgkin lymphoma, including the direct infiltration of tumour, optic nerve compression by the central nerve system mass or retinal vascular disease because of hypercoagulability and hyperviscosity.

The hyperviscosity is caused by increased levels of cellular blood components because of diseases such as poly-

cythemia vera, leukaemia and lymphoma or by the abnormality of serum protein, such as in macroglobulinemia. In either situation, the hyper viscosity reduces the rate of blood flow through the retinal vascular system. As the velocity within the retinal vessels decreases, the intraluminal pressure on the retinal vessel wall increases. The thin walled retinal veins respond to increased pressure with dilatation and tortuosity. The increased intra-vascular pressure results in pathological changes in the endothelial cell walls. This produces changes in the junctional complexes between endothelial cells and allows the vascular contents to leak into the adjacent tissues. This is seen, clinically, as intra-retinal edema and small haemorrhages (Spalter, 1959; Grindle et al., 1976; Friedman et al., 1980).

The causes of visual loss in CRVO are macular edema and retinal ischemia. The final visual acuity is dependent on the initial visual acuity. In about 50% of patients with non ischemic CRVO, vision may be 20/200 or worse. One third of patients may progress to the ischemic type, commonly in the first 6-12 months after presentation. In more than 90% of patients with ischemic CRVO, final visual acuity may be 20/200 or worse (The Central Vein Occlusion Study Group, 1997).

The first step in the treatment of CRVO is getting the systemic disease under control. Intervention is not required if the initial visual acuity is good because nonischemic CRVO may resolve completely without any complications in about 10% of cases. It was thought that anticoagulant and antiplatelet agents could be beneficial in the treatment of CRVO but then it was determined that these agents can convert the nonischemic CRVO to ischemic CRVO (Hayreh et al., 2002). Because of the presence of hyperviscosity in these patients, hemodilution may be thought as a treatment strategy but its efficacy has not been proven yet (Hayreh, 2003).

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There is increasing evidence that vascular endothelial growth factor (VEGF) plays a key role in the pathogenesis of macular edema secondary to CRVO. Therefore, VEGF appears to be a promising therapeutic target. Intravitreal bevacizumab injection is a new and effective treatment of CRVO. In the study by Iturralde et al (2006), the mean central macular thickness at the baseline was 887 μm and decreased to a mean of 372 μm at 1 month ($P < 0.001$). The mean baseline acuity was 20/600 and the mean acuity at 1 month was 20/200, a difference that was highly significant ($P = 0.001$). At the last follow-up, a mean of 3 months after the first injection, the mean visual acuity was 20/138, which was significantly better than the baseline ($P < 0.001$). (Iturralde et al, 2006) In the study of Siegfried et al, BCVA increased from 20/250 to 20/80 and macular thickness decreased from 535 \pm 148 to 323 \pm 116 μm after the intravitreal bevacizumab injection (Priglinger et al., 2007). In our patient, BCVA was $>20/50$ in both eyes initially. Before the decision for intravitreal bevacizumab injection, BCVA was $<20/200$ bilaterally. At the week 3 after the bevacizumab injection, BCVA had increased to the level between 20/200 and 20/50 bilaterally. Also the CMT decreased markedly in both eyes.

A hyperviscosity syndrome or inflammatory condition should be suspected when a patient younger than 50 years has bilateral and simultaneous central retinal vein occlusion. Intravitreal bevacizumab is a new and effective treatment for intraretinal and subretinal edema in central retinal vein occlusion secondary to hyperviscosity syndrome.

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