Central Retinal Vein Occlusion Associated With Varenicline

Vareniklinle İlişkili Santral Retinal Ven Tıkanıklığı

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ABSTRACT

Retinal venous occlusive disease is the second most common retinal vascular disorder following diabetic retinopathy.The exact pathogenesis and risk factors of RVO in younger patients—most of whom are otherwise healthy are still poorly understood. This case report shows a varenicline (Champix, Pfizer, Mumbai, India)-associated acute thrombotic CRVO in a patient without previous history of systemic inflammation or vascular occlusive disease.

Key Words: Varenicline, Thrombosis, Central Retinal Vein Occlusion.

ÖZ

Retinal ven tıkanıklığı,diyabetik retinopatiden sonra en yaygın retinal vasküler hastalıktır. Çoğu sağlıklı olan genç hastalarda retinal ven tıkanıklığının patogenezi ve risk faktörleri henüz tam olarak anlaşılamamıştır.Bu olgu sunumu, daha önce sistemik inflamasyon veya vasküler tıkayıcı hastalık öyküsü olmayan bir hastada vareniklinle(Champix, Pfizer, Mumbai, India) ilişkili akut trombotik SRVO'yu göstermektedir.

Anahtar Sözcükler: Vareniklin,Tromboz, Santral Retinal Ven Tıkanıklığı

INTRODUCTION

Retinal venous occlusive disease is the second most common retinal vascular disorder following diabetic retinopathy.[1] In older populations, there may be associated systemic vascular disease including hypertension, diabetes, hyperlipidemia and atherosclerotic cardiovascular disease.[2] Younger individuals who present with a clinical picture of CRVO may have an underlying hypercoagulable or inflammatory etiology.[3-4] Thrombosis of the central retinal vein is an end-stage phenomenon that is induced by a variety of primary lesions such as compressive or inflammatory optic nerves or orbital problems including structural abnormalities in the lamina cribrosa or hemodynamic changes. The occlusion is believed to be the result of a thrombus in the central retinal vein at or posterior to the lamina cribrosa.[1]

CASE REPORT

A 34-year-old male patient presented to our clinic with sudden painless vision loss in his right eye for three days. He had left smoking three months ago. He had been taking varenicline (Champix, Pfizer, Mumbai, India) 1 mg twice daily since that time. On the ophthalmologic examination, we documented best corrected visual acuities of 5/20 OD and 20/20 OS. The intraocular pressures were 13 mmHg in the right, and 14 mmHg in the left.

Slit lamp exam showed normal anterior segment structures with open angles bilaterally. There was a subtle, relative afferent pupillary defect on the right eye. Fundoscopy showed marked optic nerve head edema, tortuous retinal veins with intraretinal hemorrhages, retinal nerve fiber layer infarctions, flame-shaped retinal hemorrhages along the superior

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and inferior vascular course compatible with right central retinal vein occlusion. (Fig. 1) Left fundoscopic examination was normal. Flourescein angiogram of the right eye showed blocked venous fluorescence from the retinal hemorrhages as well as vessel wall staining and extensive areas of capillary non-perfusion. (Fig.2) There was no sign of ischemia.

Cystoid macular edema including the fovea was shown by optical coherence tomography (OCT-Heidelberg Spectralis®, Germany) on the right eye. (Fig 3) Based on these findings, the patient was diagnosed with non-ischemic central retinal vein occlusion in the right eye. Subsequently, laboratory tests were done including hypercoagulability, platelets, MCV, RDW, hemoglobin, prothrombin time, INR, aPTT, ANA, anti dsDNA, rheumatoid factor, sedimentation, CRP, serum lipid profile, serum protein-hemoglobin electrophoresis, angiotensin converting enzyme, VDRL, TPHA, HIV, HBsAg, HBV IgM, HCV RNA, functional protein S, C, antithrombin III assay, Factor V Leiden PCR assay, antiphospholipid antibody titer, lupus anticoagulant, anticardiolipin antibody, homocysteine, folate level, B12 level, PPD and electrocardiography were completed. In addition to these tests, the patient was consulted to the department of hematology and cardiology. All tests and consultation results were normal.

The use of twice per day Varenicline (Champix 1mg Pfizer, Mumbai, India) was immediately stopped. The patient was prescribed acetylsalicylic acid 100 mg daily. On the fifth day of vision loss aflibercept (Eylea-Bayer AG, Leverkusen, Germany) 2 mg/0.05 mL and alteplase (recombinant tissue-type plasminogen activator rt-PA Activase, Roche, CA, USA) 50 µg/0.1 mL were injected intravitreally for macular edema and to solve the venous thrombus. One week after these injections, the patient's visual acuity become full on the right eye with mild myopic correction. There was regression in the right optic nerve head edema, retinal hemorrhage and macular edema shown by control color fundus photograph and OCT scanning.(Fig. 4). There was no recurrence of reinal vein occlusion in our follow-up of 1 year.

DISCUSSION

Although the vast majority of RVOs are found in the elderly, it can affect young adults as well. Risk factors are glaucoma, syphilis, sarcoidosis, vasculitis, increased intraorbital or

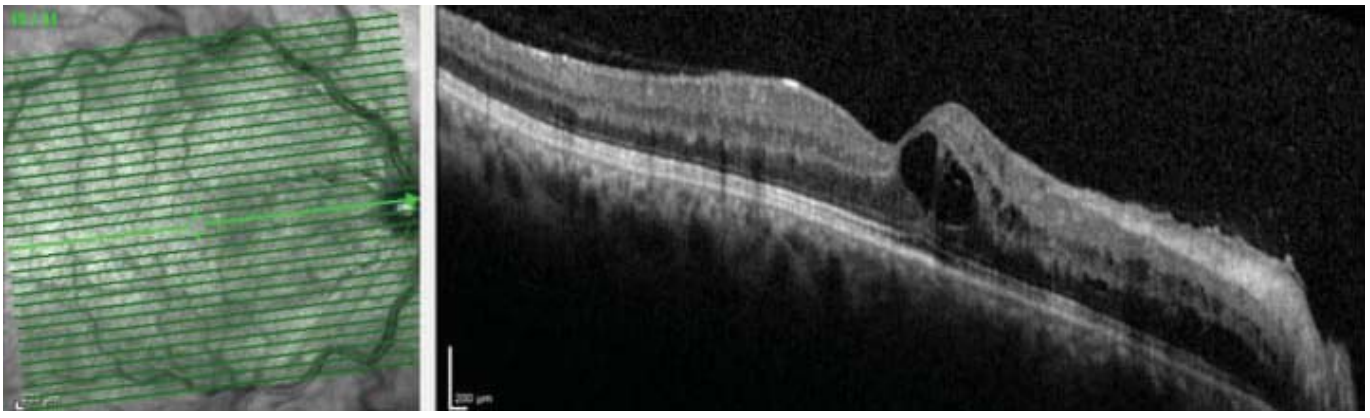
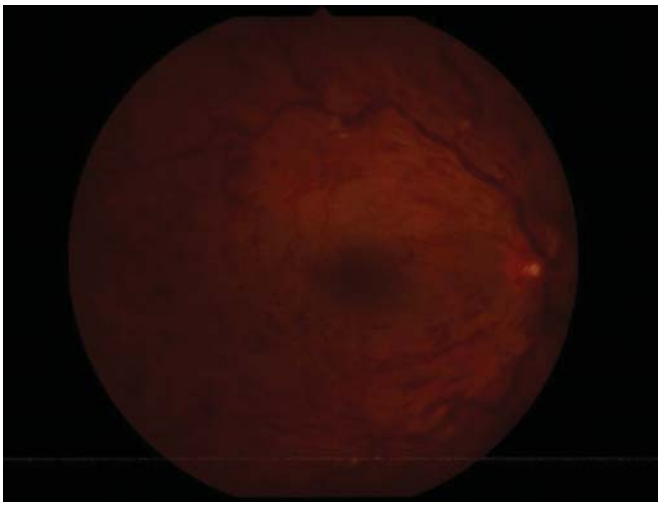


Figure 1.



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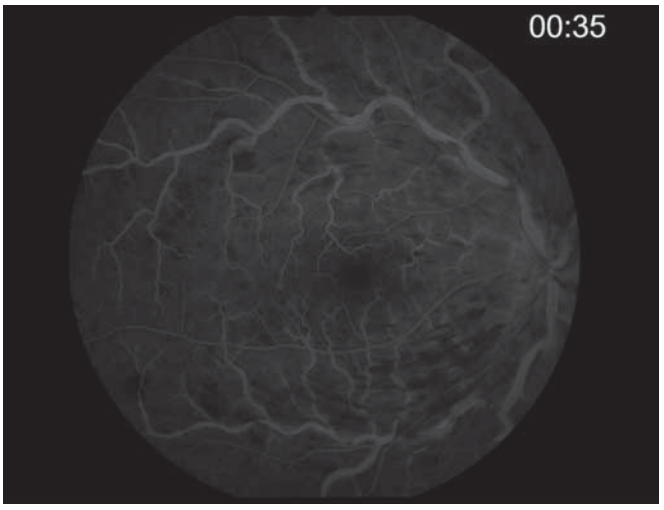

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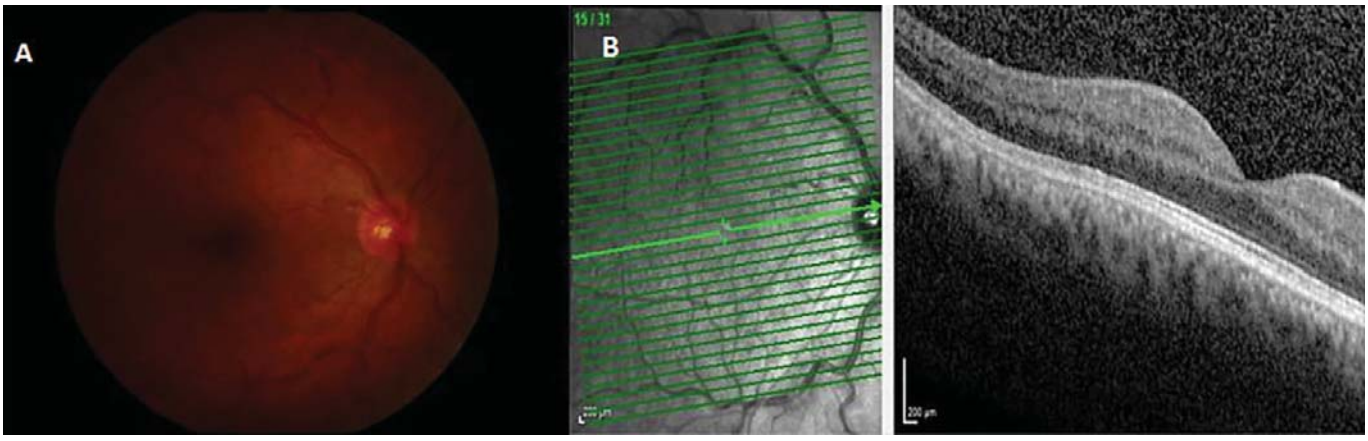

Figure 4.

intraocular pressure, hyphema, hyperviscosity syndromes (multiple myeloma, Waldenstrom's macroglobulinemia, and leukemia), high homocysteine levels, sickle cell, and HIV.[5] Smoking increases the incidence of RVO.[6] Some systemic medications such as the contraceptive pill and atypical antipsychotic agents can cause thrombotic vascular occlusion.[7-8]

Varenicline is a selective α4β2 nicotinic acetylcholine receptor partial agonist.[9] Varenicline is one of the most widely used drugs for smoking cessation and has been available since 2006.[10] This drug has been associated with adverse cardiovascular (CV) events.[11] Potential mechanisms for this association include modulation of parasympathetic output from the brainstem to the heart, release of catecholamines, and prothrombotic effects.[12] Koga et al. studied the effect of long-term varenicline treatment on atherosclerotic plaque formation in apolipoprotein E knockout (ApoE KO) mice. They showed that varenicline aggravates plaque formation by stimulating α7 nAChR and may consequently increase the risk of cardiovascular events.[13]

Kalaycı et al. reported a 30-year-old man with no known cardiac disease who developed thrombotic occlusion of the left anterior descending (LAD) artery and presented with acute coronary syndrome secondary to treatment with varenicline.[14] The Food and Drug Administration reported an increased risk of major CV events (a combined outcome of CV-related death, nonfatal stroke and nonfatal heart attack) in patients taking varenicline versus placebo.[15]

The varenicline product information also indicates that thrombosis can be seen infrequently.[16] A thrombus has also been observed in each case of CRVO in histopathological studies.[17] These findings suggest that outflow obstruction is due to thrombotic events and that fibrinolytic agents could be an appropriate treatment for retinal vein occlusion.[18-19] Thus, we added alteplase 50 µg/0.1 mL to treat the thrombus. This combination treatment contains aflibercept (Eylea-Bayer AG,Leverkusen,Germany) 2 mg/0.05 mL and alteplase (recombinant tissue-type plasminogen activator rt-PA Activase Roche, CA, USA) 50 µg/0.1 mL and showed beneficial effects on retinal blood flow and macular thickness in less than a week.

In conclusion, this case report shows a varenicline-associated acute thrombotic CRVO in a patient without previous history of systemic inflammation or vascular occlusive disease. Ophthalmologists should be aware of this side effect when using varenicline. Recombinant tissue-type plasminogen activator and anti-VEGF combination treatment may provide an effective alternative for the reduction of the thrombotic material and early resorption of macular edema.

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