Bilateral Retinal Vein Occlusions In Primary Antiphospholipid Syndrome

Primer Antifosfolipid Sendromlu Olguda Bilateral Retinal Ven Okluzyonu

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ABSTRACT

Our aim is to describe an atypical case of primary antiphospholipid syndrome with bilateral retinal vein occlusions. A detailed clinical course with a 19-month follow-up is covered in the current case. The patient presented with retinal vein occlusion as a prevailing sign. He had hyperhomocysteinemia, methylene-tetrahydrofolate-reductase enzyme (MTHFR) C677T mutation and lupus anticoagulant (LA) seropositivity. He underwent several surgical interventions, and resulted in legal blindness in one eye. Ocular manifestations of primary antiphospholipid syndrome is variable, can be the first clinical sign, and result in legal blindness despite treatment.

Keywords: Primary antiphospholipid syndrome, bilateral retinal vein occlusions; subdural hemorragia

ÖZ

Bu olguyu sunmadaki amacımız bilateral ven okluzyonu ile başvuran atipik bir primer antifosfolipid sendromu hastasını tanımlamaktır. Hastamız 19 ay boyunca ayrıntılı şekilde takip edilmiştir. Hastanın başlangıç bulgusu bilateral retinal ven okluzyonu idi. Hastada hiperhomosisteinemi, metilen-tetrahidrafolat redüktaz enzimi (MTHFR) C677T mutasyonu ve lupus antikoagülan seropozitifliği mevcuttu. Hastaya birçok cerrahi uygulanmasına karşın tek gözde yasal körlük ile sonuçlandı. Primer antifosfolipid sendromunun okuler özellikleri farklılık arzetmekte olup ilk bulgu göz rahatsızlığı olabileceği gibi yasal körlükle de sonuçlanabilmektedir.

Anahtar kelimeler: Primer antifosfolipid sendromu, bilateral retinal ven okluzyonu; subdural hemoraji

INTRODUCTION

Antiphospholipid syndrome (APS) is an autoimmune disease characterized by presence of antiphospholipid (aPL) antibodies or lupus anticoagulants (LA) together with one of the following clinical manifestations: venous and/or arterial thrombosis, repetitive fetal loss and thrombocytopenia.[1] This condition is usually associated with other autoimmune dise-

ases mostly the systemic lupus erythematosus (SLE). If the syndrome is without an another recognizable autoimmune disease, however, the syndrome is named as primary antiphospholipid syndrome (PAS).[2] The ocular manifestation of APS includes retinal vein or artery occlusions, monocular or binocular transient visual loss, diplopia, visual field loss, and ischemic optic neuropathy.[3] We herein want to present a patient with primary APS who had other protrombotic genetic disorders with bilateral ocular involvement as a prevailing sign.

CASE REPORT

A 20-year old man presented complaining of bilateral sudden painless loss of vision. His complaint was started in the left eye (LE) first 11 days ago than in the right eye (RE) a week later. His best corrected visual acuity (BCVA) was finger counting at 2 meters in the RE, and finger counting at 1 meter in the LE. Biomicroscopic evaluation revealed +1 cells in the anterior vitreous in both eyes. Fundus examination revealed macular edema, tortuous veins, and flame blurry intraretinal haemorrhages, cotton-like exudates and vascular sheating in posterior pole and in the periphery in both eyes. (figure-1-A-B) Intraocular pressure (IOP) was within normal limits in both eyes. Spectral-domain optical coherence tomography (SD-OCT, Spectralis, Heidelberg) showed bilateral severe macular edema. Fluorescein angiography of both eyes disclosed venular occlusion and capillary dropout. (figure-1-C-D) Laboratory investigation revealed erythrocyte sedimentation rate (70mm/hr; 0-15), white blood count (12.2/mm3; 4-10), C-reactive protein (14; 0-3), homocysteine (27.4 mikromol/liter; 5-14), platelet count (483/mm3; 150-450). Fibrinogen, rheumatoid factor, antinuclear antibodies, anti-double-stranded DNA antibodies, antineutrophil cytoplasmic antibodies, and C3 and C4 complement components, activated partial thromboplastin time (13.4; 9-14), international normalized ratio (INR) were normal, and HLA B5 and HLA B27 were negative . MTHFR C677T heterogeneity was detected by PCR . The antibody assay for lupus anticoagulant (LA) was positive, and IgG and IgM anticardiolipin antibodies were negative for both isotypes. Protein C (70-140) and protein S (55-160 IU/dL) activity was 139 and 140 (in

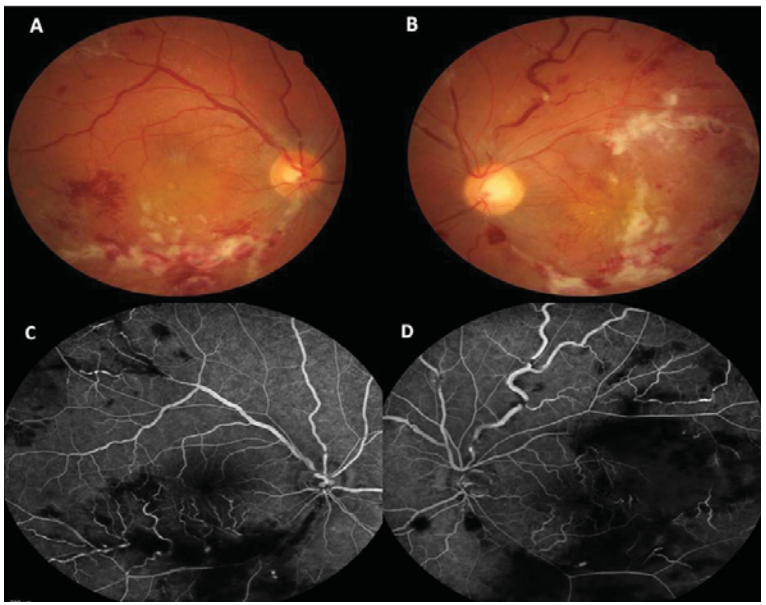

Figure-1. ***(A-B)****-Fundus photographs of right and left eye showing bilateral retinal vein occlusions.* ***(C-D)****- Fluorescein angiography of both eyes disclosing venular occlusion and capillary dropout.*

normal ranges), respectively.β2 microglobulin (1.55mg/liter; 0, 6-2, 5) was normal. Based on these findings and consultations with other clinics (rheumatology, haematology and pulmonology) the patient was diagnosed as having bilateral retinal vein occlusions secondary to primary APS. Laser photocoagulation treatment was applied to both ischemic areas in the periphery of the retina. A dosage of 1 mg/kg oral prednisolone, and an anticoagulant treatment with warfarin was started with a target INR of 2.0–3.0. His BCVA improved to 80/200 in both eyes within 2 weeks. After one month BCVA remained same in RE but improved to 200/200 in LE. Before the second month visit the patient had subdural hemorragia, and was operated in neurosurgery clinic immediately. This cranial complication resulted in a left-sided hemiplegia and the patient was followed up in physical medicine and rehabilitation clinic. At the third month visit his BCVA was light perception in the RE and 40/200 in the LE. The right fundus could not be seen due to intravitreal hemorrhage. Fundus examination of the LE showed moderate intravitreal hemorrhage and widespre-

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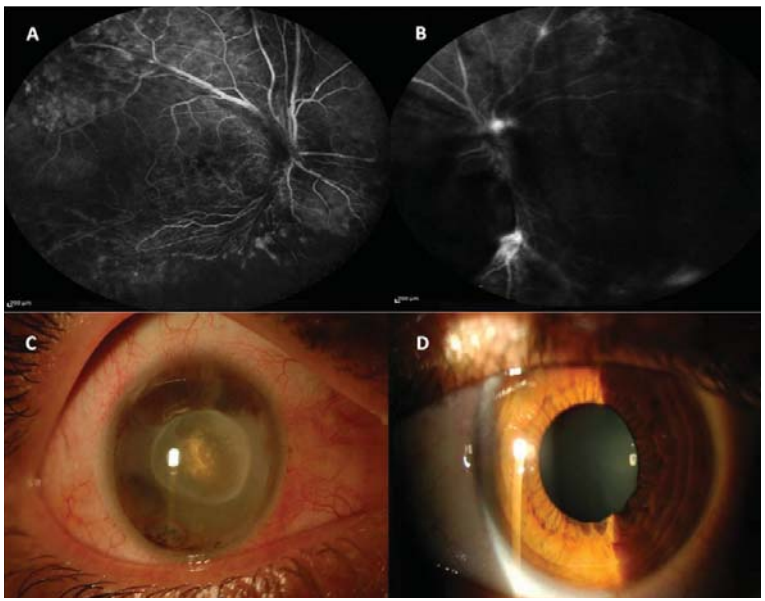

Figure-2. ***(A-B)****- Fluorescein angiography showing ischemic areas and neovascularization in the periphery of both retinas 4 months after his admission.* ***(C-D)*** *Anterior segment photographs of the patient at his final visit showing silicone oil in the anterior chamber and rubeozis iridis in the RE and normal findings in LE.*

ad retinal hemorrhages. As intravitreal hemorrhage persisted in the RE at the fourth month visit, patient underwent a pars plana vitrectomy and silicone oil injection. At the fifth month visit his BCVA was hand movement in the RE and 40/200 in the LE. LE was unremarkable at this point. There was iris neovascularization and optic atrophy in the RE. The intraocular pressure was 60 mmhg in the RE and 12 mmhg in the LE. The patient underwent silicone oil exchange in the RE. At the seventh month visit his BCVA was finger counting at 3 meters in the RE, and finger counting at 1 meter in the LE. A relative afferent pupillary defect was present in the RE. Biomicroscopic evaluation revealed thin keratic precipitates, (+1) anterior chamber cells, widespread posterior synechia and posterior subcapsular cataract in the RE. LE was unremarkable on biomicroscopic examination. Fundoscopy disclosed intravitreal and extended preretinal hemorrhages in the LE. IOP was normal in both eyes. Fluorescein angiography disclosed ischemic areas and neovascularization in the periphery of both retinas. (Figure-2-A-B) Intravitreal ranibizumab injection was applied to the LE. After one month BCVA remained the same in RE but improved to 160/200 in LE. The patient underwent cataract extraction with IOL implantation, silicone oil removal and sulfur-hexafluoride (SF6) gas injection in the RE. One month after the surgery BCVA was light perception in the RE. Dilated fundus examination showed grade C PVR and total retinal detachment in the RE. Fundoscopy of LE revealed non-clearing vitreous hemorrhage and finally PPV was applied. At his final visit on the 19. month, his BCVA was light perception in the RE and 20/20 in the LE. A relative afferent pupillary defect and sensorial exotropia of 20-25 prism diopters was present in the RE. Biomicroscopic evaluation revealed silicone oil in the anterior chamber, rubeozis iridis and centralized intraocular lens in the RE. LE was unremarkable. (Figure-2-C-D) Dilated fundus examination showed grade C PVR and total retinal detachment in the RE, and attached retina in the LE.

DISCUSSION

Our case is atypical in many ways. First of all the presentation of the APS was with ocular signs alone. The patient was diagnosed as APS with ocular examination. The APS affects predominantly women but our patient was male. P-C Chang[4] et al have reported a case of unilateral combined central retinal artery occlusion and central retinal venous occlusion in a patient with APS secondary to SLE. Also we reported unilateral combined central retinal artery and vein occlusion in a patient with APS secondary to SLE who had given a birth 5 days before the event.[5] Furthermore, veins were predominately affected in our case. However, arterial occlusions seem to be more commonly associated with antiphospholipid syndrome than venous occlusive disease in the literature.[6] False positivity of LA is usually related with syphilis but rapid plasma reagin (RPR) was negative in our case. On the other hand our patient had HCV seropositivity which can cause false positive of LA. Marcucci[7] et al reported a prevalence of 9.7% for LA and 14.6% for aCL in a group of 41 unselected patients with retinal artery occlusion. In the same study hyperhomocysteinemia among thrombophilic factors seemed to be an indepen-

dent risk factor for retinal artery occlusion. The pathogenesis of the thrombosis is still discussed, with direct action by antiphospholipid antibody (aPL) on platelet membranes, on clotting proteins and on the endothelium all being described. APS estimated to be responsible for 10% of all deaths in many non-industrial countries.[8] We think that hyperhomocysteinemia in our case is due to MTHFR C677T mutation. Our patient had a subdural hemorragia and contralateral hemiplegia. This neurological complication is very rare. In a study of Etemadifar et al they reported that ischemic thrombotic stroke was the leading neurological manifestation in patients with antiphospholipid syndrome.[9] We argue that this unfortunate complication affected the visual prognosis of RE because the patient was not under our clinical observation during this period. Development of PVR and retinal detachment was the major problem that guarded the visual prognosis in the RE. Neovascularization of the retina was resolved with panretinal argon laser photocoagulation succesfully in the LE. We think that this treatment is also benefitial to prevent complications caused by general ischemia of the ocular fundus (i.e. neovascular glaucoma). To the best of our knowledge, this is the first case report of APS which was complicated with serious ocular and neurosurgical abnormalities, and resulted in legal blindness.

CONCLUSION

Primary APS is a multisystem autoimmune disorder which can be seen with unexplained ocular manifestations as a first clinical sign. Especially in vein occlusions in younger population without any trigger factors such as arterial hypertension, cardiovascular atherosclerotic disease, or diabetes mellitus; ophthalmologists should keep APS in mind. This disorder can progress asymmetrically and can be refractory to treatment. Management of ocular complications should be more aggressive in APS patients.

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