Antiphospholipid Syndrome in the Differential Diagnosis of Retinal Ischemia: A Case Report with OCT-Angiography Findings

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ABSTRACT

Antiphospholipid syndrome (APS) is an autoimmune disease characterized by arterial and venous thrombosis. Early diagnosis and initiation of thromboprophylaxis reduce the risk of recurrent thrombosis. In this report, we presented a case with no known systemic disease but diagnosed as primary APS based on retinal ischemia findings in fluorescein angiography and optic coherence tomography angiography. The aim of this report is to emphasize that APS, which causes thrombosis in vital organs, can occur with retinal ischemia and that the diagnosis of the disease by an ophthalmologist can be life-saving.

Keywords: Antiphospholipid syndrome, OCT- Angiography, Primary, Retinal ischemia

INTRODUCTION

Antiphospholipid syndrome (APS) is an autoimmune disease characterized by presence of anti-phospholipid antibodies, arterial and venous thrombosis.[1] Although deep vein thrombosis is the most frequent finding seen by 29-55%, any organ can be affected by acute or chronic ischemia.[2] The APS can be either primary or present in association with connective tissue diseases. Although ocular involvement ranges from 8% to 88%, it can be first sign of the disease.[3-5] In ophthalmological examination, the APS can lead both anterior and posterior segment findings; in addition, it may cause neurophthalmological conditions.[6] Here, it was aimed to present a case with no known systemic disease which was diagnosed as primary APS by test performed due to retinal ischemia detected on fluorescein angiography (FA) and optical coherence tomography angiography (OCT-A).

CASE REPORT

A 46-years old woman without history of known systemic disease and medication presented to our clinic with progressive loss of vision started in right eye one year ago. In her history, it was found out that she had history of recurrent abortion. The best-corrected visual (BCVA) was 0.2 in the right eye and 0.9 in the left eye. Light reflexes were bilaterally normal and intraocular pressure was 12 mmHg in the right eye and 14 mmHg in the left eye. In the anterior segment examination, there was bilateral posterior subcapsular cataract, as being more prominent in the right eye. In the fundus examination, illumination was unclear in the right eye and soft macular exudates were observed in the left eye (Figure 1). On FA, capillary non-perfusion areas were observed in the left eye (Figure 2). On optical coherence tomography (OCT), there were hard exudates on foveal section (Figure 3a) while hypo-perfused areas were detected in both superficial and deep capillary plexuses on OCT-A in the left eye (Figure 3b). Clear images could not be captured in the right eye due to cataract. In blood tests, complete blood count and biochemical parameters were found to be normal; thus, the patient was consulted to rheumatology and hematology departments. In the rheumatology department, the patient was diagnosed as primary APS with history of recurrent abortion, ischemic ophthalmological findings, and positive

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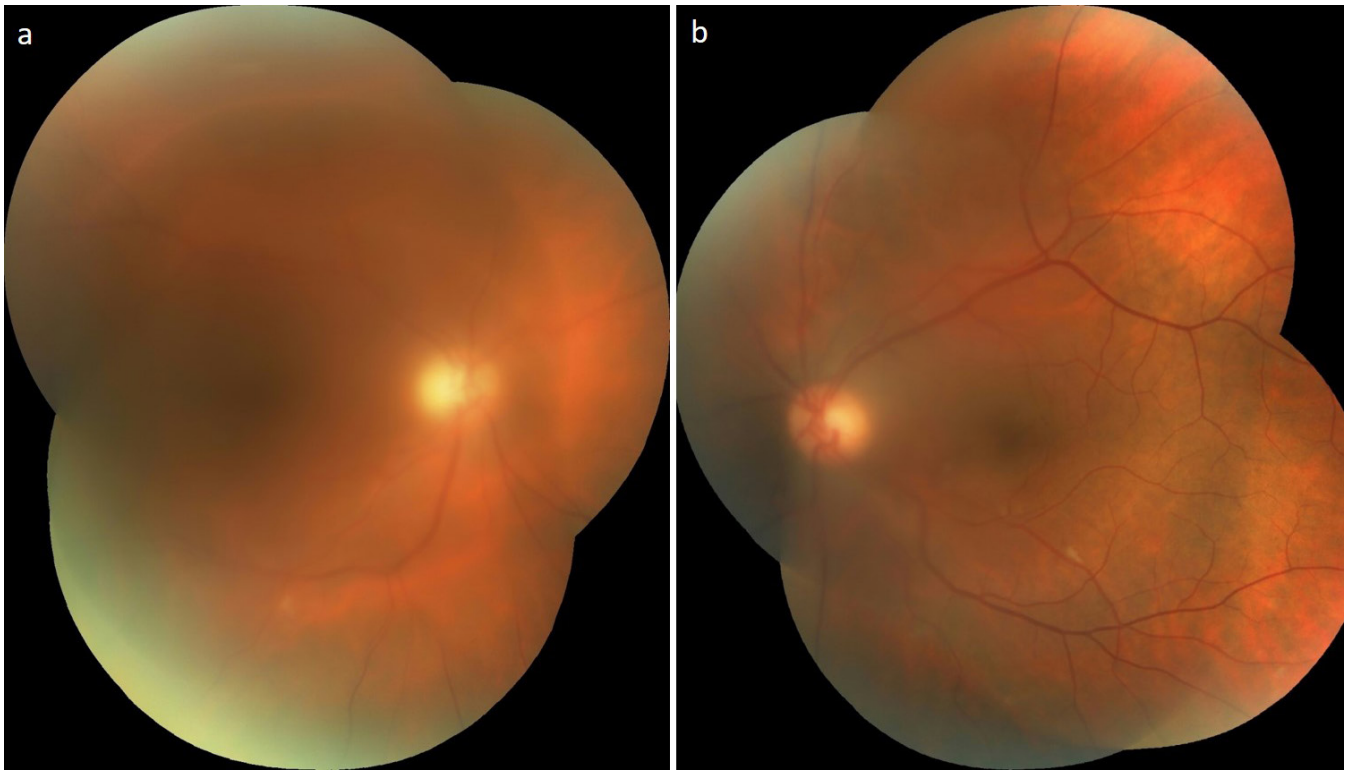

Figure 1: a) *Color fundus image at baseline: The right eye was illuminated in a blurred manner due to cataract;* **b)** *macular soft exudates are seen in the left eye.*

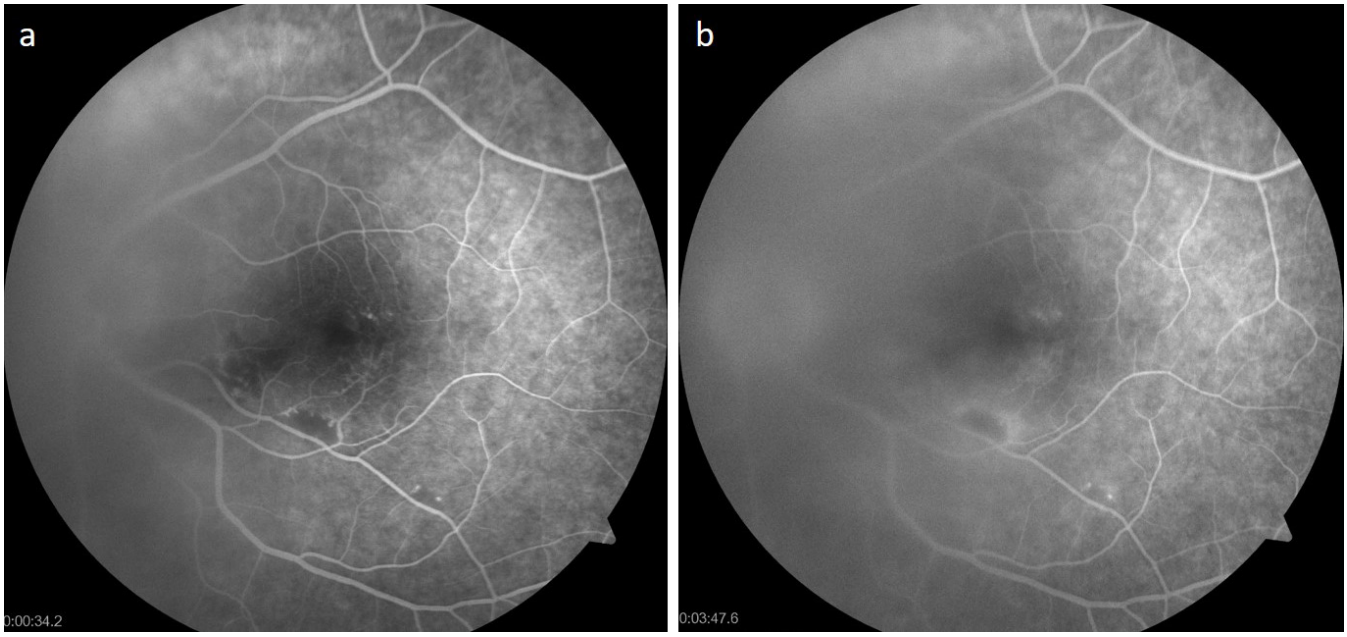

Figure 2*: Non-perfused capillary areas are seen in the fovea of left eye on early and late phase fluorescein angiograph images.*

antiphospholipid antibody titers by 12-weeks interval (β2 glikoprotein IgM; 48,32 RU/mL at presentation and 41,31 RU/mL on week 12). The patient was prescribed hydroxychloroquine, enoxaparin sodium and warfarin. Cataract surgery was performed in the right eye. In control visit on month 6, BCVA was 1.0 in the right eye and 0.8 in the left and it was noted that cataract was progressed in the left eye. In the fundus examination, soft exudate adjacent to infero-temporal arcuate and intraretinal hemorrhage were observed; soft and hard exudates could be identified in the left eye although it was flu (Figure 4). On control FA, it was seen that foveal avascular zone was highly wide in the right eye and that left eye appeared similar to previous FA (Figure 5). On OCT, there were derangement at inner

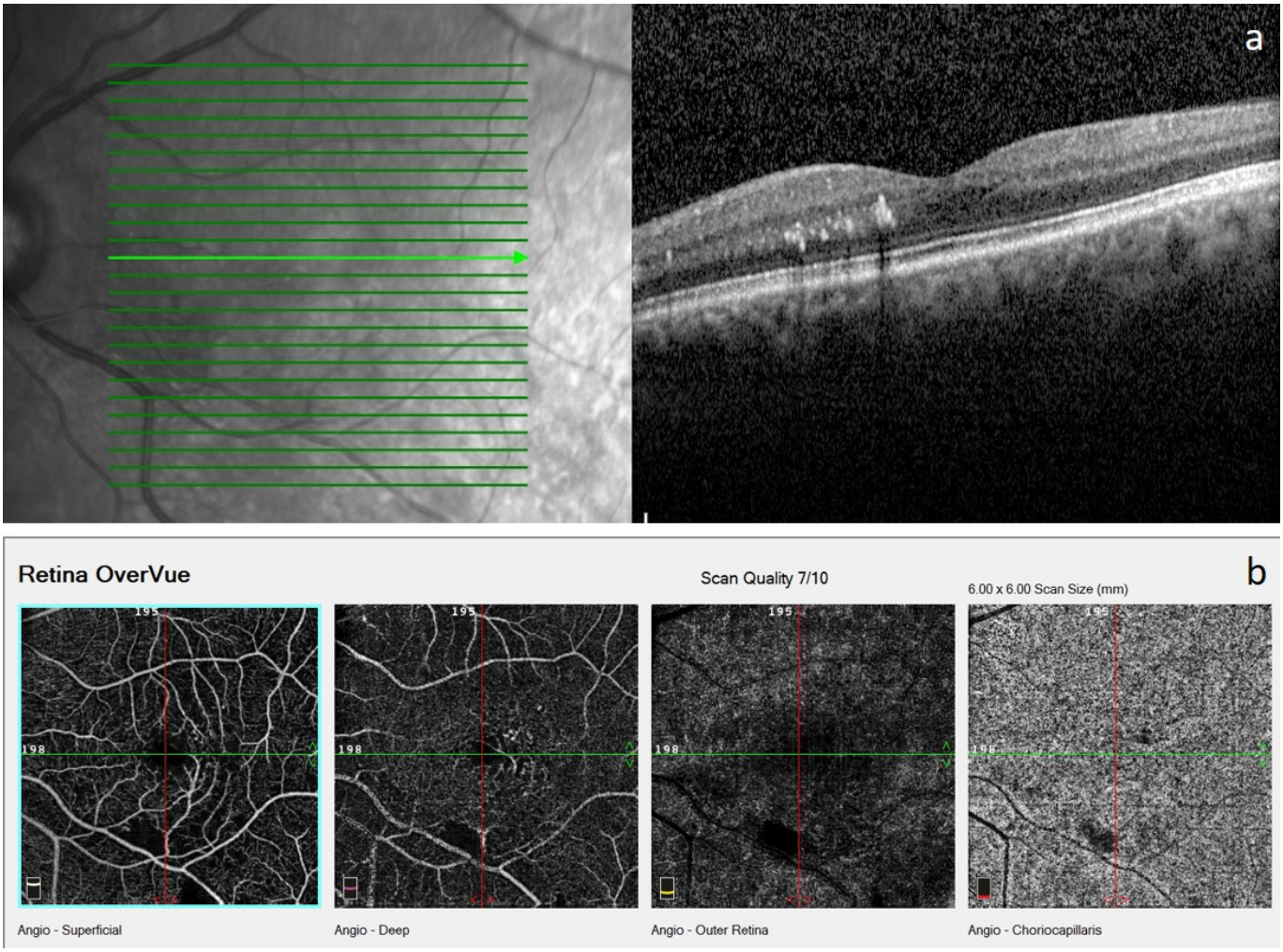

Figure 3: a) *Hard exudates are seen on foveal OCT section in the left eye.* **b)** *on OCT-A images of same eye, hypo-perfusion areas are seen in both superficial and deep capillary plexuses.*

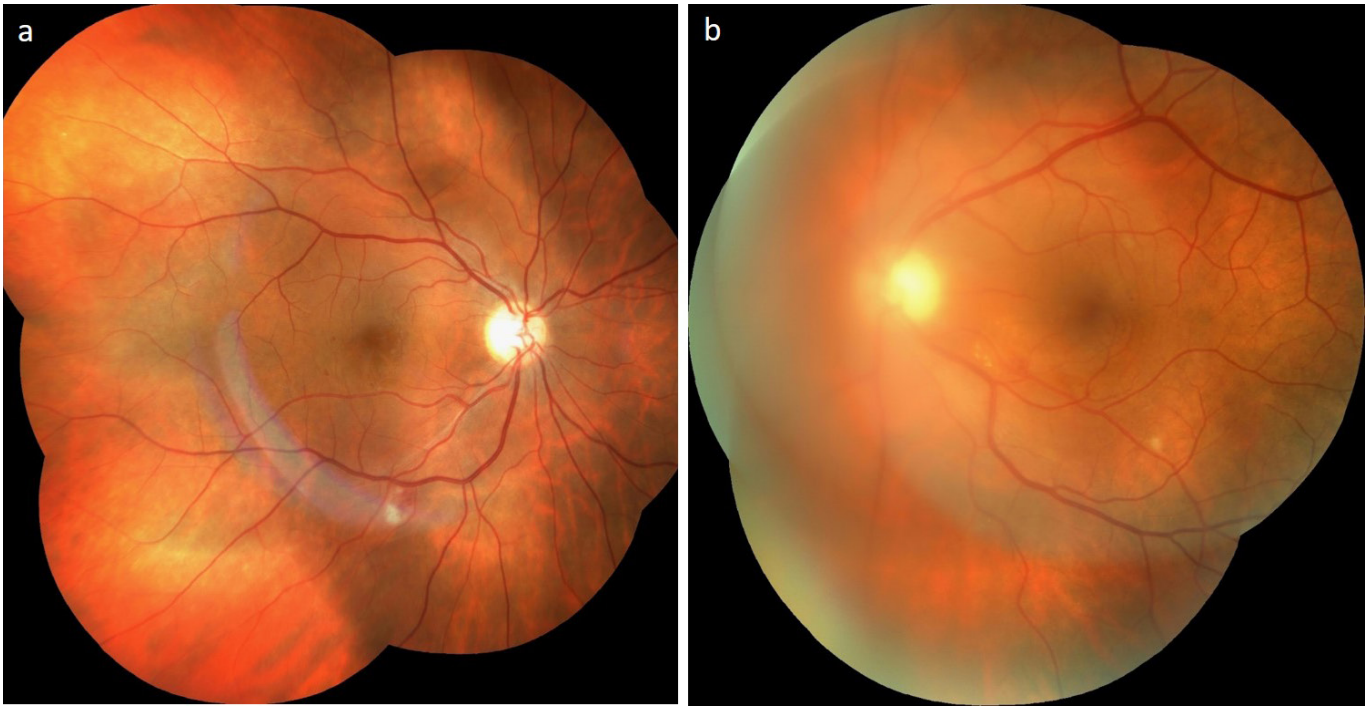

Figure 4: *Color fundus images on month 6:* **a)** *soft exudate and intraretinal hemorrhage adjacent to infero-temporal arcuate in the right eye,* **b)** *soft and hard exudates are seen in the left eye although images are blurred.*

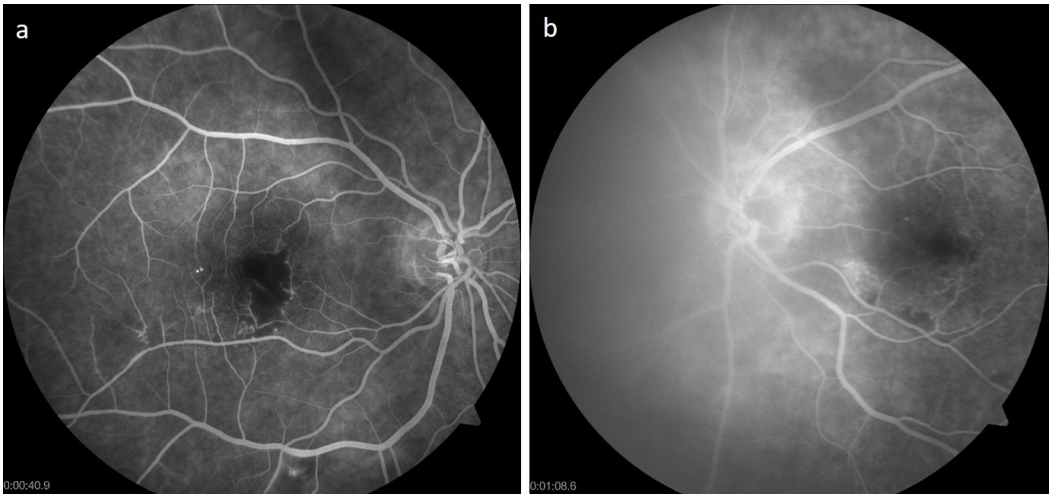

Figure 5: *Fluorescein angiograph on month 6:* **a)** *it is seen that foveal avascular zone was wide in the right eye; and* **b)** *that finding remained unchanged.*

nuclear layer and outer plexiform layer and exudates in the left eye were resolved (Figure 6). On OCT-A, it was seen that foveal zone was wide in right eye and there was hypo-perfusion areas in both superficial and deep capillary plexus while there was no change in the left eye when compared to previous scan (Figure 7). The treatment is ongoing in the patient.

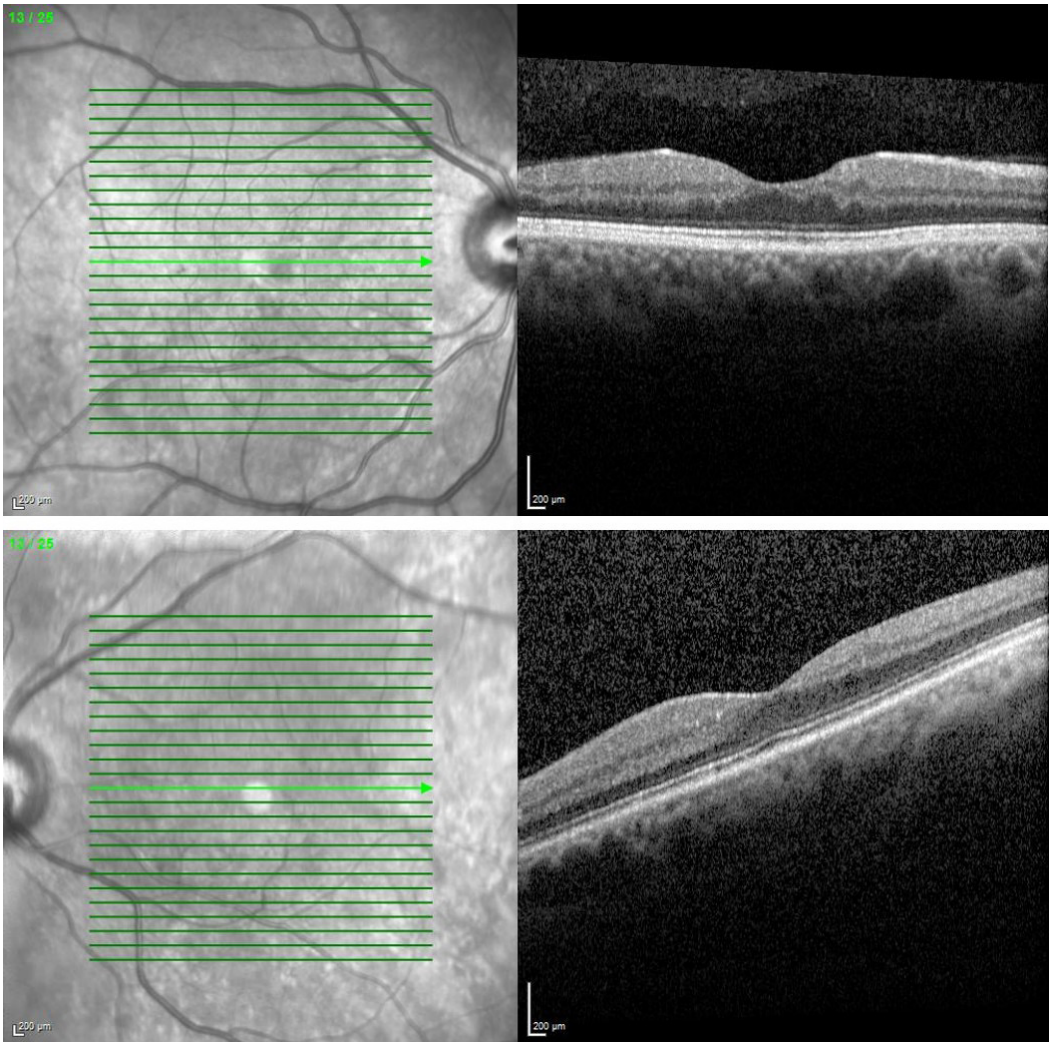

Figure 6: *OCT images on month 6:* **a)** *derangement in the inner nuclear and outer plexiform layers of right eye;* **b)** *it is seen that exudates disappeared in the left eye.*

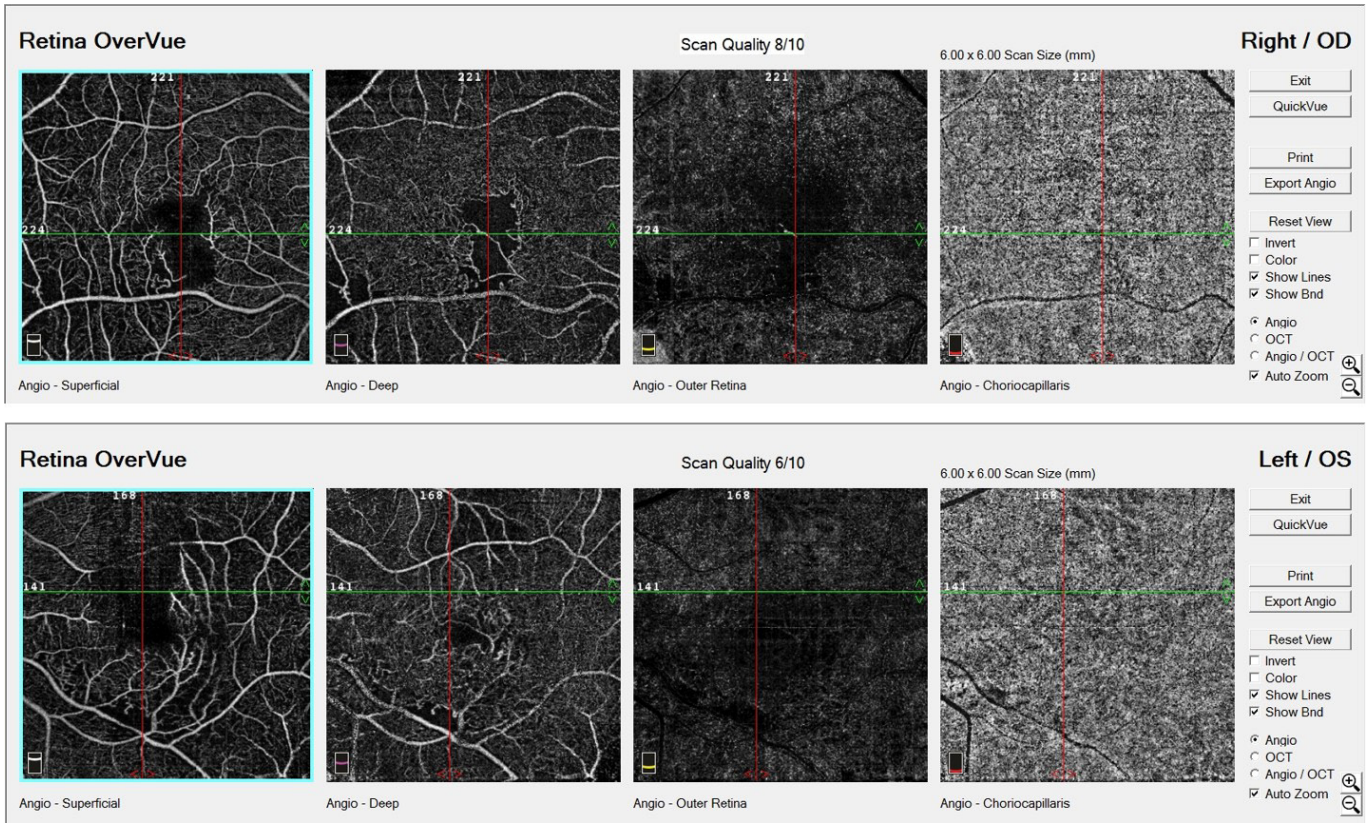

Figure 7: *OCT-A images on month 6:* **a)** *wide foveal avascular zone in the right eye and hypo-perfusion area in both superficial and deep capillary plexuses; and* **b)** *the findings remained unchanged in the left eye.*

DISCUSSION

Antiphospholipid syndrome (APS) is an acquired autoimmune disease presenting with ischemic events caused by arterial and venous thrombosis. Based on modified Sappora criteria, the APS diagnosis is made by presence of at least one clinical and one laboratory finding.[1] Antiphospholipid antibodies include lupus anticoagulant, anti-cardiolipin and ß2 glycoprotein antibodies. Two positive antibody test by 12-weeks interval is considered as relevant. APS can cause ischemia and thrombosis in central nervous system as well as it may progresses with pulmonary embolism, thrombocytopenia, nephropathy and recurrent abortion.[6]

Although APS is a rare disease, ocular involvement is common. Posterior segment is the most commonly affected component in ocular involvement of APS. There may be increased tortuosity, venous dilatation and intraretinal hemorrhage as well as retinal vein and artery occlusions.[3,7-10] It has been reported that APS leads two clinical retinopathy presentations with mild and severe courses.[11,12] In the mild form, soft exudate and intraretinal hemorrhage occur while peripheral retinal ischemia and neovascularization are seen in the severe form. Although clinical findings were compatible with mild retinopathy, OCT-A images showed severe ischemia in the fovea. It was seen that there was no change in non-perfused retinal areas on month 6 during treatment.

OCT-A is a novel, non-invasive imaging modality which allows visualization of choroid and retinal vascularity without need for dye injection.[13,14] The working principle is based on blood flow-related changes in the OCT signal resulting from blood flow. It perceives erythrocyte movement by repeated scans and shows retinal circulation indirectly by calculating difference across scanning signals. The OCT-A ensures calculation of several parameters such as blood flow, vascular intensity of superficial and deep capillary plexus and extent of foveal avascular zone.

In recent years, OCT-A has been introduced as a procedure used in the differential diagnosis of retinal and choroidal diseases and plays an important role in studying effects of systemic vascular and inflammatory disorders on retinal micro-vasculature.[15-17] As it was the case in our patient, ischemia findings on OCT-A can be alarming in patients with no known systemic disease. Although FA also showed retinal ischemia in our case, OCT-A can more clearly identify extent and localization of ischemia of superficial and deep capillary plexuses without using dye. In the paper on multi-modal imaging findings in a patient with primary

APS, Trese et al. emphasized the importance of OCT-A in demonstrating deep capillary plexus ischemia.[18] Deep capillary plexus ischemia is an important imaging finding in patients with primary APS since it may lead permanent loss of vision at long-term.[19]

It is important to initiate treatment as soon as possible in preventing complications in systemic disorders progressing with multi-organ involvement such as APS. In the treatment of APS, agents such as enoxaparin sodium, warfarin and acetyl salicylic acid are used to prevent thromboembolic events.[6] In a review on importance of thromboprophylaxis, it was reported that the risk for recurrent thrombosis is around 30% in APS patients not using anticoagulant therapy.[20]

In conclusion, APS is one of the rare causes retinal ischemia, can manifest with ocular findings alone. OCTA plays an important role in demonstrating extent and localization of retinal ischemia. Recognition of the disease by an ophthalmologist is important for rapid diagnosis and treatment and can be life-saving.

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