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CASE REPORT

Bilateral Choroidal Occlusion in Antiphospholipid Syndrome Associated with Systemic Lupus Erythematosus

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Abstract This article reports a rare case of bilateral choroidal occlusion that occurred in a 24-year-old woman with antiphospholipid syndrome (APS) associated with systemic lupus erythematosus (SLE). This young lady concurred with aorta ventralis thrombosis and bilateral iliac artery occlusion when presented, and experienced a rapid deterioration of vision. She also has a history of recurrent miscarriage. Corticosteroid, immunosuppression and anticoagulation therapy were administered. Patients with APS associated with SLE are at risk for thrombotic phenomena, which may affect the ocular vessels of all sizes, including choroidal vessel. Our case alerts ophthalmologists and rheumatologists that bilateral choroidal occlusion may indeed be developed in patients with APS associated with SLE, and is a potential cause of visual morbidity.

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ANTIPHOSPHOLIPID syndrome (APS) is an autoimmune disease with moderate to high levels of antiphospholipid antibodies (aPL) in the blood. Its main clinical characteristics include arterial and venous thrombosis and recurrently spontaneous abortion.¹ APS may occur primarily in the absence of systemic disease, or accompany with a known systemic autoimmune disease, such as systemic lupus erythematosus (SLE).^{2,3} In the current paper, we report a rare

case of bilateral choroidal occlusion as a complication of APS associated with SLE in a woman.

CASE DESCRIPTION

A 24-year-old female was referred to our clinic, complaining of bilateral progressively reduced visual acuity in the past 2 months. The patient had been suffering from general fatigue, inappetence and intermittent fever for 3 months, and went to see rheumatologists prior to the presence at our clinic. She had no history of malar or discoid rash, no history of photosensitivity, arthralgias, or Raynaud's phenomenon. She had an experience of four

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miscarriages for unknown reason.

Clinical work-up was conducted for diagnosis. Laboratory investigation (Table 1) revealed prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT). Antinuclear antibodies (ANA) was 1:80, Coombs test was positive. Levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), anticardiolipin antibody (aCL), and the antibody titer to β -2-glycoprotein 1 (β 2GP1) were elevated. Complement levels of C3 and C4 were reduced. Thrombocytopenia was present with an extremely low count of platelet ($11 \times 10^9/L$). Analyses for anti-double-stranded DNA (anti-dsDNA) antibodies, anti-neutrophil cytoplasmic antibodies with cytoplasmic staining pattern (c-ANCA) and with peripheral staining pattern (p-ANCA), rheumatoid factor, anti-Ro (SSA) and anti-ribonucleoprotein were all negative.

Contrast enhanced abdominal CT revealed thrombosis in aorta ventralis and bilateral iliac arteries. There was no evidence of deep vein thrombosis or pulmonary embolism. No abnormality was found in chest CT, brain MRI, carotid Doppler sonography and colonoscopy.

The best-corrected visual acuity was 40/200 OD and counting fingers OS. Binocular Goldmann applanation

intraocular pressures were 10 mmHg OD and 8 mmHg OS. Examinations of cornea, anterior chamber and lens were unremarkable. Clear vitreous was present. Bilateral pupils were equal in diameter with good direct and indirect reactions. Fundus examination revealed slightly pale optic discs. Multifocal choroidal infarction was bilaterally widespread, and choroidal atrophy was seen in all quadrants of both eyes. There were a few retina folds at the posterior pole of the left eye, with macular involvement. Retinal pigment epithelium atrophy in the areas of infarcted choroid was shown. No vasculitis or periphlebitis was found (Fig. 1).

Fluorescein angiography showed normal perfusion of retinal vessels in the early stage, and hypofluorescence in the areas of choroidal infarction; in the late stage, hyperfluorescence was present in the areas around the choroidal infarction and the left foveolar avascular zone (Fig. 2). The indocyanine green angiography (ICGA) of both eyes revealed large wedge-shaped and lobular areas of hypofluorescence corresponding to the location of choroidal non-perfusion lesion (Fig. 3). Optical coherence tomography (OCT) revealed that the thicknesses of bilateral choroid, especially in areas of choroidal infarction, reduced distinctly (Fig. 4).

Table 1. Results of laboratory examination of a 24-year-old patient with APS associated SLE

Items of laboratory examination	Tested value	Normal range
Prothrombin time (PT) (s)	17.8	10.4-12.6
Activated partial thromboplastin time (APTT) (s)	120	22.7-31.8
C-reactive protein (CRP) (mg/L)	76.45	≤ 10 mg
Erythrocyte sedimentation rate (ESR) (mm/h)	125	0-20 mm
Anticardiolipin antibody (aCL) (U/ml)	120	<10U
β -2-glycoprotein 1 (β 2GP1) (U/ml)	155	<5U
Complement C3 (g/L)	0.40	0.80-1.20
Complement C4 (g/L)	0.048	0.10-0.40
Platelet count (/L)	11×10^9	$100-300 \times 10^9$

APS, antiphospholipid syndrome; SLE, systemic lupus erythematosus.

Figure 1. Fundus photography of both eyes.

Slightly pale optic discs, bilaterally multiple areas of choroidal atrophy (white arrow), a few retina folds at the posterior pole (black arrow), and atrophy of the retinal pigment epithelium.

Figure 2. Fluorescein angiography (FA) of both eyes.

Hypofluorescence at the choroidal infarcted areas (asterisk), hyperfluorescence around the choroidal infarctions and the foveolae avascular zone.

Figure 3. Indocyanine green angiography (ICG) of both eyes.

Large wedge-shaped and lobular areas of hypofluorescence (asterisk) correspond to the choroidal lesions of non-perfusion

Figure 4. Optical coherence tomography (OCT) of the non-perfused choroid.

A. The scan line. B. The choroidal thickness of the infarcted area decreased distinctly (white arrow).

According to the results of above examinations, the diagnosis of APS associated with SLE was established. The patient had not been on anticoagulation therapy or any other offending medications prior to the consultation. Anticoagulant treatment, corticosteroid and immunosuppression were then given. Anticoagulation therapy began with intravenous heparin 0.4 ml once a day for

10 days, followed by oral warfarin 5 mg once a day, for the purpose of preventing from further vaso-occlusion. Intravenous pulsed methyl-prednisolone was followed by oral corticosteroids and cyclophosphamide therapy.

After 4 weeks of therapy, the best-corrected visual acuity recovered slightly to 60/200 OD and 20/200 OS. However, the fundus appearance did not improve signifi-

cantly. The six-month follow-up showed no further visual acuity improvement.

DISCUSSION

The diagnosis of this patient, APS associated with SLE, was established according to American College of Rheumatology classification criteria and the strict diagnostic criteria established in 1998 at the International Symposium on antiphospholipid antibodies in Sapporo, Japan.⁴

APS is an autoimmune disorder characterized by arterial or venous thrombosis, which can affect any organs, and develop systemic and cerebral thromboembolism, with the results of deep vein thromboses, pulmonary emboli, myocardial infarction, cerebral stroke and increase of miscarriage rate.⁵⁻⁷

APS could be a primary pathogenesis, or secondary to some systemic autoimmune diseases, such as SLE. The clinical features of SLE vary, with musculoskeletal and cutaneous disorders being the most common. Both APS and SLE have a high frequency of ocular involvement, which even may be the initial manifestation of the disease.^{8,9} Generally, the anterior segment is not likely to be involved. The most common ocular findings are optic neuropathy and retinopathy that are due to ocular vessel disorder, such as anterior ischemic optic neuropathy, vessel obstruction and capillary non-perfusion, and are always correlate with the activity of SLE disease.

Retinal vascular occlusive diseases have been documented in patients with APS or SLE. Although vascular occlusion can occur in any part of retinal vessels, choroidal vessel occlusion is rare. Very few reports have described choroidopathy in primary antiphospholipid syndrome and SLE.^{10,11} Retinopathy in SLE always manifests as a benign form, which has been attributed to immune complex-mediated vasculitis, and the prognosis of vision deterioration in most cases is favorable. However, the most common ocular feature of APS is vaso-occlusive retinopathy, where the histology of the lesion is thrombosis. We proposed that the ocular symptoms of our patient were caused by vascular thrombosis secondary to APS rather than vasculitis from SLE.

Meanwhile, the clinical features of ocular involvement seem to be different between primary and secondary APS. Ocular vasculopathy is the typical manifestation of primary APS, whereas thrombophilia is more common in APS secondary to SLE.¹² The latter is consistent with the characteristics of the current case.

Antibodies associated with APS include aCL, lupus anticoagulant, and antibodies directed against β 2GP1.

These molecules all play roles in inhibiting the coagulation cascade, promoting thrombosis, causing a hypercoagulable state. The characteristic feature of APS is retinal vessel occlusion, which is more common in individuals with high titer of aCL.¹³ Several studies suggested that a moderate-to-high titer of aCL was associated with an increased risk of thrombosis.¹⁴ Our presented case had a high titer of aCL, which implied her high risk of thrombosis.

Although the exact role of antiphospholipid antibodies in the development of thrombosis is unclear, anticoagulation therapy consisting of intravenous heparin followed by oral warfarin was recommended as the initial therapy, which should be implemented as early as possible, and last for at least 6 months; otherwise, recurrent thrombosis may occur, and even develop thrombotic complications while still staying on the treatment.²

In our case, immunosuppression therapy was given for controlling SLE; meanwhile, anticoagulation therapy was performed for APS to prevent further thrombophilia and complications caused by neovascularization. However, after 4 weeks of therapy, visual acuity showed slight improvement and no change in the fundus defects. We believe that the unsatisfactory therapeutic effects may be due to that the patient did not have regular treatment during the two months of her visual loss before the diagnosis. Therefore, early diagnosis and timely treatment are important for a better prognosis in this situation.

Our case raises an alert to ophthalmologists and rheumatologists that in APS associated with SLE, bilateral vascular occlusion occurs not only in retina, but also in choroid, and both could constitute the potential causes of visual morbidity. Fundus phyfluoresce angiography is necessary to evaluate the vessels of patients with ocular symptoms. Furthermore, full thrombophilic panel work-up is strongly recommended for young patients who present occlusive ocular and/or vascular disorders, but have no conventional risk factors for thrombosis, especially when they have concomitant syndromes that are suspicious for SLE and/or APS.

REFERENCES

1. Greaves M. Antiphospholipid antibodies and thrombosis. *Lancet* 1999; 353:1348-53. doi: 10.1016/S0140-6736(98)10362-8.
2. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera R, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost* 2006; 4: 295-306. doi: 10.1111/j.1538-7836.2006.01753.x.

3. Bernard AG, Bayani N, Chretien P, Cochard C, Lelong F, Coscas G. Antiphospholipid antibodies in retinal vascular occlusions: a prospective study of 75 patients. *Arch. Ophthalmol* 1994; 112: 790-5. doi: 10.1001/archophth.1994.01090180088041.
4. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis & Rheumatism* 1997; 40: 1725. doi: 10.1002/art.1780400928.
5. Durrani OM, Gordon C, Murray PI. Primary anti-phospholipid antibody syndrome (APS): current concepts. *Surv Ophthalmol* 2002; 47: 215-38. doi: 10.1016/S0039-6257(02)00289-8.
6. Utz VM, Tang J. Ocular manifestations of the antiphospholipid syndrome. *Br J Ophthalmol* 2011, 95: 454-9. doi: 10.1136/bjo.2010.182857.
7. Levine JS, Branch DW, Rauch J. The antiphospholipid syndrome. *N Engl J Med* 2002; 346: 752-63. doi: 10.1056/NEJMra002974.
8. Miserocchi E, Baltatzis S, Foster CS. Ocular features associated with anticardiolipin antibodies: a descriptive study. *Am J Ophthalmol* 2001; 131:451-6. doi: 10.1016/S0002-9394(00)00884-9.
9. Bisighini S, Zerilli-Zavgorodni T. Branch retinal artery occlusion secondary to antiphospholipid syndrome. *Optom Vis Sci* 2012; 89: e78-84. doi: 10.1097/OPX.0b013e31826abc1a.
10. Ang LP, Yap EY, Fam HB. Bilateral choroidal infarction in a patient with antiphospholipid syndrome: a case report. *Clin Experiment Ophthalmol* 2000; 28: 326-8. doi: 10.1046/j.1442-9071.2000.00322.x.
11. Edouard S, Douat J, Sailler L, Arlet P, Astudillo L. Bilateral choroidopathy in systemic lupus erythematosus. *Lupus* 2011; 20: 1209-10. doi: 10.1177/0961203311398510.
12. Lima Cabrita FV, Foster CS. Anticardiolipin antibodies and ocular disease. *Ocul Immunol Inflamm* 2005; 13: 265-70. doi: 10.1080/09273940490912434.
13. Rodrigues CE, Carvalho JF, Shoenfeld Y. Neurological manifestations of antiphospholipid syndrome. *Eur J Clin Invest* 2010; 40: 350-9. doi: 10.1111/j.1365-2362.2010.02263.x.
14. Tanne D, Hassin-Baer S. Neurologic manifestations of the antiphospholipid syndrome. *Curr Rheumatol Rep* 2001; 3: 286-92. doi: 10.1007/s11926-001-0032-3.