CASE REPORT

Necrotising scleritis, keratitis and uveitis in primary antiphospholipid syndrome

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SUMMARY

Ocular manifestations of antiphospholipid syndrome typically include thromboembolic and neuro-ophthalmic complications. In this report we present a case of inflammation of the ocular coats in a patient diagnosed with antiphospholipid syndrome 16 years prior. We discuss management of the case and the possible aetiology of the rare association.

BACKGROUND

Antiphospholipid syndrome (APLS), previously known as Hughes syndrome, is typically characterised by thromboembolic complications or pregnancy-related morbidity. Serology reveals persistent antiphospholipid antibodies inclusive of lupus anticoagulant or anticardiolipin or antibeta2-glycoprotein 1 antibodies. APLS may secondarily occur due to other immune disorders, most commonly systemic lupus erythematosus (SLE). Rarely, systemic vasculitis may coexist with APLS, and there is increasing consensus that some manifestations of the disorder are due to its autoimmune nature and not entirely due to vascular thrombosis.^{1 2}

We discuss a case of primary APLS that had initially presented as classical systemic disease, but two decades later developed inflammation of the ocular coats. The possible aetiological links between APLS and scleritis are also discussed.

CASE PRESENTATION

A 50-year-old woman had been diagnosed with Hughes syndrome 16 years ago. She had history of multiple spontaneous abortions, renal infarction, digital gangrene, Raynaud's phenomenon and secondary hypertension, all occurring over 2 years. Lupus anticoagulant had been present in serum and had been confirmed 3 months after the first evaluation. Serum work-up was negative for anticardiolipin antibody, antibeta2-glycoprotein 1 antibody, antinuclear antibodies and Double-stranded Deoxyribonucleic acid (dsDNA). Serum cytoplasmic antineutrophil cytoplasmic antibody (cANCA) was positive while perinuclear antineutrophil cytoplasmic antibody (pANCA) was negative, and complement levels were normal. She had been treated with oral steroids and cyclophosphamide earlier. At presentation, she was being treated with oral antihypertensive medication, oral anticoagulation (warfarin), methotrexate and mycophenolate mofetil.

She presented to us with acute redness and low vision in the right eye (RE). She had recurrent untreated redness in this eye for the past 5 years. Best corrected visual acuity was counting fingers close to face in RE, while it was 6/6 in left eye (LE). Ocular examination revealed necrotising anterior scleritis with uveal show (figure 1) in RE. Peripheral stromal keratitis was present at the temporal limbus, measuring 6×1 mm. She had non-granulomatous anterior uveitis with 1+ cells in the anterior chamber (standardised uveitis nomenclature grading system) with a dense posterior subcapsular cataract. Fundus examination revealed localised anterior retinal detachment with choroidal effusion corresponding to the area of scleritis (figure 2). Ultrasound confirmed the choroidal effusion and ruled out T-sign (figure 3). Intraocular pressure was normal in both eyes, while the LE was unremarkable on examination.

INVESTIGATIONS

Lupus anticoagulant: partial thromboplastin time (PTT)=60.7 s, control=34.0 s; dilute Russell's Viper Venom test (DRVV) screen time=77.1 s, DRVV screen time ratio=2.01; DRVV confirmatory time=55.2 s, DRVV confirmatory ratio=1.65; cANCA: positive

erythrocyte sedimentation rate (ESR): 66 mm/hour

C-reactive protein

Total and differential leucocyte counts: normal

Renal function test (repeated many times): urea/creatinine (mg/dL)=31/1.2 initially; 46/0.9 at presentation (always within laboratory's normal range)

Other antiphospholipid antibodies, pANCA, anti-nuclear antibody (ANA), dsDNA, rheumatoid factor: negative; complement levels: normal

Chest X-ray: normal

CT chest and sinus: maxillary polyp, rest normal

ECG and echocardiogram: normal

Urine examination (repeated many times): occasional white blood cells, no red blood cells

Ultrasound kidney, ureter and bladder (KUB) and renal artery Doppler: normal

international normalized ratio (INR): 2.3

DIFFERENTIAL DIAGNOSIS

Granulomatosis with polyangiitis (GPA) was unlikely as chest and sinus imaging was negative, as well as the non-suggestive urine and blood investigation result. An otorhinolaryngologist was consulted

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Figure 1 Clinical photograph of the right eye depicting severe uveal show through the necrotic temporal sclera. The deep scleral vessels can be seen prominently due to the inflammation.

but no evidence of GPA was found. Rheumatoid arthritis was ruled out with serology and absence of arthritis. SLE was ruled out by non-fulfilment of the systemic lupus international collaborating clinics classification criteria.

TREATMENT

She was diagnosed with necrotising scleritis with keratouveitis associated with APLS and prescribed with topical steroid, artificial tear, cycloplegia and oral indomethacin. She was immediately referred to a rheumatologist colleague and treated as primary APLS with coexisting primary systemic vasculitis. Oral steroid of 1 mg/kg/day was initiated, dosage of mycophenolate mofetil was increased, and methotrexate, antihypertensive as well as anticoagulants were continued.

OUTCOME AND FOLLOW-UP

On this regimen, her ocular symptoms were improving with resolution of scleritis (figure 4), anterior uveitis, keratitis, choroidal effusion and retinal detachment over a period of 2 months. The uveal show persisted while cataract had worsened. Oral and topical steroids were slowly tapered down, while cycloplegia and indomethacin were discontinued. Methotrexate, mycophenolate

Figure 2 Ultra-wide fundus image of the right eye showing temporal exudative retinal detachment while posterior pole appears normal.

Figure 3 Ultrasound image of the right eye depicting choroidal effusion in the temporal quadrant, seen as thickened choroid.

mofetil, antihypertensive and anticoagulant were continued. Long-term plan included cataract extraction with steroid cover after the inflammation had been controlled. She was clinically stable at 4 months of follow-up with best corrected visual acuity of 3/60. She is currently under regular combined ophthalmic and rheumatology care.

DISCUSSION

Classically, APLS results in occlusive vasculopathy even in cases presenting with other ocular symptoms.^{2 3} It is uncommonly associated with vasculitis, although retinal vasculitis has been reported before. However, scleritis and uveitis are rare.^{1 2} Descriptive studies done on ocular findings in cases positive for serum anticardiolipin antibodies have found rare occurrence of posterior scleritis, filamentary keratitis and iritis.^{4 5} Although relapsing anterior scleritis as a presenting sign of APLS has been reported, the report did not further elaborate on systemic condition or vasculitis status during the follow-up.¹ Thus, scleral necrosis seen in our patient is highly unusual for APLS.

ANCA is a marker of vasculitis and is very useful for diagnosing GPA.² It has been reported that up to 75% cANCA-positive patients develop scleritis, with more than 20% having the necrotising type, while others develop peripheral keratitis and uveitis.⁶ This could explain the severe ocular pathology in our patient. Moreover, the hypercoagulable state in APLS could

Figure 4 Clinical photograph of the right eye showing resolution of active scleritis, with persistent uveal show.

lead to ischaemia, complicating the necrotising condition of the sclera. Phospholipid layer in the sclera contains cardiolipin, which might induce autoimmune reaction by the circulating autoantibodies in APLS.⁷ This unproven hypothesis then could lead to vasculitis and necrosis of the scleral collagen tissue.

APLS can rarely be complicated by systemic vasculitis involving small, medium or large vessels. The relation between ANCA-associated vasculitis and APLS has been suggested by multiple reports.² Coexistence of GPA and APLS with atypical manifestations has also been documented prior.^{2,8} Further, APLS and GPA can have common presentations like pulmonary vasculitis.⁹ Antiphospholipid antibodies are known to be present in patients with GPA.^{2,10} The frequency and amount however are usually low.¹⁰ Higher incidence of thromboembolism was noted in patients of GPA in the Wegener's Clinical Occurrence of Thrombosis (WeCLOT) study.¹¹ However, anticardiolipin antibodies and antibeta2-glycoprotein in the WeCLOT cohort and other studies too have been analysed not to have a role in the hypercoagulable state seen in GPA.^{2,10} It is possible that the presence of these antibodies in GPA is an epiphenomenon or due to vascular damage itself.²

Ocular manifestations can be the initial presentation of GPA, which may eventually evolve into systemic disease. Considering that our patient had been on long-term therapy, it is possible that GPA may have been present in our patient in a subtle subclinical form. In fact scleritis is a well-known presentation of GPA and

has very rarely been seen in APLS.^{1,12} However, given the typical systemic symptoms of APLS, and consistently present lupus anticoagulant with negative work-up for GPA, APLS with systemic vasculitis is a more likely explanation for these ocular manifestations in our patient.

Contributors BT, PV and UK contributed to diagnosis and management of the patient. BT and PV wrote the script, and SK supervised and performed critical revision. PV is the overall guarantor of the work.

Competing interests None declared.

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Learning points

- Scleritis is an uncommon presentation of antiphospholipid syndrome; thorough examination and investigation are needed to rule out other possible secondary associations (eg, antineutrophil cytoplasmic antibody-associated vasculitis, granulomatosis with polyangiitis, rheumatoid arthritis, systemic lupus erythematosus).
- Prompt management with interdisciplinary care could lead to better systemic control and prevent ocular sequelae (eg, scleral perforation, panophthalmitis).

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