Sir,

Scleritis as the presenting sign of primary antiphospholipid syndrome

Antiphospholipid antibody syndrome (APS) is an important cause of arterial and venous thrombosis. Ophthalmic manifestations result from cerebral and retinal vascular occlusion.[1] Visual field loss and ocular motility defects occur secondary to involvement of intracranial vasculature,[2] whilst retinal vascular occlusion results in retinopathy characterised by venous tortuosity, cotton wool spots and retinal capillary abnormalities.[3] We describe a previously unreported ophthalmic association of primary APS, namely bilateral sclerokeratitis.

Case report

A 39-year-old Caucasian woman presented to eye casualty with severe pain and photophobia of the right eye of gradual onset over 5 days. There was no significant past ophthalmic history. Medical history included three spontaneous late first-trimester miscarriages.

Initial ocular examination documented right scleritis, inferotemporal corneal infiltrate with neovascularisation and mild anterior uveitis. Fundus examination was normal. A diagnosis of right scleritis was made. The patient was commenced on dexamethasone 0.1% drops and flurbiprofen (Lagap, France). The patient presented 6 months later with a second episode of pain, at which point the scleritis had migrated to the temporal quadrant. She was re-commenced on dexamethasone and flurbiprofen. Over the next 2½ years there was further circumferential spread of a sclerokeratitis, which left areas of thinned and partially avascular sclera and corneal nebula. The left eye developed identical signs 2 years after onset of the condition in the right eye (Fig. 1).

An incidental referral to Rheumatology led to a diagnosis of primary antiphospholipid antibody syndrome based on the previous miscarriages and positive ELISA (Cambridge Life Sciences, UK) for anticardiolipin IgG antibody (34 and 41.2 GPLu/ml) on two occasions 18 months apart. Coagulation profile and platelet count were normal. The patient did not meet the criteria for systemic lupus erythematosus with absence of antibodies to double-strandard DNA and antinuclear antibodies. C-reactive protein and C3 and C4 complement levels were within normal levels.

Currently, there are frequent relapses of the sclerokeratitis in either eye (Fig. 1).

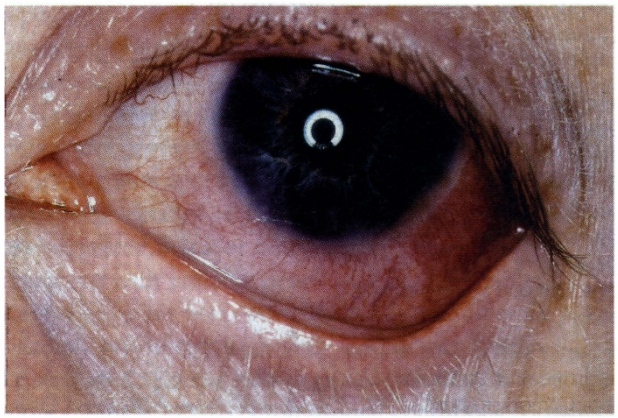

Fig. 1. *There is deep injection of the temporal sclera, which does not blanch with phenylephrine. The adjacent peripheral cornea contains multiple deep vessels with loss of transparency.*

Comment

APS is an important cause of thrombophilia with arterial and venous thrombosis occurring in any organ system.[4] It is characterised by recurrent thrombosis, pregnancy loss, thrombocytopenia and the presence of lupus anticoagulant and/or antiphospholipid antibodies.[1]

Thrombophilia in APS results from binding of antiphospholipid antibodies (APL) to protein–phospholipid complexes on vascular endothelial cells, enhancing expression of tissue factor. This results in activation of platelets and the coagulation cascade.[5] APL also interferes with natural anticoagulants such as the protein C system and antithrombin III–heparin pathways.[5,6] Beta-2-glycoprotein I is considered the primary target of the antiphospholipid antibodies.[1] Other targets include prothrombin, annexin V, protein C and protein S.[7] APS may be associated with connective tissue diseases such as systemic lupus erythematosus (secondary APS), but may also occur in isolation (primary APS).[1]

Antiphospholipid antibodies may be of IgG, IgM and IgA isotypes, though the IgG is found more commonly and in higher titre in APS.[8,9]

Diagnosis is based on one or more confirmed episodes of arterial and/or venous thrombosis, recurrent pregnancy loss and the presence of lupus anticoagulant or anticardiolipin antibodies to β2-glycoprotein I plasma protein.[10]

The most common systemic presentation is with deep vein thrombosis, whereas retinal venous tortuosity, dilatation, exudates and haemorrhages are the most common ocular finding.[1,3] Signs of ocular occlusive disease have been reported in 8–15% of the patients with APS while visual symptoms are reported in 33–59%.[2,3] Other posterior segment signs include retinal arterial or venous occlusion, choroidal infarction, vaso-occlusive retinopathy and ischaemic optic neuropathy.[3,9] Anterior segment disease reported in association with APS includes conjunctival telangiectasia, episcleritis, limbal keratitis and dry eye.[3] The most common reported ophthalmic symptoms are of transient visual loss, visual field defect or diplopia due to transient cerebral ischaemia.[2] Fong *et al.*[11] suggest scleritis is an immune complex mediated (type III hypersensitivity) disease with T cell involvement seen in autoimmune diseases such as rheumatoid arthritis: such a state exists in APS.

Severe necrotising or non-necrotising inflammation characterises scleritis. The initial lesion typically involves a segment of the globe and circumferential spread is

common. About 45% of the patients have associated systemic disease. Severe pain is also a prominent feature and is not typically seen in episcleritis or marginal keratitis, which need to be differentiated from scleritis.[12] There were several findings in our patient that supported the diagnosis of scleritis, including characteristic pain, lack of blanching with vasoconstrictor, circumferential spread and residual scleral changes. The response to intensive topical steroid and the corneal signs were somewhat atypical, but these features support the likely association between APS and scleritis, as they resemble some of the anterior segment features previously described in APS.[3]

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Sir,

Recurrent cerebral lupus heralded by an unusual combination of ocular manifestations

A 41-year-old Chinese woman presented with spontaneous progressive painless blurring of vision and facial swelling for a week. She had a history of systemic lupus erythematosus (SLE) for 3 years, initially presenting with oral ulcer, leucopenia, serositis, positive antinuclear antibody and cerebral lupus.[1] The disease was stabilised clinically and serologically with hydroxychloroquine 200 mg daily and prednisolone 2.5 mg on alternate days. On examination, visual acuity was 20/50 in both eyes. There was bilateral non-tender periorbital oedema (Fig. 1A, B) and conjunctival chemosis (Fig. 1C, D). There was no sign of scleritis. The anterior chamber and vitreous were clear. Contact lens biomicroscopy revealed a bilateral symmetrical macular oedema, with multiple foveal fine yellowish dots at the level of the retinal pigment epithelium (RPE) (Fig. 2). The discs and vessels appeared unremarkable. Blood pressure and serum albumin were normal.

A few hours later she became drowsy, which lasted for 4 days. She was further managed in the intensive care unit. Computed tomography of the brain was normal. Lumbar puncture showed an opening pressure of 10.4 cm H_2O, raised protein of 2.5 g/l (reference range 0.15–0.45 g/l) and a negative smear. She was treated as having recurrent cerebral lupus with intravenous methylprednisolone 500 mg daily for 3 days and a single pulse of cyclophosphamide 500 mg.

Two weeks later, the macular oedema, periorbital swelling and conjunctival chemosis were partially resolved. A fluorescein angiogram showed faint hyperfluorescence in the fovea in the early phase with no leakage in the late phase, which was compatible with RPE dysfunction secondary to choroidopathy. There was no evidence of retinal vasculitis or scleritis. A month later the macular oedema, periorbital swelling and conjunctival chemosis all subsided. Visual acuity was 20/30 in the right eye, 20/20 in the left. Twenty months later, visual acuity was 20/20 in both eyes. There were fine macular RPE stippling changes in both eyes (Fig. 3).