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Sir,

Central retinal artery occlusion and bilateral choroidal infarcts in Wegener's granulomatosis

Up to 77% of patients with Wegener's granulomatosis (WG) develop ocular manifestations during the course of their disease. However, clinically identifiable retinal involvement is rare and only three cases of central retinal artery occlusion (CRAO) occurring in patients with WG have been reported. We describe the case of a patient with WG who developed unilateral CRAO associated with bilateral choroidal infarcts.

Case report

A 58-year-old Caucasian man presented to a respiratory clinic with a 10 month history of productive cough with dyspnoea on exertion. He had general malaise with poor appetite and weight loss, night sweats and arthralgia. He had been attending an ENT clinic with symptoms of stuffy nose, postnasal drip and decreased hearing in his left ear. He had a strong family history of lung cancer and also had contracted tuberculosis as a child.

General examination was normal. Investigations revealed a leucocytosis, ESR 94 mm/h and a high CRP (464 mg/l). Chest radiograph showed a prominent right hilum and small right pleural effusion. A differential diagnosis of bronchial carcinoma and tuberculosis was considered. Sputum samples for AFB were negative. A week later he was admitted to hospital with a 3 day history of forgetfulness, disorientation, slurred speech and painless loss of vision in the left eye. Apart from slight ataxia there were no abnormal neurological signs. No focal endobronchial lesion was evident on bronchoscopy but the mucosa was congested and the biopsy revealed ulceration with non-specific granulomatous inflammation with no suggestion of malignancy.

Vision was 6/9 in the right eye, and hand movements in the left eye. A left relative afferent pupillary defect was present. Orbits and anterior segments were normal with clear vitreous in both eyes. Fundoscopy of the left eye showed attenuated arterioles, a pale oedematous retina, and a cherry-red spot at the fovea. In the right eye multiple, discrete, round, yellow-white, choroidal lesions were scattered around the posterior pole. The lesions in the left eye showed gradual resolution of the retinal oedema to reveal discrete lesions similar to those present in the right eye (Fig. 1). The fundus lesions regressed to leave atrophic pigmented areas, with the vision remaining unchanged during follow-up. Fundus fluorescein angiography showed blocking of choroidal fluorescence during the early phase, with little filling even in the mid- or late phase. As the disease resolved, angiography demonstrated staining of these lesions with alteration in background fluorescence due to changes in the pigment epithelium (Fig. 2). These findings were consistent with a left CRAO and bilateral choroidal infarcts.

Considering the ocular and bronchoscopic findings with repeatedly negative sputum samples, tuberculosis and bronchial carcinoma were unlikely. Serology for cANCA was positive to a 1:80 dilution and blood urea was 11.2 mmol/l with normal serum electrolytes. A CT scan of the chest demonstrated multiple cavitating nodules in both lungs, a right pleural effusion and right

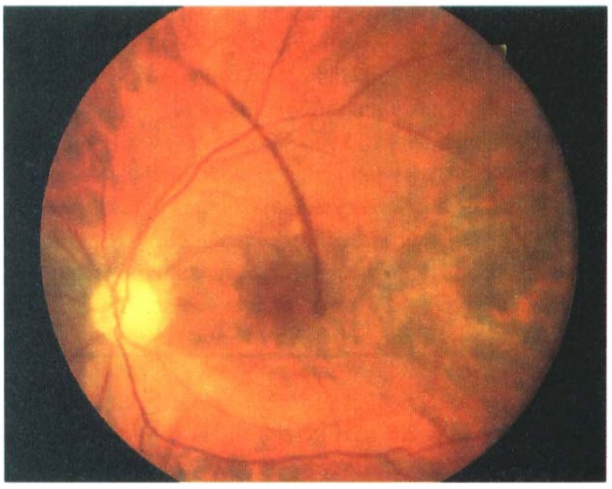

Fig. 1. *The left eye showing the pale optic disc and discrete choroidal lesions with alteration in the retinal pigment epithelium at the posterior pole.*

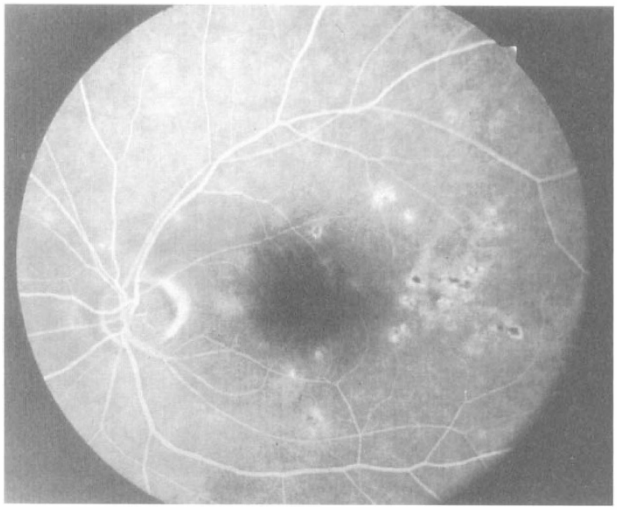

Fig. 2. *Mid-phase of fundus fluorescein angiography of the left eye showing staining of choroidal lesions in the margins with lack of choroidal fluorescence in the centre.*

lower lobe collapse with consolidation. A CT of the head showed a normal brain, nasal cavities, paranasal sinuses and orbits.

A diagnosis of Wegener's granulomatosis was made and the patient commenced on 60 mg of oral prednisolone daily with the addition, 3 days later, of cyclophosphamide 100 mg per day. The patient's general condition improved over the next few days and he was discharged on a tapering dose of oral prednisolone and cyclophosphamide. Six weeks later he was re-admitted with a diagnosis of relapsing WG and secondary pneumonitis with oliguria. Despite intensive steroids, antibiotics and assisted ventilation he rapidly deteriorated into respiratory and renal failure with a fatal outcome. An autopsy request for histopathological confirmation was refused by the relatives.

Comment

WG is a rare disorder of unknown aetiology characterised by necrotising vasculitis and granulomatous infiltration of respiratory and renal systems. cANCA is positive in 90% of cases and is highly specific for WG.[1] The effect of treatment with systemic steroids is variable, but response to cyclophosphamide and other cytotoxic drugs is usual.

Ocular involvement is seen in 40–77% of patients.[2] The manifestations can be classified into the contiguous type, with direct spread from the paranasal sinuses causing orbital infiltration with proptosis, nasolacrimal duct obstruction and optic nerve involvement, and the focal type presenting with conjunctivitis, episcleritis, scleritis, peripheral ulcerative keratitis, anterior uveitis and posterior segment inflammation.[2,3–6] Choroidal and retinal involvement is rare, with only three cases of CRAO being reported.[5,6] Of these, two cases were bilateral and in the third an impending CRAO in the second eye was thought to be reversed by treatment.[1,5,6] The pathology of the ocular manifestations is a necrotising obliterative vasculitis. Histopathology often shows inflammatory changes in the choroid and retinal vessels with thickening of the media and prominent endothelial cells in the choroidal vessels which can lead to choroidal vascular occlusion and infarcts.[4] Hayreh[9] demonstrated the lobular pattern of the choriocapillaris in the submacular region in the posterior pole of primates. Other studies have supported the conclusion that lobules of choriocapillaris in the submacular region are supplied by short pre-capillary arterioles without functioning anastomosis between capillary units. Small multifocal infarcts are also found in temporal arteritis and Goodpasture's syndrome and are presumed to be caused by vasculitis leading to occlusion of pre-capillary arterioles.[10]

Our patient had unilateral CRAO but evidence of bilateral choroidal vascular involvement. Timely and aggressive treatment prevented the retinal vascular involvement and visual loss in the second eye. This, as far as we are aware, is the first reported case of multiple bilateral choroidal infarcts in a case of Wegener's granulomatosis, although delayed and irregular filling of the choroid has been described in a case of anterior ischaemic optic neuropathy caused by focal vasculitis of the posterior ciliary arteries.[8] Systemic inflammatory causes such as WG should always be considered in the differential diagnosis of CRAO. Multiple organ involvement in WG tends to carry a worse prognosis, but there is no definite evidence in literature to suggest that the severity of ophthalmic involvement is in any way a predictor of survival. It is possible that patients may present with ocular features before the diagnosis of WG has been made, as in our case. Ophthalmologists should be aware of the spectrum of ophthalmic manifestations of this condition.

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Sir,

Interferon-associated retinopathy in a diabetic patient

Manifestations of retinal ischaemia are rarely reported complications of interferon alpha treatment.

Case report

A 59-year-old man was initially referred to the diabetic screening clinic with a 7 week history of decreasing visual acuity in both eyes and right retinal haemorrhage noticed by his optician.

Three months previously he had been found to have cerebral and pulmonary metastases from a renal cell carcinoma that had been diagnosed in 1992. At this time his full blood count, urea and electrolytes and liver function tests were normal. He was treated with oral dexamethasone, radiotherapy for the cerebral metastases and subcutaneous interferon alpha for the pulmonary metastases, and was soon found to have maturity-onset diabetes mellitus. His blood sugars were reported to be well controlled on oral gliclazide. In addition he was taking allopurinol and lansoprazole and he was an ex-smoker. At this time his blood pressure was noted to be normal.

On examination in the Eye Clinic his corrected visual acuity in each eye was 6/9. Both anterior segments were normal without significant lens opacities. Fundoscopy revealed four cotton wool spots in the left eye only, without any other evidence of changes associated with diabetes. The right fundus was unremarkable, and there was no evidence of the haemorrhage previously noted by the optician. A diagnosis of diabetic retinopathy was made at this time.

The patient was reviewed 4 months later, which was 2 weeks after his interferon alpha-2A course had been stopped by the oncologists. There had been no further deterioration in his vision or any other new symptoms, although he had now developed a few cotton wool spots in both eyes (Fig. 1), still without any other diabetic changes. He was reviewed 2 months later, when the cotton wool spots had begun to fade (Fig. 2).

Comment

The most commonly reported retinal changes described with interferon therapy are cotton wool spots, splinter haemorrhages, retinal haemorrhages[1,2] and arteriolar occlusion,[3] which the manufacturers claim occur in about 1 per 10 000 patients (Roche). Other rarely reported ocular complications include oculomotor paralysis,[4] hypertrichosis,[5,6] corneal allograft rejection,[7] papilloedema[8] and AION.[9] Most of the cases described in the literature are incidental findings in asymptomatic patients and occur within the first few weeks of starting therapy: e.g. 86% within 8 weeks.[1]

Some studies report the disappearance of cotton wool spots and haemorrhages while still on interferon treatment;[1,2] however, there are few data on the persistence of cotton wool spots after treatment has stopped, as in our case.

It is interesting to note that one study[1] found that the incidence of ischaemic retinopathic signs was increased in diabetic and hypertensive patients on interferon, suggesting a microcirculatory disturbance as the underlying pathological mechanism of retinal damage.

Interferon-associated retinopathy is a well-recognised if uncommon phenomenon, and in diabetic patients could easily be mistaken for diabetic retinopathy, as was the case with our patient initially.

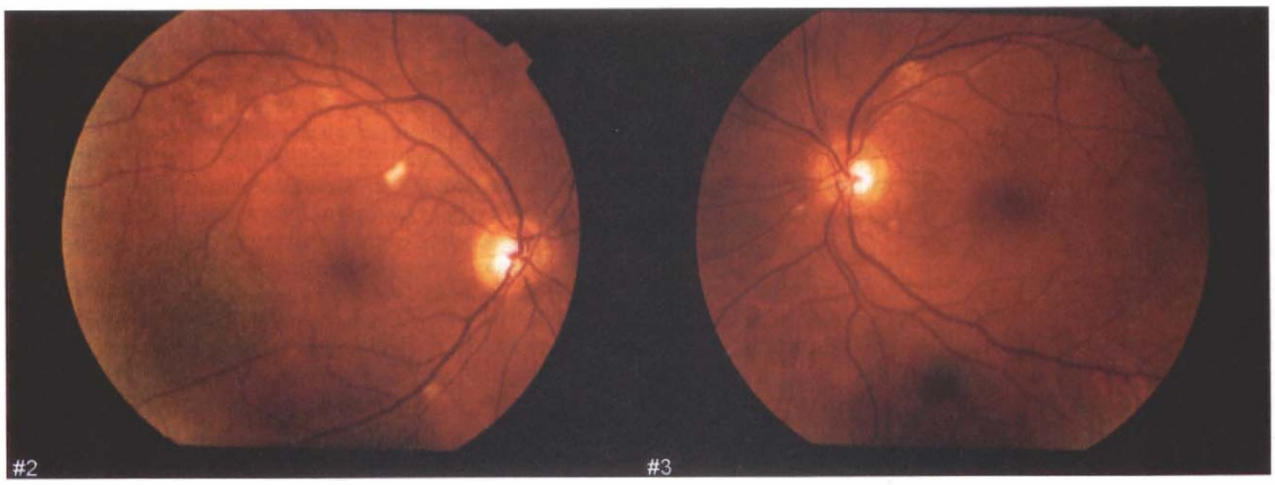

Fig. 1. *Cotton wool spots without any other evidence of diabetic retinopathy.*