

Acute posterior multifocal placoid pigment epitheliopathy and sarcoidosis

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SUMMARY We report on a patient with acute posterior multifocal placoid pigment epitheliopathy and sarcoidosis. A review of the literature suggests that sarcoidosis may occur more commonly in this condition than previously suspected.

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) was originally defined by Gass¹ and is characterised by the acute onset of multiple lesions of the posterior pole at the level of the retinal pigment epithelium. It has become clear that this condition may be only one feature of more generalised disease, and various reports have linked APMPPE with transient cerebral disturbances, cerebral vasculitis,^{2,4} erythema nodosum,^{5,6} subclinical nephropathy,⁷ and thyroiditis.⁸ A review of the ocular fundus findings in a series of patients with sarcoidosis⁹ found retinal pigment epithelial changes in 36% of 36 cases. In this group, the lesions were usually not at the posterior pole, and in no patient was vision affected by the retinal pigment disturbance. APMPPE has not been previously thought to be associated with sarcoidosis.

Case report

In March 1981 a 24-year-old male trainee designer became unwell with an influenza-like illness followed 10 days later by the development of multiple scotomata in his visual field. Examination of the fundi revealed multifocal placoid grey/white lesions at the posterior pole of both eyes (Fig. 1). A subsequent fluorescein angiogram displayed the typical features of APMPPE, namely, hypofluorescence in the early dye transit and marked hyperfluorescence in the late dye transit phase. The features were those of APMPPE. The visual symptoms improved without specific therapy, and

the lesions regressed. Six weeks later he presented with bilateral anterior uveitis. Topical steroid treatment was begun, but he remained systemically unwell and developed recurrent small buccal ulcers. Two weeks prior to his admission to the Neurological Centre he was noted to have a generalised lymphadenopathy and complained of an ascending sensory disturbance involving the left leg. For 24 hours before admission he had hesitancy of micturition.

Examination revealed cervical, inguinal, and axillary lymphadenopathy. The blood pressure was 120/80 mmHg. The visual acuity was 6/6 bilaterally, and paracentral scotomata were present in both visual fields. The fundal appearances were unchanged. Neurological examination showed him to have increased tone in both lower limbs, pathologically brisk reflexes, and flexor plantar responses. There were also radicular signs, with fifth lumbar motor weakness and disturbed sensation in the first to fourth sacral dermatomes on the left side. Clinically he was thought to have a myeloradiculopathy.

He had a haemoglobin of 10.7 g/dl, with normal normochromic normocytic indices, a raised erythrocyte sedimentation rate of 61 mm/h (Westergren), and raised serum urea and creatinine concentrations of 11.3 mmol/l and 207 µmol/l respectively. Serum proteins with electrophoresis and urine microscopy were normal. A chest radiograph revealed bilateral hilar enlargement, but plain radiology of the abdomen and intravenous nephrograms were normal. A myelogram and subsequent examination of the cerebrospinal fluid showed no abnormality. A lymph node biopsy was performed, and histological examination showed multiple epithelioid granulomata

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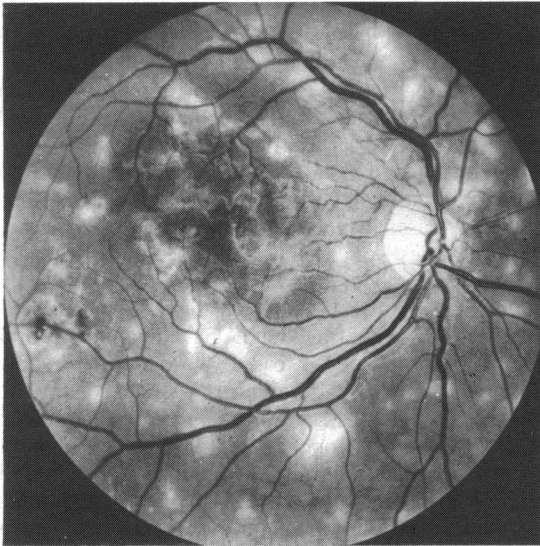


Fig. 1. Right eye.

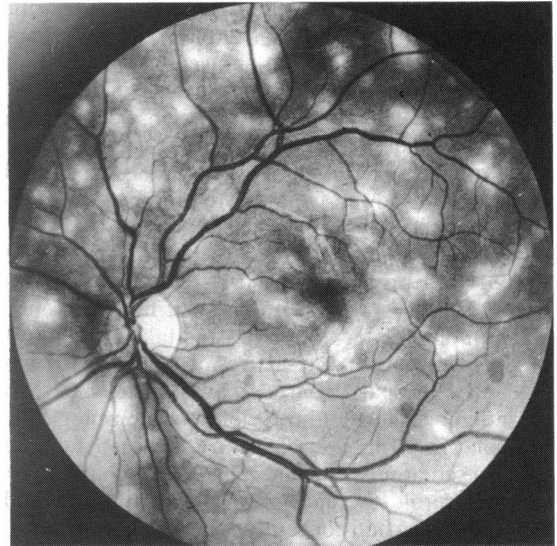


Fig. 2. Left eye.

Fig. 1 Fundal appearances of both eyes showing multifocal grey/white lesions at the posterior poles.

containing numerous Langhans giant cells and occasional central necrosis. No acid fast bacilli were seen and a Mantoux test was negative. Serum angiotensin converting enzyme activity was $52 \text{ nmol ml}^{-1} \text{ min}^{-1}$ (normal 16-52).

A renal biopsy showed a cortico-medullary sample with II glomeruli (Fig. 2). There were focal capsular adhesions, slight wrinkling of some basement

membranes, considerable numbers of non-caseating granulomata with multinucleate giant cells, and occasional crystalline inclusions. The majority of these granulomata were present interstitially and occasionally surrounded tubules. There was a moderate diffuse interstitial infiltrate of lymphocytes and plasma cells. Early tubular atrophy involved some 20% of the tubules. The appearances were

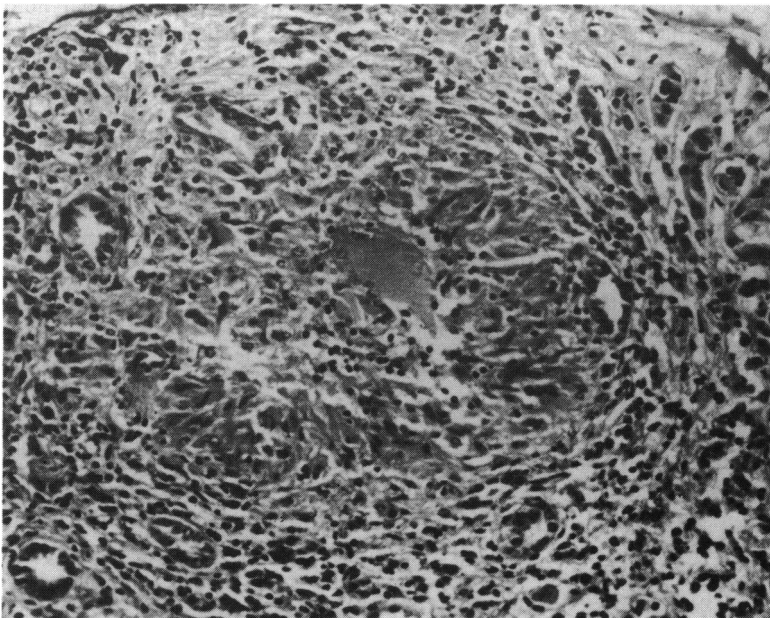


Fig. 2 Renal biopsy containing non-caseating granuloma. See text for details. Haematoxylin and eosin. $\times 236$.

those of an interstitial granulomatous nephritis with features suggestive of sarcoidosis. Immunofluorescence examination showed no significant immunoglobulin deposition. Electron microscopy showed a small number of electron dense deposits on the glomerular basement membrane with focal thickening and wrinkling. Examination of sarcoid granulomata showed lymphocytes and macrophages and considerable fibroblastic activity.

A diagnosis of sarcoidosis was made and treatment started with prednisolone 60 mg daily, which was followed by a gradual resolution of his symptoms. Three months later, when he was taking 20 mg of prednisolone daily, no active ocular disease was evident, and apart from a small area of disturbed sensation over the left buttock he was neurologically normal. The serum urea concentration was 9.2 mmol/l and the creatinine 126 µmol. Eighteen months after starting steroid therapy he was asymptomatic, and the serum urea and concentration were normal.

Discussion

Sarcoidosis affects the eye and optic nerve in many ways, and some 20% of patients will have ocular involvement at the time of their first examination. In established disease the incidence is even higher.¹⁰ Anterior segment disease occurs most commonly and usually takes the form of a chronic granulomatous uveitis. Posterior segment involvement occurs less frequently and rarely in isolation – chorioretinitis, periphlebitis, and chorioretinal nodules are the lesions most frequently described.^{10,11} Retinal pigment epithelial changes usually occur peripherally and are not associated with a disturbance of vision.⁹ Vitreous opacities¹² and choroidal granulomas¹³ also occur. Disease outside the globe is equally varied – conjunctival and lacrimal gland involvement, papilloedema, and direct granulomatous involvement of the optic nerve or chiasm¹⁴ are all well described.

APMPPE usually occurs in young adults, who develop an acute bilateral disturbance of vision. Funduscopy reveals multiple, grey-white, flat placoid retinal lesions at the level of the retinal pigment epithelium, and there may also be an associated low grade uveitis. Characteristically, fluorescein angiography shows hypofluorescence in the early dye transit and hyperfluorescence in the late transit phase. Gass¹ thought the disease originated in the retinal pigment epithelium, although later authors suggested that the lesions may be due to an underlying choroidal vasculitis.¹⁵ The pathophysiological mechanism is now thought to be choroidal ischaemia, which leads to a disturbance of the retinal pigment – epithelium barrier.^{16,17}

Several disorders have been reported to occur with

APMPPE. Symptoms suggestive of an antecedent viral attack are common,¹⁸ but firm serological evidence of definite infection has only been occasionally documented.¹⁹ The central nervous system (CNS) has been unequivocally involved in several cases, and the symptoms included headache, drowsiness, and focal neurological deficit due to lesions of the cerebral hemisphere.²⁴ Investigations in these cases have shown minimal, non-specific abnormalities of the electroencephalogram, a lymphocytic pleocytosis in the cerebrospinal fluid,²⁰ and cerebral infarction shown by a computerised tomography scan of the head.⁴ Carotid and vertebral angiography in three cases purported to show changes of cerebral vasculitis²⁴ and led to the suggestion that APMPPE may be part of a systemic vasculitis. Some support for this suggestion comes from its association with erythema nodosum^{5,6} and the presence of cellular casts in the urine of patients with APMPPE.⁷ Erythema nodosum may be due to a cutaneous vasculitis, and urinary casts might indicate a subclinical microvascular nephropathy.

There can be no doubt that our patient suffered from renal and central nervous system sarcoidosis, and to our knowledge this is the first report which links this disorder with APMPPE. It is important to review the neurological case reports in the light of this association. In fact many of the non-specific symptoms described such as headache and drowsiness may occur in CNS sarcoid, and cerebral infarction with focal neurological deficit may be the result of granuloma formation with blood vessel walls.²¹ Abnormalities of the electroencephalogram and a lymphocytic pleocytosis in the cerebrospinal fluid also occur in sarcoidosis. Furthermore, erythema nodosum is a common cutaneous manifestation of the disease. None of the patients described in these reports had specific tests for sarcoidosis. We suggest that some of these cases may have had sarcoidosis and that this disorder should be considered when investigating patients with APMPPE in future.

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Accepted for publication 11 August 1986.