

Acute multifocal placoid pigment epitheliopathy associated with erythema nodosum and a flu-like illness

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ABSTRACT

Acute multifocal placoid pigment epitheliopathy (AMPPE) is a rare inflammatory vasculitis of the choroid. Despite primarily being a disorder of the eye, a number of extra-ophthalmological features have been described in AMPPE and may accompany the visual disturbances. Such patients may be admitted under the care of physicians for evaluation of a systemic illness. We report AMPPE occurring in a 37-year-old man in his thirties admitted with a flu-like illness, erythema nodosum, visual disturbances and raised inflammatory markers. Conditions such as bacterial endocarditis and vasculitis, were considered before a diagnosis of AMPPE was made. The case illustrates how AMPPE can be a diagnostic dilemma, particularly when associated with extra-ophthalmological features. The epidemiology, clinical features, diagnosis and therapy of AMPPE are also discussed.

Keywords: acute multifocal placoid pigment epitheliopathy, choroid vasculitis, epitheliopathy, erythema nodosum, placoid

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INTRODUCTION

Acute multifocal placoid pigment epitheliopathy (AMPPE) is a choroidal vasculitis that is uncommonly seen by ophthalmologists and even less so by physicians. The diagnosis of AMPPE can be a challenging one, especially in the presence of extra-ophthalmological features. We present a case of a systemically-unwell man with AMPPE whose clinical presentation created a diagnostic dilemma.

CASE REPORT

A 37-year-old man presented with a one-week history of general malaise, sweats, myalgias, visual disturbance and a headache. He had a history of migraine, but this episode was completely different from his usual migraine headache. He had initially noticed three dark spots around his left lateral visual field while watching television. An ophthalmologist diagnosed retinal emboli.

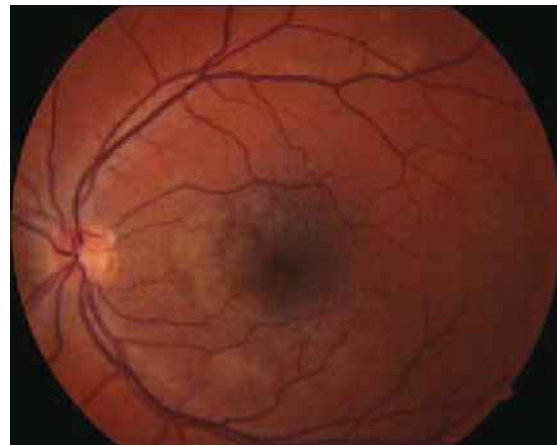


Fig. 1 Fundoscopic photograph of the left eye shows focal choroiditis and multiple creamy white plaques.

He then developed multiple dark spots in his right eye followed by sweats, a frontal headache and arthralgias in the ankles and the right wrist. There was no muscle weakness, obvious joint swelling, or oral and genital ulcers. His erythrocyte sedimentation rate was elevated; this, in combination with his systemic illness and the diagnosis of retinal emboli, raised the possibility of infective endocarditis. This prompted admission to the hospital. On examination, he was afebrile and had a painful erythematous macular rash on the anterior aspect of both lower legs, clinically consistent with erythema nodosum. A large left paracentral scotoma and multiple dark spots in his right visual field affected his vision. He was alert and oriented with no stigmata of infective endocarditis. The remainder of the examination was unremarkable.

He was commenced on empiric antibiotic therapy for infective endocarditis as well as intravenous acyclovir and fluconazole. Later that day, an ophthalmologist examined him and saw signs consistent with bilateral retinal arteriolaritis. He believed that vasculitis was more likely than an infective cause. On this basis, the patient received three days of daily methylprednisolone 1 g intravenously. Within hours of the first dose of methylprednisolone, the erythema nodosum spontaneously resolved. His antibiotics were ceased after endocarditis was excluded on the basis of three sets of negative blood cultures and a normal transthoracic echocardiogram. Serological tests

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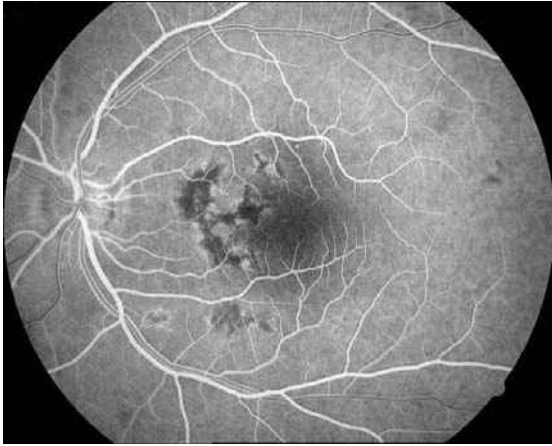


Fig. 2 Early phase fluorescein angiogram of the left eye shows plaques blocking the fluorescence.

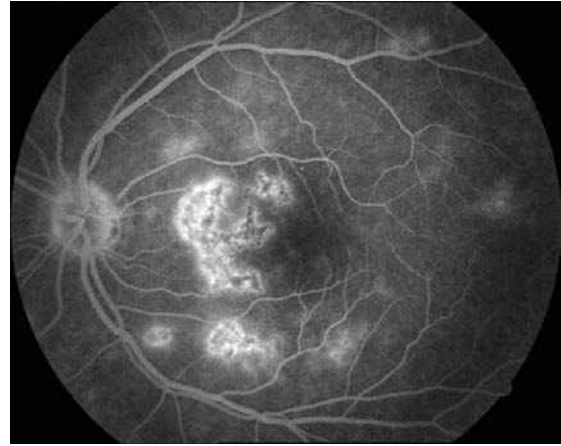


Fig. 3 Late phase fluorescein angiogram of the left eye shows staining of plaques.

for a wide range of viruses were all unremarkable. There was no proteinuria. His vasculitic and thrombophilic screens were unremarkable. The angiotensin converting enzyme assay was normal. HLA-B27 was negative. Due to technical difficulties, only sufficient cerebrospinal fluid was obtained for a cell count: this showed $114 \text{ erythrocytes} \times 10^6/\text{L}$ and $2 \text{ polymorphonuclear cells} \times 10^6/\text{L}$. Magnetic resonance imaging and magnetic resonance angiography of the brain were unremarkable.

He gradually felt much better systemically with resolving inflammatory markers, although his vision did not improve much. At this time, fundoscopy and fluorescein angiography were performed by another ophthalmologist. Fundoscopy showed focal choroiditis with multiple subretinal creamy white plaques scattered throughout the posterior pole of both eyes (Fig. 1). Fluorescein angiography showed early block of fluorescence and late staining (Figs. 2 & 3). On this basis, a diagnosis of AMPPE was made. The patient was discharged with a tapering dose of oral prednisolone. Since discharge, his visual acuity has remained stable at 6/6 bilaterally. The fundal lesions have settled to stable pigmented scars. He has not experienced distortion or further deterioration in his vision.

DISCUSSION

AMPPE is a rare idiopathic inflammatory disease and obstructive vasculitis of the choroid that affects the choroidal capillaries, retinal pigmentary epithelium and outer retina. Healthy adults aged 20–50 years tend to be affected; there is no sex predilection.⁽¹⁾ AMPPE is a bilateral visual disorder, which presents with subacute unilateral visual impairment. The combination of AMPPE's rarity as an ophthalmological disorder and the presence of a number of extra-ophthalmological features can create a diagnostic dilemma, as this case demonstrated. In this case, diagnoses such as infective endocarditis, viral encephalitis and cerebral

vasculitis were entertained, before AMPPE was finally diagnosed. AMPPE can be associated with a variety of extra-ophthalmological features, such as erythema nodosum (as with this patient),⁽²⁾ thyroiditis,⁽³⁾ cerebral angiitis,⁽⁴⁾ and a flu-like prodrome in about one-third of the patients.⁽⁵⁾ When cerebral vasculitis accompanies AMPPE, a wide range of neurological sequelae can occur, including headaches, meningitis, cerebral venous thrombosis and stroke. Deaths due to cerebral vasculitis in AMPPE have been documented. Headache is the most frequent symptom of central nervous system involvement accompanying AMPPE, occurring in over two-thirds of cases.^(4,6)

The aetiology of AMPPE is uncertain, despite being associated with a number of infective and immunological conditions. Infective associations include viral illnesses⁽⁷⁾ and vaccines.^(8,9) A genetic basis has been postulated in some cases.^(10,11) The differential diagnosis is broad and includes a variety of autoimmune and infective disorders, such as cytomegalovirus, syphilis, histoplasmosis, sarcoidosis, systemic lupus erythematosus, Behcet's disease, Vogt-Koyanagi-Harada disease, and metastatic malignancy.⁽¹²⁾ With regard to the retinal findings alone, the differential diagnosis includes acute retinal pigment epithelitis, diffuse unilateral subacute neuroretinitis, birdshot choroidopathy, multifocal evanescent white dot syndrome and serpiginous choroiditis.⁽¹³⁾

The diagnosis is a clinical one, made through fundoscopic examination with fluorescent angiography. Fundoscopic examination typically reveals multifocal, yellow-white, creamy placoid lesions at the level of the retinal pigment epithelium and choroid.⁽⁵⁾ The lesions are mainly at the posterior pole, never being anterior to the equator. After beginning to fade within a few days, the lesions will have been replaced with areas of partly deep-pigmented pigment epithelium with irregular pigment clumping. The characteristic findings on fluorescein angiography are hypofluorescent lesions

in the early phase followed by late hyperfluorescence of the same regions.⁽¹²⁾ Indocyanine green angiography is another technique that may be used, where the acute lesion shows hypofluorescence.⁽¹⁴⁾

The outcome of AMPPE is spontaneous improvement with almost complete visual recovery over weeks.⁽¹⁾ Uncommonly, patients have recurrences within the first six months,⁽¹⁵⁾ and rarely, significant visual loss with choroidoretinal atrophy can occur.⁽¹⁶⁾ In our patient, the deterioration of his vision seemed to halt after administration of corticosteroids, but it is unclear whether this was coincidental. His erythema nodosum did rapidly resolve within hours of the first dose of intravenous methylprednisolone, suggesting that corticosteroids might have an impact on some of the extra-ophthalmological features of AMPPE. This is supported by the recommendation that corticosteroids must be used when AMPPE is complicated by cerebral vasculitis.⁽⁴⁾

In summary, AMPPE is a rare inflammatory vasculitis of the choroid that can pose diagnostic difficulties to clinicians, particularly when it presents in association with extra-ophthalmological features. While the natural history in uncomplicated AMPPE tends to be one of spontaneous resolution, the use of intravenous corticosteroids, especially in the presence of cerebral vasculitis, is not unreasonable.

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