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Clinical Study

Neurological complications of acute multifocal placoid pigment epitheliopathy

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ABSTRACT

Acute multifocal placoid pigment epitheliopathy (AMPPE) is an autoimmune chorioretinal disease that can be complicated by neurological involvement. There is limited information on this potentially treatable condition in the neurological literature. The objective of this patient series is to describe the neurological complications of AMPPE. We retrospectively identified patients with neurological complications of AMPPE seen at Auckland Hospital between 2008 and 2013 and summarised cases in the literature between 1976 and 2013. We identified five patients with neurological complications of AMPPE at Auckland Hospital and 47 reported patients. These patients demonstrated a spectrum of neurological involvement including isolated headache, stroke or transient ischaemic attack, seizures, venous sinus thrombosis, optic neuritis, sensorineural hearing loss and peripheral vestibular disorder. We propose criteria to define AMPPE with neurological complications. A cerebrospinal fluid (CSF) lymphocytosis in a patient with isolated headache may predict the development of cerebrovascular complications of AMPPE. Patients with cerebrovascular complications of AMPPE have a poor prognosis with high rates of death and neurological disability among survivors. Predictors of poor outcome in those who develop neurological complications of AMPPE are a relapsing course, generalised seizures and multifocal infarction on MRI. All patients with neurological complications of AMPPE, including headache alone, should be investigated with an MRI brain and CSF examination. Patients with focal neurological symptoms should receive intravenous (IV) methylprednisolone followed by a tapering course of oral steroids for at least 3 months. Patients with AMPPE and an isolated headache with a CSF pleocytosis should be treated with oral steroids.

1. Introduction

Acute multifocal placoid pigment epitheliopathy (AMPPE) is an uncommon inflammatory chorioretinal disorder [1,2]. AMPPE presents in young adults with the acute onset of photopsias and painless visual loss that is frequently bilateral. Characteristic retinal changes are creamy lesions that evolve over several weeks leaving retinal pigmentary changes. On fluorescein angiography, acutely these areas demonstrate early hypofluorescence and late hyperfluorescence consistent with impaired choroidal blood flow thought to be due to an inflammatory choriocapillaritis [2]. It remains unclear whether the characteristic retinal lesions are exudative or ischaemic in nature. The course is usually self-limiting with recovery of vision, although there may be residual retinal scarring. The visual prognosis is related to the degree of foveal involvement. The cause of AMPPE is uncertain, but several lines of evidence suggest that it is immune-mediated: association with other ocular and systemic inflammatory diseases, post-infectious and post-vaccination cases and the association with certain HLA types [2].

Patients with AMPPE can develop neurological complications but usually present with retinal disease before headache or focal neurological deficits develop. Imaging studies suggest the cause is cerebral vasculitis and this has been confirmed in three pathological cases showing granulomatous inflammation in the large, medium and small vessels in the brain and meninges [3–6].

Articles on AMPPE are rarely published in the neurological literature. The objective of this patient series is to describe the neurological complications of AMPPE so as to facilitate early recognition of this disorder and to summarise the clinical and radiological characteristics of neurological complications of AMPPE from the literature.

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2. Methods

We report five patients with AMPPE and neurological complications presenting to our institution and collected retrospectively between 2008 and 2013. Patients were included if they had AMPPE confirmed ophthalmologically and experienced neurological symptoms which included headache, focal neurological deficit, seizure or reduced level of consciousness. The findings of 47 published patients are combined with our five patients to examine the spectrum of neurological complications of AMPPE. To obtain the published cases of AMPPE, we performed an online medline search of the English literature. We used the search terms "AMPPE" and "APMPPE" as key words which identified 79 publications. We included all cases of AMPPE with neurological involvement including headache. Excluded were cases with isolated ocular disease. We analysed the clinical features of the combined series of patients to identify risk factors for poor outcome, defined as residual neurological deficit or death. Missing data points were omitted from the analysis. Follow-up data was collected from the most recently available clinic letter with a range of one to ten months following initial presentation, or as detailed in the published case reports.

3. Patient reports

3.1. Patient 1

A previously well 26-year-old man presented to an ophthalmologist with headache and photopsia. Visual acuity was 20/50 bilaterally. The optic discs were normal and mild swelling was identified at the macula. He was diagnosed with central serous chorioretinopathy. Two days later he awoke with worsening headache and visual disturbance, difficulty with language and right arm weakness. A neurological examination showed an expressive dysphasia, right homonymous hemianopia and mild right hemiparesis. MRI, including diffusion-weighted imaging (DWI) of the brain was normal and a lumbar puncture showed a normal opening pressure at 190 mm H_2O, a lymphocytic meningitis (white cell count 61×10^6/L [normal range $\leqslant 5 \times 10^6$/L]: 75% lymphocytes [normal range 60–80%], protein 92 mg/dl [normal range 0.15–0.45 mg/dl] and glucose 61.2 mg/dl [normal range 2.8–4.4 mg/dl]). A further ophthalmology opinion was arranged. He was noted to have subretinal fluid over the maculae, ill-defined choroidal lesions in both eyes and early pigmentary changes. A fluorescein angiogram showed early hypofluorescence followed by later hyperfluorescence consistent with delayed choroidal filling (Fig. 1). He was treated with 1 g intravenous (IV) methylprednisolone for five days followed by a tapering dose of oral prednisone over two weeks. The patient's expressive dysphasia, hemianopia and hemiparesis began to improve prior to starting corticosteroids and resolved within 24 hours. At follow up four weeks later his visual acuity had improved to 6/6 bilaterally and he reported no further headaches.

3.2. Patient 2

A previously well 38-year-old man presented to an ophthalmologist with a two week history of headache, malaise and visual blurring. The visual acuity was 20/40 in the right eye and 6/6 in the left eye. There were patchy retinal changes around the macula in the right eye. These changes were seen in the area of the optic disc and more peripherally in the left eye (Fig. 2). There was no visual field defect and the rest of the neurological examination was normal. MRI showed a small acute infarct in the right parietal lobe. MR angiography was normal. The patient was diagnosed with AMPPE with neurological complications and he was started on prednisone 60 mg/day. Four weeks later, while receiving prednisone 30 mg/

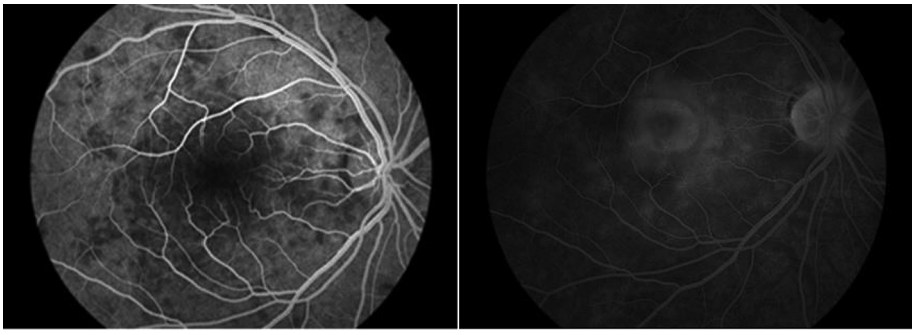

Fig. 1. Fluorescein angiogram performed in patient 1 showing early hypofluorescence followed by late hyperfluorescence characteristic of AMPPE.

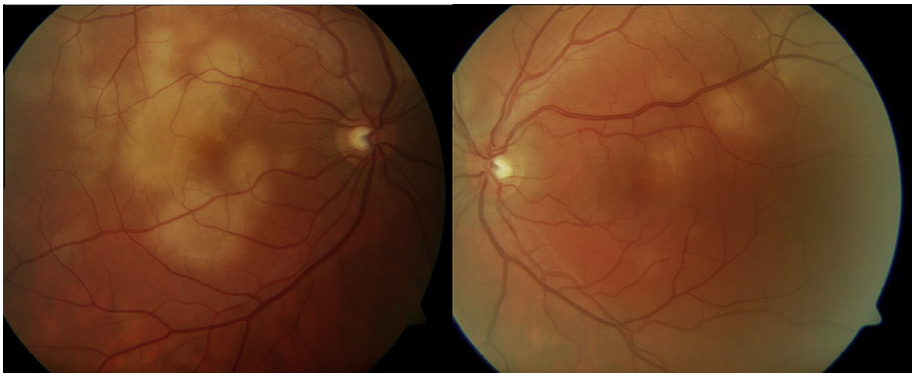

Fig. 2. Fundus photography of patient 2 showing patchy retinal changes around the macula in the right eye and around the optic disc and more peripherally in the left eye.