Acute posterior multifocal placoid pigment epitheliopathy with cerebral involvement

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Abstract
In a patient with angiographically proven cerebral vasculitis five months after acute posterior multifocal placoid pigment epitheliopathy (APMPPE) neurological symptoms promptly responded to steroid treatment. Cerebrospinal fluid (CSF) showed a lymphocytic pleocytosis. Magnetic resonance imaging (MRI) revealed multifocal white matter lesions in the hemispheres and the brain stem suggesting a diffuse subcortical vasculitis.

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) originally described by Gass in 1968 is characterised by sudden, usually binocular, blurring of vision. At the level of the pigment epithelium multifocal yellowish-white placoid lesions occur. Usually the visual outcome is good and the disease has a self-limited natural course. Serious complications, however, may evolve from systemic manifestations which occur occasionally such as cerebral vasculitis, nephritis, thyroiditis, Crohn’s disease and erythema nodosum. We report the first MRI documentation of multiple white matter foci in APMPPE with angiographically proven cerebral vasculitis.

Case report
A 54 year old man had had influenza type symptoms and fever for many weeks and awoke on 9 December 1988 with acute loss of vision in his left eye followed within 12 hours by his right eye. The diagnosis of APMPPE was made on the basis of typical fundoscopic and fluorescein angiographic findings (fig 1). He was treated with defibrase (TM) for 40 days without improvement in visual acuity.

On 31 March 1989 he was admitted as he had developed dysarthria, unsteadiness of gait and weakness of his left arm and leg overnight. His past medical history was completely normal. On examination visual acuity was 0.1 in both eyes and fundoscopy revealed pigmental scars of both maculae typical for late stages of APMPPE. Neurologically, he exhibited severe dysarthria, pyramidal signs on both sides, and a moderate left sided hemiparesis. His gait was unsteady without further evidence of cerebellar dysfunction. A CAT scan performed on the day of admission was normal. CSF showed a pleocytosis of 18 mononuclear cells per µl and an increased protein level of 0.67 g/l. The IgG index (0.32) was normal and oligoclonal bands were negative. MRI (5 April 1989) revealed multiple hemispheric white matter foci (fig 2a, b). Additional non-space occupying lesions were found in the pons and left thalamus (fig 2c, d).

Angiography showed string-like arterial narrowing of all basal cerebral arteries which was most prominent in areas close to the subarachnoid space. Laboratory findings including ESR were normal except for low complement levels (C3 18 mg/dl, C4 54 mg/dl). Anti-mitochondrial, anti-nuclear, and anti-smooth muscle antibodies as well as levels of C-reactive protein and rheumatoid factor were negative. Dexamethasone (24 mg) was administered iv for six days followed by oral methylprednisolone (80 mg) for eight days. Within five days of treatment clinical symptoms resolved completely, except for visual acuity and increased reflexes. Steroid treatment was continued with 40 mg, later 20 mg methylprednisolone for an additional two months and the patient was put on azathi-
oprine (150 mg per day) for long term immunosuppression.

His neurological condition was stable until February 1990 when he was last seen. Visual acuity of his right eye had finally improved from 0-1 to 0-7 between October 1989 and February 1990. The size of the multiple white matter foci seen on MRI in April 1989 had decreased as revealed by a control scan in February 1990, and no additional lesions had developed under immunosuppression.

Discussion

APMPPE is an inflammatory disorder of unknown aetiology which is usually self limited. Associated neurological complications have been reported such as severe headache, neck stiffness, transient aphasia, hemianopia, limb weakness, ataxia, tremor, and swelling of optic disks and in one case sudden coma and death. Neurological signs usually occurred simultaneously or within one month after onset of ocular symptoms, in one case there was a delay of 5-5 years, and in our case of four months.

In the six cases with CNS involvement where angiograms have been performed five showed cerebral vasculitis and only one angiogram was normal most likely because the patient was having steroid treatment. In the one fatal case vasculitis was confirmed by histopathology which revealed a focal granulomatous infiltration of medium-sized leptomeningeal arteries and patchy confluencing areas of vascular congestion in the grey matter of both cerebral hemispheres. All patients had elevated CSF protein levels and/or lymphocytic pleocytosis, but CSF abnormalities have also been found in the absence of neurological symptoms. Oligoclonal bands when tested were negative.

In our patient, clinical symptoms can be sufficiently explained by the brainstem lesion seen on MRI. Moreover, additional extensive hemispheric white matter lesions without clinical correlates could be detected which were still present as scars in the control MRI 10 months later. The distribution of these lesions is consistent with a diffuse predominantly subcortical vasculitis which has not been reported previously in APMPPE. In most cases with proven vasculitis CAT scans were normal, in two cases posterior lobe infarctions indicating occlusion of a major cerebral artery were found.
We suggest that an MRI should be performed on every patient with APMPPE as a non-invasive screening procedure for early detection of a potentially harmful CNS involvement. Unlike other types of vasculitis ESR is not a reliable indicator of cerebral vasculitis since it was normal in almost all cases of APMPPE with neurological symptoms, including ours. In accordance with previous cases neurological symptoms promptly responded to steroid treatment. Recurrences, however, were observed in two of four cases and one patient died after the steroid dose was lowered. We therefore kept our patient on methylprednisolone for two months and concomitantly prescribed azathioprine for long-term immunosuppression. With this treatment no further infarctions have occurred as shown by MRI. Moreover, visual acuity had even improved one year after the onset of APMPPE. This case again stresses that APMPPE is not a "benign" disorder. Aetiologically, it seems to represent a systemic inflammatory disease with an initial and preferential ocular manifestation.

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