BMJ Case Reports

Rare disease

Recurring meningoencephalitis in sinusitis-associated acute posterior multifocal placoid pigment epitheliopathy under prednisone tapering

H Joswig,[1] C Flueckiger,[2] A Infanger,[3] B Tettenborn,[1] A Felbecker[1]

[1]Department of Neurology, Cantonal Hospital St. Gallen, St. Gallen, Switzerland;
[2]Department of Ophthalmology, Cantonal Hospital St. Gallen, St. Gallen, Switzerland;
[3]Department of Otorhinolaryngoscopy, Cantonal Hospital St. Gallen, St. Gallen, Switzerland

Correspondence to Dr Ansgar Felbecker, ansgar.felbecker@kssg.ch

Summary

The authors describe a case of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) with recurrent neurological complications.

A 24-year-old man experienced subacute bilateral visual loss. Based on the characteristic findings in funduscopy and fluorescin angiography and after the exclusion of the differential diagnoses, APMPPE was diagnosed. During the course of the disease recurrent episodes of meningitis and encephalitis occurred when tapering of prednisone was attempted. Secondary to encephalitic lesions, the patient developed partial epileptic seizures, which made an anticonvulsive medication necessary. The authors considered a chronic sinusitis to be an aetiological factor of the underlying autoimmune process. Due to the complicated course of APMPPE, they decided to start long-term immunosuppressive therapy with azathioprine under which the patient remained stable and prednisone could be tapered successfully.

Neurological complications of APMPPE are rare. Nevertheless, this case demonstrates that long-term immunosuppressive treatment might be necessary to prevent recurrent neurological complications in some cases.

BACKGROUND

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is a rare ophthalmologic disease usually occurring in young adults presenting with mostly binocular retinal lesions that result in a reduction of visual acuity.[1] The aetiology is unknown and an autoimmune process is still a matter of speculation as reports of concomitant autoimmune disorders or vasculitis[2–6] and preceding flu-like symptoms[5] and vaccinations[7] have been made. Up to date choroidal vasculitis is generally believed to play the main role in the pathogenesis of APMPPE.[5 6 8–10] Nevertheless, prognosis of APMPPE is mostly good with or without treatment unless the central nervous system is involved,[4 11] which has been reported in only a few cases worldwide.

A limited number of case reports exist in which APMPPE is associated with neurological complications. We present a case of severe neurological complications successfully treated with azathioprine. To the best of our knowledge we are the first to describe a chronic sinusitis maxillaris to be the underlying cause of APMPPE.

CASE PRESENTATION

A 24-year-old man with APMPPE was repeatedly admitted with neurological symptoms of headache and partial epileptic seizures.

Initially, the patient presented to the department of ophthalmology with an increasing flickering and bilateral loss of vision. The results of investigations are given below.

Two and a half weeks later, after discharge from hospital, the patient was admitted to the department of neurology. While under prednisone tapering he developed persistent cephalgia, the most common symptom of APMPPE,[12] which was not accompanied by a reduction in visual acuity. Because of clinical and laboratory findings APMPPE-associated meningitis was diagnosed. However, an episode of somnolence and global aphasia followed shortly after. Thus, the diagnosis of an APMPPE-associated meningoencephalitis was established.

INVESTIGATIONS

At the first examination in the department of ophthalmology, visual acuity was reduced to finger counting OD, 0.2 OS and funduscopy revealed a macular oedema and multiple white-coloured lesions in its vicinity with early hypofluorescence and late hyperfluorescence (figure 1A and B) supporting the diagnosis of APMPPE.

Differential diagnoses such as cytomegalovirus-retinitis, Epstein–Barr virus, hepatitis B virus, hepatitis C virus, Frühsommer-Meningoenzephalitis, tuberculosis (TB), Borrelia, Treponema, Leptospira, Toxoplasma and vasculitis (Rheumatoid factor, antinuclear antibodies and antineutrophil cytoplasmic antibodies negative) were ruled out. After re-admission to the department of neurology 2½ weeks later, bacterial, TB, viral or fungal meningitis were also taken into consideration, but were not laboratory-confirmed in the cerebrospinal fluid examination, which revealed a moderate lymphocytic inflammatory reaction with moderate pleozytosis of 29 cells/µl and a mildly elevated protein of 0.47 g/l (normal value 0.15–0.45 g/l). Cerebral MRI at that time was normal and the diagnosis

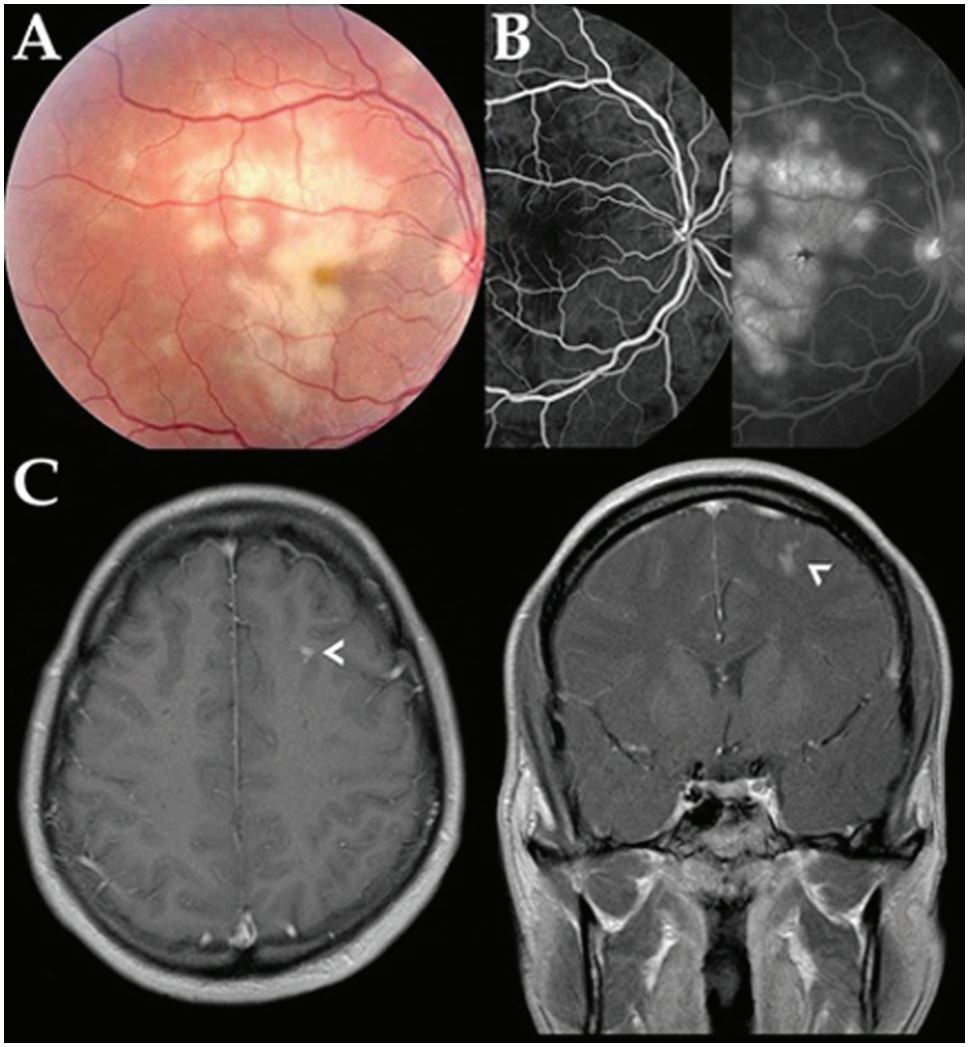

Figure 1 (A) Funduscopy of the right eye showing multiple white-coloured lesions. (B) Fluorescin angiography of the right eye showing early hypofluorescence (left) and late hyperfluorescence (right) of the placoid lesions. (C) Horizontal (left) and coronar (right) MR image of the APMPPE associated contrast-enhanced vasculoencephalopathic lesions.

of APMPPE-associated meningitis was made. After an episode of somnolence and global aphasia, the cerebrospinal fluid cell count rose up to 95/µl and protein to 1.67 g/l. Cerebral MRI showed a new restricted diffusion in the right precunius and a pachymeningeal enhancement.

DIFFERENTIAL DIAGNOSIS

The initial presentation with acute bilateral visual loss in a young patient as well as characteristic funduscopic and fluorescin angiography findings led to the diagnosis of APMPPE. Afterwards, the severe headache without focal neurological signs in view of normal MRI findings and cerebrospinal fluid pleocytosis had to be classified as APMPPE-associated meningitis.

The following admission with additional focal neurological signs and focal hyperintensities in contrast-enhanced MRI led us to the diagnosis of APMPPE-associated meningoencephalitis. At this point, relevant differential diagnoses included APMPPE-induced cerebral vasculitis. Because of the normal MR angiography and the cortical location of the lesions, however, we explained the encephalitic lesions as focal spreading of the meningitic reaction.

TREATMENT

After the diagnosis of APMPPE was made, a systemic immunosuppressive therapy with prednisone 100 mg/day as well as a local therapy with prednisone and indometacin eye drops was initiated. The decision for immunosuppressive therapy was based on the foveal involvement, which is significantly associated with a poor outcome.[1 8] Prednisone was tapered by 20 mg every 2 days to 10 mg.

During the following course of the disease the patient experienced recurrent meningitis and meningoencephalitis while under prednisone tapering. Therefore, the prednisone dose was re-adapted to 1 mg/kg body weight under which the patient recovered rapidly.

OUTCOME AND FOLLOW-UP

Following initial treatment, visual acuity promptly increased to 0.25 OU and a regression of the retinal lesions was noted. A new onset of persistent headaches took place 4 months after the initial symptoms, while the patient was on prednisone 2.5 mg/day. Thus, prednisone dose was increased to the last effective dose of 10 mg/day. Visual acuity was unaffected and had improved to 0.3 OU.

BMJ Case Reports 2011; doi:10.1136/bcr.02.2011.3820

The following month, the patient was admitted to our department once again after having experienced a speech arrest of about 5 min. Furthermore, he reported intermittent paraesthesias of the right arm that occasionally spread to the right leg and right part of the mouth. The patient underwent cerebrospinal fluid examination, which now revealed 10 cells/µl and a protein level of 0.26 g/l. The cerebral MRI demonstrated new lesions of restricted diffusion in the left precunius and in the left frontal medial gyrus (figure 1C) with diffuse correlating enhancement in contrast images. A MRI-angiography was normal without evidence of cerebral vasculitis and a routine EEG was normal. Because of the typical semiology of the spreading paraesthesias and speech arrest we diagnosed partial epileptic seizures and decided to start an anticonvulsive treatment with carbamazepine.

Because of the postulated parainfectious autoimmune cause of APMPPE, we searched for a concomitant or precedent infection. The only significant finding in this regard was a chronic sinusitis maxillaris and ethmoidalis, which had been persistent for a year and had been treated with antibiotics in the acute periods. As there are reports of a linkage between infectious processes or vaccinations and APMPPE in the literature,[5 7 12] we considered the patient's sinusitis to be an underlying cause or trigger of his symptoms. Therefore, the patient was subjected to otorhinolaryngologic surgery. A septumplasty, an infundibulotomy and an anterior ethmoidectomy were performed on both sides. Histological findings showed normal respiratory epithelium with chronic plasmacellular inflammation and eosinophilia as it is commonly seen in chronic sinusitis.

Prednisone tapering was 5 mg/day at the time of last relapse of the disease. In view of the patient's history so far and taking into account reports of complications under prednisone tapering[11–15] we regarded prednisone alone to be insufficient to prevent further incidents of neurological manifestations. We started with azathioprine 150 mg/day and continued with prednisone 70 mg/day for 1 month. Subsequent prednisone tapering was now done very slowly over a period of 6 months. Under this regimen the patient has remained free of symptoms and was able to return to work.

DISCUSSION

This case reports demonstrates the necessity for long-term immunosuppressive therapy in some cases of APMPPE in order to control recurrent meningoencephalitis. Whereas a benefit of the use of corticosteroids in APMPPE without involvement of the central nervous system cannot be clearly stated,[1] there is no doubt about the benefit of immunosuppressive therapy in cases with neurological complications.[2 11–12 16] Although extremely rare, neurological complications of APMPPE had proved to be severe[4 5 9–12 16] or even fatal.[2 15] Attempts to control neurological complications in patients with recurrences under corticoid tapering have been made with azathioprine,[4 9 14] cyclophosphamide[12 14] or mitoxantrone.[17] Considering the side-effects of all long-term immunosuppressive medication for this young adult, we chose azathioprine under which no further relapses were observed.

In our opinion, the search for and therapy of underlying infectious processes is vital in the treatment of this presumably parainfectious autoimmune disease. Concomitant inflammatory diseases of APMPPE such as Lyme disease, systemic lupus erythematodes, juvenile rheumatoid arthritis, sarcoid, Wegener's granulomatosis, schistosomiasis, adenovirus, thyroiditis, Crohn's disease, uveitis, papillitis, erythema nodosum and nephritis[5 6] have been reported. To the best of our knowledge, we are the first to describe a case of associated chronic sinusitis maxillaris.

Several authors[2 3 11–12 14] reported an associated cerebral vasculitis, which could not be shown by intracerebral MR-angiography in our patient. In general, we agree with other authors,[4 14 15] who suggest that an MRI should be performed in any APMPPE patient presenting with neurological symptoms.

Clearly, this case report highlights the potential malignancy of APMPPE and the urgency of aggressive treatment in some cases.

Learning points

- APMPPE is a potentially harmful disease.
- Cerebral MRI should be performed in APMPPE patients with neurological symptoms.
- Prednisone tapering should be done very carefully and long-term immunosuppressive therapy might be necessary.
- APMPPE might be – among other infectious causes – triggered by sinusitis maxillaries.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Fiore T,** Iaccheri B, Androudi S, *et al*. Acute posterior multifocal placoid pigment epitheliopathy: outcome and visual prognosis. *Retina (Philadelphia, Pa)* 2009;**29**:994–1001.
2. **de Vries JJ,** den Dunnen WF, Timmerman EA, *et al*. Acute posterior multifocal placoid pigment epitheliopathy with cerebral vasculitis: a multisystem granulomatous disease. *Arch Ophthalmol* 2006;**124**:910–13.
3. **Prokosch V,** Becker H, Thanos S, *et al*. Acute posterior multifocal placoid pigment epitheliopathy with concurrent cerebral vasculitis and sarcoidosis. *Graefes Arch Clin Exp Ophthalmol* 2010;**248**:151–2.
4. **Stoll G,** Reiners K, Schwartz A, *et al*. Acute posterior multifocal placoid pigment epitheliopathy with cerebral involvement. *J Neurol Neurosurg Psychiatr* 1991;**54**:77–9.
5. **Comu S,** Verstraeten T, Rinkoff JS, *et al*. Neurological manifestations of acute posterior multifocal placoid pigment epitheliopathy. *Stroke* 1996;**27**:996–1001.
6. **Hsu CT,** Harlan JB, Goldberg MF, *et al*. Acute posterior multifocal placoid pigment epitheliopathy associated with a systemic necrotizing vasculitis. *Retina (Philadelphia, Pa)* 2003;**23**:64–8.
7. **Mendrinos E,** Baglivo E. Acute posterior multifocal placoid pigment epitheliopathy following influenza vaccination. *Eye (Lond)* 2010;**24**:180–1.
8. **Vedantham V,** Ramasamy K. Atypical manifestations of acute posterior multifocal placoid pigment epitheliopathy. *Indian J Ophthalmol* 2006;**54**:49–52.
9. **Bewermeyer H,** Nelles G, Huber M, *et al*. Pontine infarction in acute posterior multifocal placoid pigment epitheliopathy. *J Neurol* 1993;**241**:22–6.
10. **Bugnone AN,** Hartker F, Shapiro M, *et al*. Acute and chronic brain infarcts on MR imaging in a 20-year-old woman with acute posterior multifocal placoid pigment epitheliopathy. *AJNR Am J Neuroradiol* 2006;**27**:67–9.
11. **Weinstein JM,** Bresnick GH, Bell CL, *et al*. Acute posterior multifocal placoid pigment epitheliopathy associated with cerebral vasculitis. *J Clin Neuroophthalmol* 1988;**8**:195–201.

12. **O'Halloran HS,** Berger JR, Lee WB, *et al*. Acute multifocal placoid pigment epitheliopathy and central nervous system involvement: nine new cases and a review of the literature. *Ophthalmology* 2001;**108**:861–8.
13. **Gibelalde A,** Bidaguren A, Ostolaza JI, *et al*. [Pigmentary epitheliopathy multifocal acute placoid associated with paralysis of VI cranial par]. *Arch Soc Esp Oftalmol* 2009;**84**:159–62.
14. **Luneau K,** Newman NJ, Srivastava S, *et al*. A case of acute posterior multifocal placoid pigment epitheliopathy with recurrent stroke. *J Neuroophthalmol* 2009;**29**:111–18.
15. **Hammer ME,** Grizzard WS, Travies D. Death associated with acute, multifocal, placoid pigment epitheliopathy. Case report. *Arch Ophthalmol* 1989;**107**:170–1.
16. **Jaramillo A,** Gaete G, Romero P, *et al*. Acute pontine infarct in a 16-year-old man with acute posterior multifocal placoid pigment epitheliopathy. A case report. *J Stroke Cerebrovasc Dis* 2009;**18**:164–6.
17. **Massé H,** Guyomard JL, Baudet D, *et al*. Mitoxantrone therapy for acute posterior multifocal placoid pigment epitheliopathy with cerebral vasculitis. *Case Report Med* 2009;**2009**:481512.