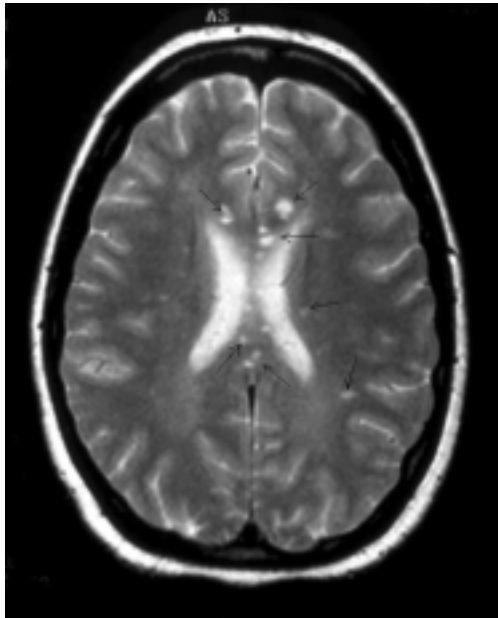
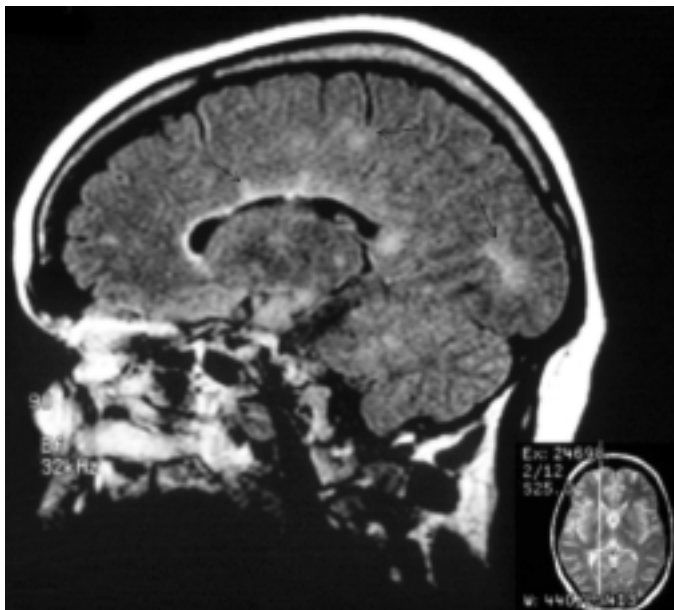


NEUROLOGICAL RARITIES

A blinding headache



(a)



(b)

Figure 1 Multiple small high signal lesions on (a) T2-weighted and (b) FLAIR MR images, involving mainly the fronto-parietal white matter, corpus callosum and cerebellum.

THE STORY

A 23-year-old woman, who had just completed a degree in adventure tourism at university and started working as a video librarian, presented with a 6-week history of a throbbing bi-frontal headache, nausea, photophobia and increasing confusion. She had been getting lost even in her own flat and was found outside wandering about aimlessly. Her family commented that her gait was unsteady and her speech had become slurred. The patient's past medical history was unremarkable apart from mild asthma treated with inhalers when required. There was no history of foreign travel, recent illness, vaccinations, alcohol or drug misuse.

THE EXAMINATION AND INVESTIGATIONS

On admission she was found to be encephalopathic with drowsiness, cognitive impairment [Mini Mental State Examination (MMSE) = 13/30] and cerebellar signs, in particular lateral gaze evoked nystagmus, dysarthria and an ataxic gait. She had myoclonus. Initial blood tests, including ESR, CRP, auto-immune profile, ANCA, dsDNA and complement levels were all normal or negative. Her MRI showed multiple small high signal lesions on T2-weighted and FLAIR images, involving mainly the fronto-parietal white matter, corpus callosum and cerebellum (Fig. 1), thought to be compatible with demyelination. MR angiography and venography were normal. Cerebrospinal fluid (CSF) examination revealed no cells but a raised protein of 3.6 g/L and no oligoclonal bands. At this stage the working diagnosis was that of acute disseminated encephalomyelitis (ADEM).

THE TREATMENT

The patient received a 3-day course of intravenous methylprednisolone, 1 g/day. Within a few days of starting treatment there was marked improvement. Her conscious level became normal, the headaches resolved and her ataxia lessened. She was discharged on a course of oral steroids reducing over 3 weeks. When seen in outpatients a month later she had continued to improve. Note was made for the first time that she complained of mild hearing problems.

THE RECURRENCE

She re-presented 2 months following her discharge with very similar symptoms, in particular recurrence of headaches, nausea and vomiting and increasing unsteadiness. Examination showed

e falling on deaf ears (Susac's syndrome)

bilateral asymmetrical sensory-neural deafness, bilateral cerebellar signs and slurring dysarthria. A repeat MR scan again revealed multiple high signal lesions on T2-weighted and FLAIR sequences. Some lesions had decreased in size but additional new lesions were noted. A repeat CSF showed a protein level of 1.2 g/L with matched CSF and serum oligoclonal bands. Some of the blood tests including a vasculitic screen were repeated with normal results. She again responded to a further course of intravenous methylprednisolone and was discharged on a more slowly reducing course of oral steroids.

ANOTHER RECURRENCE

Six weeks later, following the reduction of prednisolone from 20 to 10 mg daily, she relapsed with more headaches and increasing ataxia. Audiometry had shown predominantly low tone hearing loss (Fig. 2) and she had been fitted with a hearing aid. On this occasion, examination showed additional variable visual field deficit affecting particularly the peripheral field of the right eye. Her MMSE was 24/30. A repeat MRI was unchanged and her CSF showed 1.4 g/L protein with negative oligoclonal bands. A thrombophilia screen, serum ACE and white cell enzymes were normal.

THE DIAGNOSIS

Until this point the diagnosis had remained obscure. In a young women presenting with a relapsing–remitting neurological disorder and in whom the MRI appearances and response to steroids were compatible with demyelination, we thought that multiphasic disseminated

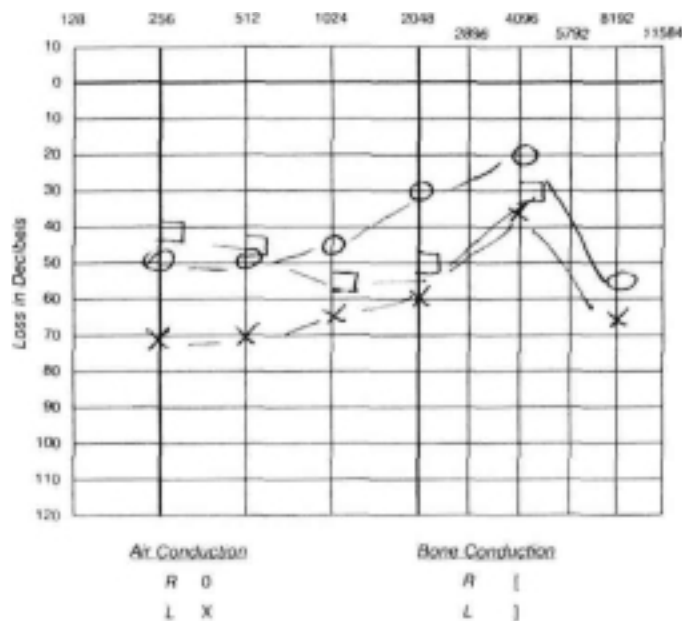


Figure 2 Audiometry showing low tone hearing loss.

encephalomyelitis (MDEM) was the most likely diagnosis. Despite the MRI findings, a diagnosis of multiple sclerosis was thought to be unlikely because of her clinical presentation with headache, encephalopathy and deafness and a CSF with markedly raised protein but persistently negative oligoclonal bands (note that encephalopathy and headache are not uncommon with MDEM; Dale *et al.* 2000.)

Ophthalmologic examination provided the correct diagnosis. Visual acuity was mildly reduced to 6/12 in the right eye and was normal at 6/6 in the left eye. There was an area of retinal infarction in the upper temporal quadrant of the right fundus involving the macula (Fig. 3).

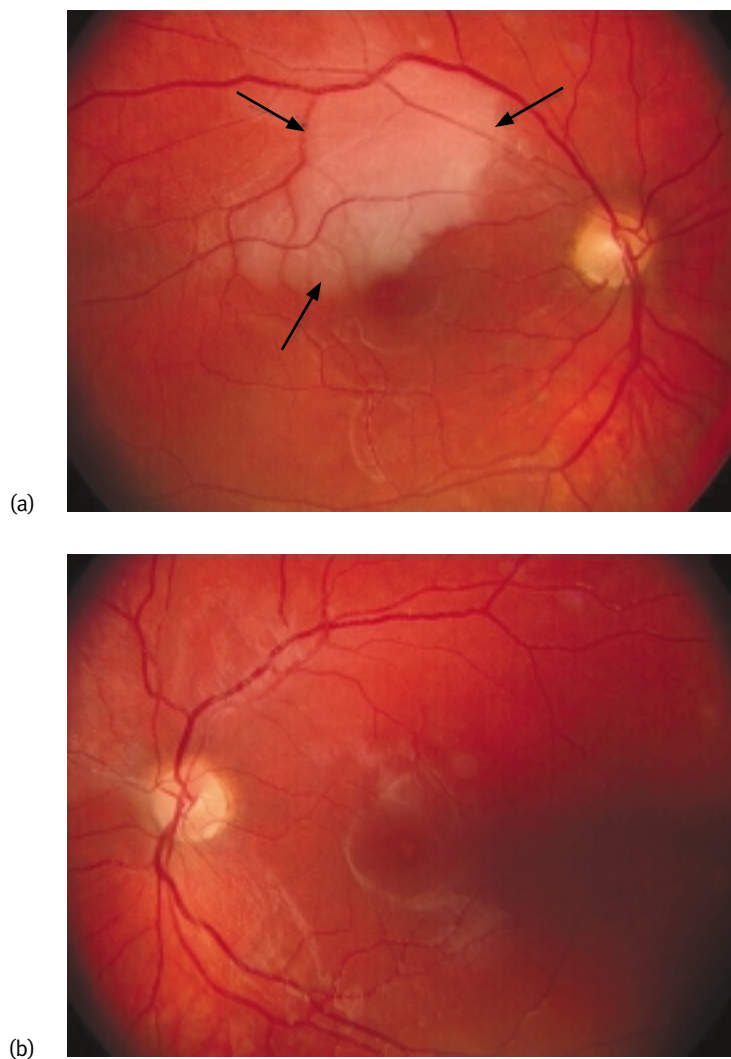


Figure 3. Retinal photographs of the patient's (a) right and (b) left fundus during the third relapse of her illness. It shows an area of retinal infarction in the upper temporal quadrant of the right fundus involving the macula (arrows). The left fundus appears normal.

Fluorescein angiography showed areas of focal arteriolar wall hyperfluorescence in both eyes (Fig. 4). These appearances indicated multifocal retinal arterial disease with retinal branch arterial occlusion in the right eye. We investigated for the possibility of emboli to the retina but an echocardiogram and carotid Doppler examination were normal. There was no evidence to suggest a systemic small-vessel vasculitis, such as systemic lupus erythematosus, Churg–Strauss vasculitis or Goodpasture's syndrome.

SUSAC'S SYNDROME

Susac *et al.* (1979) described two women who presented with a triad of encephalopathy, sensory-neural hearing loss and retinal branch artery occlusions. Different terms have subsequently been suggested for this syndrome such as RED-M (retinopathy, encephalopathy, deafness associated microangiopathy; Nicolle & McLachlan 1991) and SICRET (small infarctions of cochlear, retinal, and encephalic tissue; Schwitter *et al.* 1992) but most authors now refer to this entity as Susac's syndrome. The under-

lying pathology is a non-inflammatory microangiopathy causing small infarcts in the brain, cochlea and retina. To date, more than 100 cases have been reported in the literature. The disease is more common in young women in the third and fourth decade but male (Saw *et al.* 2000) and older patients (Barker *et al.* 1999) have been described. Not all elements of the triad are necessarily present at the beginning of the illness. The disease runs a relapsing–remitting course and tends to be self-limiting although relapse after a long period of remission has been reported (Petty *et al.* 2001).

The encephalopathy usually evolves subacutely. Headache is often a prodromal symptom that can occur several months before the development of the encephalopathy (Papo *et al.* 1998). Associated features are psychiatric abnormalities, seizures and myoclonus. The hearing loss is predominantly of low-to-medium tone, suggestive of cochlear apical infarction due to occlusion of the cochlear end arterioles (Monteiro *et al.* 1985). The hearing loss is often acute, bilateral and asymmetrical. Prominent jerk nystagmus can be present, which might be related to microinfarction of the membranous labyrinth (Susac 1994). Branch retinal artery occlusions can vary in degree and visual loss depends on their position. Even severe visual loss can be missed if the patient is profoundly encephalopathic. Fluorescein angiography shows focal arteriolar wall hyperfluorescence, indicating damage to the blood–retinal barrier. This appearance may also be caused by endothelial damage from retinal emboli or retinal arteriolar involvement in a vasculitis such as in systemic lupus erythematosus, Churg–Strauss or Goodpasture's syndrome. In Susac's syndrome the hyperfluorescence occurs without occlusion of the relevant arteriole, which is not a feature of embolism (O'Halloran *et al.* 1998).

Laboratory investigations in particular for vasculitis, autoimmune disease, coagulopathy and infectious diseases are normal. The EEG is diffusely slow during the encephalopathic phase. MRI shows multiple small high signal lesions on T2-weighted images, which represent small infarcts affecting both white and grey matter with predilection for the corpus callosum (O'Halloran *et al.* 1998). These lesions can enhance in the acute and subacute stage. The imaging appearances are often suggestive of multiple sclerosis or other demyelinating diseases. The CSF invariably has a high protein content with normal cells or a minimal pleocytosis and there are no IgG

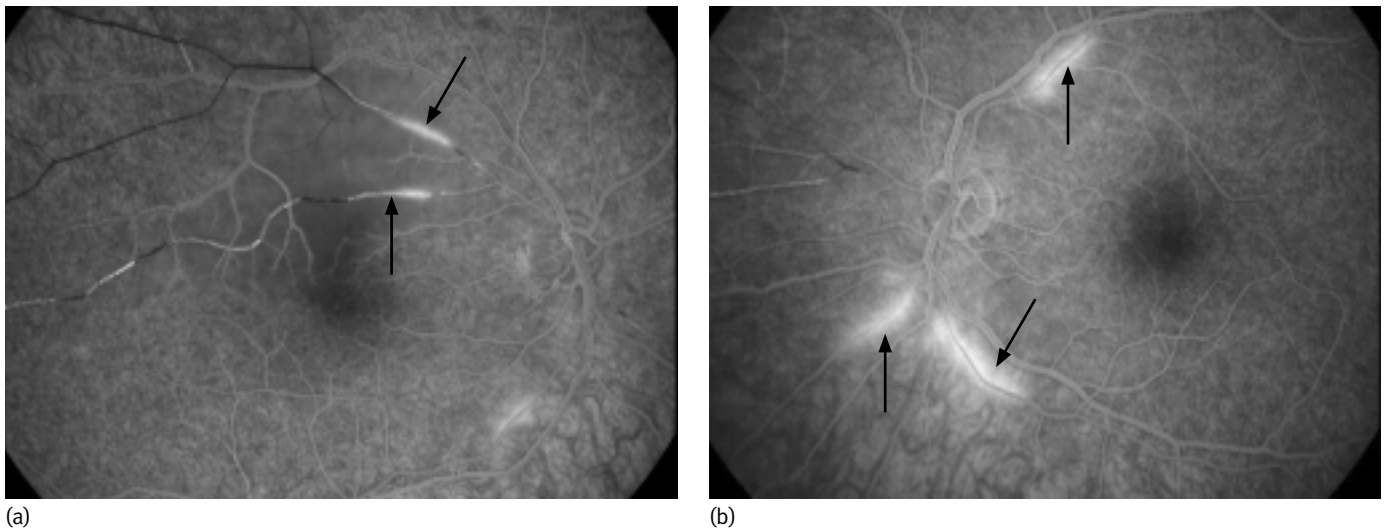


Figure 4 Fluorescein angiography of the (a) right and (b) left eye. There are multiple areas (arrows) of focal arteriolar wall hyperfluorescence in both eyes.

oligoclonal bands (O'Halloran *et al.* 1998). Histopathological studies from brain biopsies have shown microinfarcts due to arteriolar occlusion, the exact mechanism of which is unclear (Susac *et al.* 1979; O'Halloran *et al.* 1998). No vasculitis or fibrinoid necrosis has been demonstrated.

Treatment is difficult because of the rarity of this disease and there are no randomised trials. Furthermore, the self-limiting nature and spontaneous resolution of symptoms make it difficult to be certain how much of the improvement seen is due to the treatment. Management to date has included immune-suppression with steroids, cyclophosphamide and azathioprine (O'Halloran *et al.* 1998; Petty *et al.* 2001). Anti-thrombotic measures with warfarin anticoagulation have been used (Gordon *et al.* 1991). There are case reports of the use of antiplatelet agents and antivasospastic agents such as nimodipine (Schwitter *et al.* 1992; Wildemann *et al.* 1996). Plasma-exchange and intravenous immunoglobulin have also been used (Papeix *et al.* 2000; Petty *et al.* 2001). In our case the patient was maintained on a high dose of oral steroids (60 mg Prednisolone daily) for several weeks and the dose was then gradually reduced and finally stopped. There has been no further relapse since her last admission.

LEARNING POINTS

This case highlights a number of clinical points. Firstly, accurate visual assessment is a vital part of the assessment of neurological patients but may be difficult particularly if the patient is encephalopathic. Early involvement of neuro-ophthalmology colleagues may be extremely helpful. Secondly, there is a broad differential diagnosis

for brain MR lesions typical of MS. Other diagnoses must be considered when the clinical features are in any way atypical.

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