NEUROLOGICAL RARITIES

A blinding headache

THE STORY
A 23-year-old women, 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
bilateral asymmetrical sensory-neural deafness, bilateral cerebellar signs and slurring dysarthria. A repeat MRI 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 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).
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

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 & M Clachlan 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
Secondly, there is a broad differential diagnosis which the ophthalmology colleagues may be extremely helpful. Early involvement of neuro-ophtalmic services may be difficult particularly if the patient is encephalopathic. Early involvement of neuro-ophthalmology colleagues may be extremely helpful. Early involvement of neuro-ophtalmology colleagues may be extremely helpful.

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 ascertain 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 MRI lesion typical of MS. Other diagnoses must be considered when the clinical features are in any way atypical.

**REFERENCES**


