

## SHORT REPORT

## Multiphasic disseminated encephalomyelitis presenting as alternating hemiplegia

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### Abstract

**Two cases of alternating hemiparesis are reported, one in a black Sudanese woman, the other in a Saudi man, who had two episodes of alternating hemiparesis separated in time by six and three years respectively. Based on the typical appearance of the MRI and the results of brain biopsy, the diagnosis of multiphasic disseminated encephalomyelitis was made rather than that of multiple sclerosis. This entity is also differentiated from recurrent disseminated encephalomyelitis, where the relapses are symptomatically stereotyped although the appearance of the MRI is similar and in which new lesions do not occur. Because of the unusual appearance of these MRI lesions, brain biopsy is often performed but recognising their relevance should obviate that need.**

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Hemiparesis in a young adult is a diagnostic challenge because of the many potential causes. In developing countries, hemiparesis in young adults is related to pregnancy, childbirth, rheumatic heart disease, or infections<sup>1</sup> as opposed to that in western countries, where the predominant causes are atherosclerosis, cardiogenic embolism, blood disorders, and non-atherosclerosis vasculopathies.<sup>2</sup> Hemiparesis involving the face is an uncommon presentation of primary demyelinating disorders of the CNS and may cause diagnostic confusion, especially if the disease is monophasic or if the relapse rate is low. It is rare in definite multiple sclerosis.<sup>3</sup> In low risk areas for multiple sclerosis, as in high risk countries, other forms of primary demyelinating diseases are seen, in particular postinfectious disseminated encephalomyelitis (DEM).<sup>4</sup>

We report two cases of alternating hemiparesis in which stereotactic brain biopsy showed primary demyelination. It was impossible to differentiate the illness from multiple sclerosis on the basis of the history, the CSF examination, and evoked potential studies

but the MRI of the brain favoured the diagnosis of multiphasic disseminated encephalomyelitis (MDEM).

### Case reports

#### CASE 1

A 32 year old black Sudanese woman was admitted to the hospital because of sudden dysarthria. On the next day, she had a right hemiparesis without impairment of consciousness or seizures. Six years before, while living in the Sudan, she had suddenly had left sided hemiparesis and homonymous hemianopia. The hemiplegia recovered completely in one week, whereas the hemianopia persisted. She was not diabetic or hypertensive, and there was no history of cardiac disease or hyperlipidaemia. Systemic examination was normal. The neurological examination showed normal intellectual function, but she had slurred speech without aphasia. Other findings included left homonymous hemianopia, right upper motor neuron facial nerve palsy, and slight deviation of the tongue to the right without wasting or fasciculations. She had upper motor neuron weakness of the right upper and lower limbs, with hyperreflexia and Babinski sign. There was no limb ataxia or disequilibrium and all modalities of sensations were intact. She had a right hemiplegic gait.

Complete blood count, sedimentation rate, blood urea nitrogen, and serum electrolytes, liver function tests, and autoimmune screen for connective tissue disease, including lupus anticoagulant and phospholipid antibodies, were all normal. Sick cell screen was negative. The serum titres for brucella, syphilis, and hepatitis B were negative as was the tuberculin skin test. A chest radiograph, ECG, and transesophageal echocardiogram were normal. Doppler examination of the neck vessels and four vessel cerebral arteriography were normal. The CSF showed 2 white blood cells/mm<sup>3</sup>, total protein 0.26 g/l, glucose 3 mmol/l, and an IgG index of 0.6. No oligoclonal bands were seen. Tests for measles, rubella, mumps, Epstein-Barr, and herpes simplex antibodies and for the presence of fungal antigens were negative. An EEG showed focal slowing in the left frontoparietal and right occipital regions. Pattern shift visual, somatosensory, and brainstem auditory

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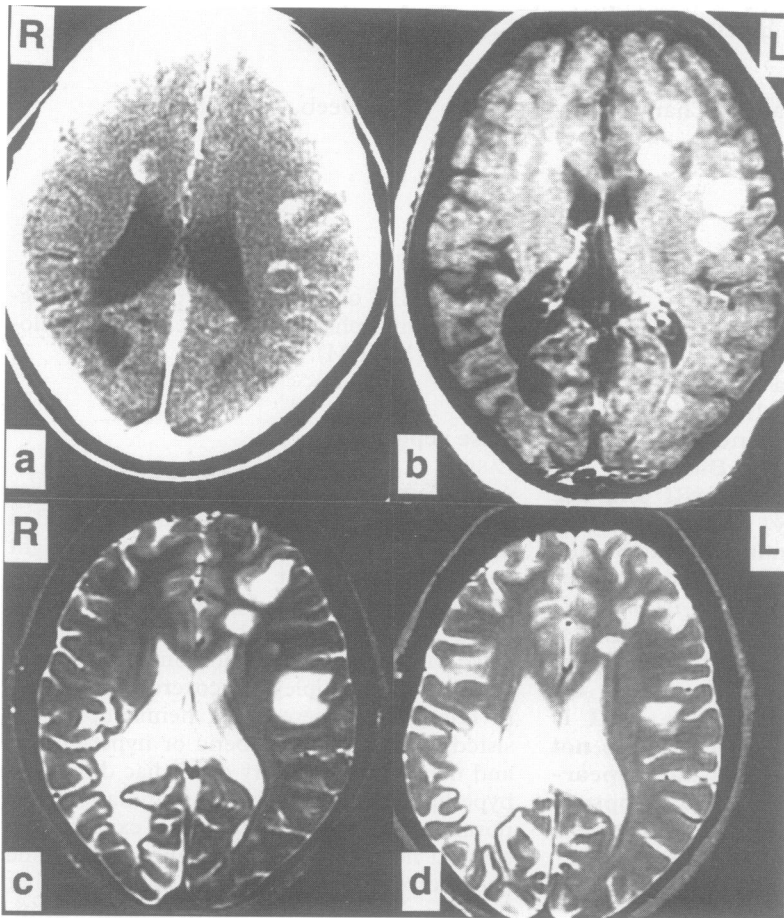
evoked potentials were normal. Computed tomography and MRI of the brain showed bilateral multiple, scattered enhancing nodular lesions in the white matter (fig 1a-c).

The diagnoses of multiple tuberculomas or

metastasis were initially considered, but brain biopsy showed inflammatory primary demyelination (fig 2), so a diagnosis of MDEM was made. She was given methylprednisolone (1 g intravenously daily for five days), followed by a course of tapering oral steroids. After one week, the hemiparesis started to improve and the dysarthria disappeared after 10 days. Four weeks later, the patient had fully recovered. The hemianopia from her previous episode had remained unchanged. The steroids were discontinued at the end of six weeks. Repeat MRI eight weeks after the onset of her illness showed considerable improvement in the white matter lesions (fig 1d), which no longer enhanced after injection of gadolinium.

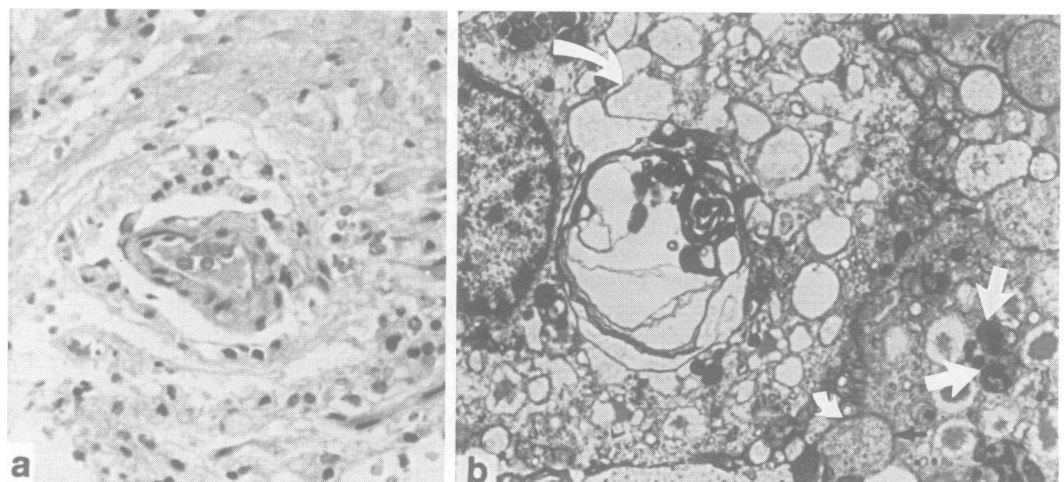
#### CASE 2

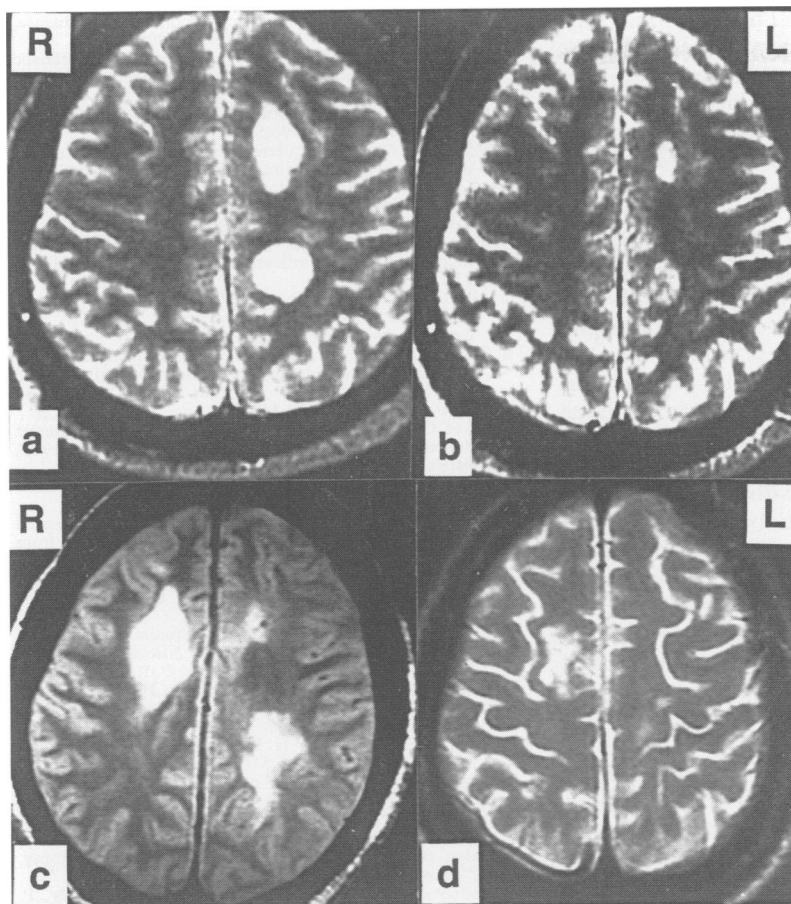
In June 1990, a previously healthy 29 year old Saudi man had acute right leg weakness, which progressed over a week to involve his right arm and face as well. He also noted numbness of his right leg. He complained of frontal headache, difficulty in concentrating, and mild weight loss. He had no seizures, fever, diplopia, or urinary difficulties. The neurological examination on admission showed mild dysnomia and right spastic hemiparesis affecting the leg more than the arm and face. There was subjective diminution of pain, temperature, and vibratory sensations. A brain MRI showed two large lesions in the left subcortical white matter and a smaller one posteriorly on the left (fig 3a). There was little adjacent oedema and no mass effect. These lesions enhanced poorly after gadolinium injection. A left internal carotid arteriogram, an EEG, and visual and somatosensory evoked potentials were negative. Blood count, sedimentation rate, electrolytes, autoimmune screen for vasculitis, serological tests for borrelia, brucella, syphilis, cryptococcus, toxoplasma, and HIV were all negative, as were the tuberculin skin test, chest radiograph, ECG, and abdominal ultrasound. A CSF examination showed 6 white blood cells/mm<sup>3</sup>, a total protein of 0.37 g/l, a raised IgG index of 1.64 (normal <0.7), IgG synthesis of 19.1 mg/24 hours (normal 0-3.5), and three oligoclonal bands.



**Figure 1** Case 1 (a) Contrast enhanced brain CT: multiple enhancing nodules in both cerebral hemispheres. There is dilatation of the atrium of the right lateral ventricle associated with a hypodense area in the parietotemporal region on the right characteristic of an old lesion. (b) MRI T1 weighted image after gadolinium injection showing five enhancing nodules in the left subcortical white matter. There is a large area of low intensity in the right parieto-occipital region indicating the site of an old, inactive lesion, which probably occurred six years previously when the patient developed left hemianopia and hemiparesis. (c) T2 weighted MRI: multifocal high signal intensity lesions in the white matter of both hemispheres. One of the lesions encroaches on the cortex on the left side. There is extensive white matter high signal intensity in the right parieto-occipital region. Note the sparing of the corpus callosum and the absence of periventricular lesions. (d) T2 weighted MRI eight weeks later: there has been a considerable reduction of the size of the left sided lesions while the one on the right remains unchanged.

**Figure 2** Case 1: brain biopsy (a) Light microscopy. Perivascular oedema, inflammation, and demyelination (haematoxylin-eosin). (b) Electronmicrograph showing complete disorganisation of the myelin sheath (white curved arrow on top) and bare axons (white curved arrow and straight black arrow at the bottom). Many macrophages contain myelin bodies within their cytoplasm (two straight white arrows at the bottom right). No viral particles were seen.





**Figure 3** Case 2 (a) T2 weighted MRI: Two very large left hemispheric lesions without mass effect. (b) T2 weighted MRI four months later. Pronounced regression of both lesions. (c) T2 weighted MRI three years later at time of second episode. Large, new lesion in the right frontal area. Note that the previous, left posterior lesion has become much larger and seems to have been reactivated. (d) T2 weighted MRI two months later. Pronounced regression of all lesions.

All CSF cultures and antiviral titres were negative. A left frontal brain biopsy was performed which showed perivascular infiltrates and demyelination, numerous foamy macrophages, and pronounced astrocytic proliferation of the white matter. Neither necrosis nor inclusion bodies were present. The histological diagnosis was primary demyelinating disorder. The patient improved without treatment and had completely recovered four months after onset. He was able to complete his studies and start work as an engineer. A follow up examination six months later was normal except for mild right hyperreflexia. A repeat MRI (fig 3b) showed no new lesions and considerable reduction in the size of the original ones. He remained free of symptoms until January 1994 when, two weeks after a flu like illness, he had rapidly progressive headache, impaired concentration, and left sided weakness. He was emotionally labile and had normal optic discs, exaggerated jaw and limb reflexes, and moderately severe left sided hemiparesis. The MRI showed a new very large lesion in the anterior right subcortical white matter, and the two old lesions on the left; the posterior one was considerably larger than it had been on the previous MRI three years earlier (fig 3c). The new lesion

enhanced faintly after gadolinium injection. The patient's weakness improved after treatment with intravenous methylprednisolone. A follow up MRI obtained three months later showed considerable regression of all the lesions (fig 3d).

### Discussion

Classically, acute disseminated encephalomyelitis (ADEM) is a monophasic neurological syndrome that may occur after vaccination against various viruses and after many viral infections.<sup>4-7</sup> Repeated episodes of postinfectious or postvaccinal neurological syndromes are rare.<sup>8,9</sup> Poser<sup>10</sup> has proposed that disseminated encephalomyelitis (DEM) with multiple episodes be classified into two types. In the first one, an initial episode of ADEM, from which there is complete or partial recovery, is followed by recurrences that are characteristically stereotyped—that is, the symptoms are always the same, although the complete original syndrome is not necessarily present. This is called recurrent DEM (RDEM). RDEM must not be confused with the pseudorecurrences seen in patients with steroid dependent ADEM when treatment is stopped. In the other type, which is represented in these two patients, there are two or more separate acute episodes that differ in clinical presentation, and that is termed multiphasic DEM (MDEM). Both cases of Poser *et al*<sup>5</sup> are examples of MDEM; MDEM is extremely difficult to differentiate from multiple sclerosis on purely clinical grounds, but it is important to do so since the prognosis of MDEM is much better.

In patients with DEM, the CSF most commonly shows a moderate pleocytosis and increase in total protein, although both may be very high. IgG is often increased but oligoclonal bands are rare. Oligoclonal bands never disappear in multiple sclerosis but may do so in DEM, and this is important in differentiating multiple sclerosis from both MDEM and RDEM.<sup>11</sup> The MRI in DEM is often abnormal and has special characteristics.<sup>9-11-14</sup> Although in some cases, the abnormalities cannot be distinguished from those of multiple sclerosis.<sup>15</sup> Unlike those in multiple sclerosis, the lesions are extensive, often follow the outline of the cortical ribbon, or may consist, as in these two cases, of very large, globular areas of increased signal intensity that do not produce a mass effect. They are often mistaken for neoplasms or abscesses. The cerebellum and cortex are often involved, as are occasionally the thalamus or the basal ganglia. The corpus callosum is usually not affected and the periventricular distribution of the lesions is not as constant.<sup>9,11</sup> An important differential point between MDEM and RDEM is that new MRI lesions invariably occur in the first but not in the second. In MDEM, the lesions tend to be of varying age, active lesions can be shown by contrast enhancement on T1 weighted image, whereas old inactive lesions appear as high signal intensities on T2 weighted image

as shown in our patients. The large lobar high intensity lesions, which may be seen in DEM, are never seen in multiple sclerosis.

The pathology in DEM is similar to that of multiple sclerosis in showing perivascular oedema, inflammation, and demyelination. The degree of inflammatory reaction will obviously depend on the time elapsed between the onset of the illness and the time of the biopsy. Because the histological differentiation between all types of DEM and multiple sclerosis is based on the topography of the demyelinating process, which is essentially histologically identical in both conditions, it cannot be dependably made on tissue obtained by means of stereotactic needle brain biopsy. In most instances, the characteristic MRI coupled with the history of recurrences, or of a multiphasic illness, mitigates the need for brain biopsy. Sometimes misunderstanding the diagnostic importance of the characteristic MRI appearance of DEM coupled with the results of needle brain biopsy may lead to the erroneous diagnosis of multiple sclerosis.<sup>16 17</sup>

As well as the distinctive MRI image, another consideration, albeit a minor one, made us veer away from the diagnosis of multiple sclerosis in case 1: our patient was a black African, in whom the disease is extremely rare, living in Saudi Arabia, an area of low multiple sclerosis incidence.<sup>18</sup>

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