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MR brain scanning in patients with vasculitis: differentiation from multiple sclerosis

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Summary. We performed MR (magnetic resonance) brain imaging on 24 patients with a systemic vasculitis. MRI proved to be a sensitive method for detecting brain lesions (clinically silent or manifest) in these patients. The most frequent abnormalities were periventricular lesions seen in 12 cases. Such changes are not specific for vascular disease, and are often seen in multiple sclerosis. However, additional changes were commonly seen which suggested the correct diagnosis.

Key words: Magnetic resonance imaging - Systemic lupus erythematosus - Behcet's disease

MRI (magnetic resonance imaging) has proved sensitive in the detection of brain lesions in patients with multiple sclerosis [1] and cerebrovascular disease [2, 3]. Previous studies have noted the similarity of scan appearances in these two conditions [2], but those with cerebrovascular disease have generally been in an older age group, where MRI changes are common in the normal population [4].

The vasculitides are a heterogeneous group of disorders with a complex system of classification. They have been of interest to us because they: (1) frequently involve the central nervous system; (2) tend to affect a younger age group than those with arteriosclerotic disease; (3) frequently cause a multifocal neurological disorder similar to multiple sclerosis.

Of the various subgroups, Systemic lupus erythematosus (SLE) and Behcet's disease are of particular importance neurologically. SLE may present with optic neuritis or transverse myelitis [5, 6], and Behcet's disease with a brainstem syndrome [7], or visual symptoms compatible with optic neuritis. Such neurological presentations in young adults suggest a diagnosis of multiple sclerosis (MS). In the present study we document the frequency, nature and specificity of MRI abnormalities in such patients. We also attempt to correlate the clinical features with the scan abnormalities, and compare the MRI with CT findings.

Methods

We chose patients in whom clinical and laboratory findings led to a diagnosis of vasculitis. Cases of SLE were diagnosed where 4 of the 11 American Rheumatism Association criteria were met [8]. Behcet's disease was diagnosed where two of the three major manifestations of the condition were present (oral ulceration, genital ulceration, and iritis), in addition to one other recognised systemic feature of the disease [9]. Most patients had clinical features suggesting involvement of the central nervous system, but a few had no such evidence.

Patients were scanned on a Picker 0.5 T superconducting system. The whole brain was scanned in all cases. All had 5 or 10 mm axial contiguous slices using one or more spin echo sequences ($SE_{2000/60}$, $SE_{2000/40}$, $SE_{2000/120}$). Many patients were also scanned with an inversion recovery sequence.

Results

We scanned 24 patients aged 14 to 62 years (mean 35 years). 10 had SLE, 9 had Behcet's disease and 5 had other categories of vasculitis (2 had polyarteritis nodosa, 2 retinal vasculitis and one Cogan's syndrome). 15 had clinical evidence of central nervous

Table 1: Clinical and MRI findings in cases with evidence of CNS involvement

	Age	Sex	Diagnosis	Neurological findings	M.R.I.
1.	40	F	SLE	Confusion, myoclonus, frontal lobe features.	Multiple, frontal discrete white matter (WM) lesions.
2.	32	F	SLE	L hemiplegia, psychosis.	R middle cerebral artery infarct.
3.	25	F	SLE	Seizures.	L anterior cerebral infarct; smooth periventricular (PV) change; discrete R frontal WM lesions.
4.	50	F	SLE	Vertigo, R hemisensory loss lasting 24 h.	Lesions R cerebellar vermis and hemisphere, R & L parietal lobes.
5.	41	F	SLE	Transient episodes of memory loss and facial numbness. R optic neuritis.	Focal cortical atrophy occipital lobes; irregular PV changes (body, frontal horn of lateral ventricles).
6.	40	M	Behcet's	Acute brainstem syndrome (see text).	Lesions L pons; R midbrain; R optic radiation/int. capsule; R putamen/int. capsule; L frontal horn.
7.	40	F	Behcet's	Transient episode of vertigo and ataxia.	Irregular PV changes; discrete L parietal WM lesions.
8.	44	M	Polyarteritis nodosa.	R hemiparesis.	Multiple deep WM and peripheral cortical lesions.
9.	22	M	Polyarteritis nodosa.	Cerebellar ataxia, extensor plantars.	Multiple, mild, irregular PV changes.
10.	25	F	Unclassified	R hemiparesis and sensory loss including face.	Discrete lesions L and R frontal and posterior parietal WM.
11.	37	F	Behcet's	Subacute transverse myelopathy (T2).	Multiple, mild, irregular PV changes.
12.	25	F	Behcet's	Recurrent meningitis; thoracic cord lesion.	Normal.
13.	37	F	Behcet's	Low thoracic cord lesion.	Normal.
14.	14	M	SLE	Subacute myelopathy.	Normal.
15.	64	F	SLE	Bilateral ischaemic optic neuropathy.	Irregular PV changes; lesions R globus pallidus.

Table 2: MRI abnormalities in the patients without CNS features.

	Age	Sex	Diagnosis	MRI
16.	64	F	Cogan's syndrome	Extensive, irregular PV changes; several discrete cerebral and cerebellar WM lesions.
17.	40	F	Behcet's	Multiple, mild, irregular PV changes.
18.	12	F	Behcet's	Multiple, mild, irregular PV changes.
19.	16	F	SLE	PV lesion body of L lateral ventricle.

system (CNS) involvement (Table 1). In 10, the clinical syndrome indicated involvement of the brain; in 4, the spinal cord; and in one, the optic nerves. 9 cases did not have clinical evidence of CNS involvement.

The 16 patients who had abnormal brain scans included all 10 with clinical evidence of a brain syndrome, but only 1 of the 4 with a spinal cord syndrome. 7 of the 10 with clinically manifest brain disease had lesions in a site appropriate to the clinical syndrome (Table 1).

4 of the 9 patients without clinical CNS features had an abnormal scan (Table 2). Asymptomatic lesions were revealed by MRI in 14.

The distribution of visible abnormalities seen was as follows: periventricular, around the lateral ventricles, in 12; cerebral hemisphere discrete from the ventricles in 9; cerebellar in 2; wedges in the recognisable territory of a major cerebral artery in 2; brainstem in one patient.

10 had multiple periventricular lesions (mean age 38 years). 3 of these had additional features strongly suggesting a vascular aetiology: one had evidence of infarction in the territory of the left anterior cerebral artery; one had a wedge shaped lesion in the occipital cortex suggesting infarction (Fig. 1a); and one had 2 wedge shaped areas of cortical atrophy in the occipital lobes. Of the remaining 7 patients, 4 had no additional lesions, while 3 had additional discrete lesions in the cerebral hemispheres. The changes in these 7 were of irregular contour and could not be distinguished from those

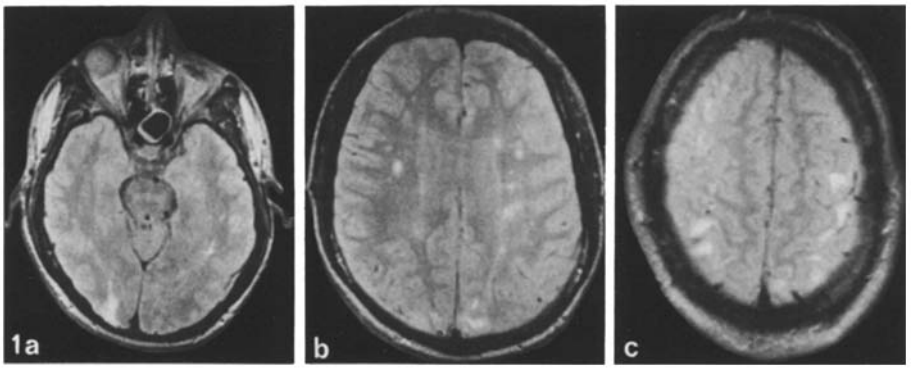

Fig. 1a–c. Polyarteritis nodosa (case 8): Axial slices at 3 different levels using a spin echo sequence ($SE_{2000/60}$). (**a**) shows a wedge shaped lesion in the occipital cortex. (**b**) shows several lesions adjacent to the body of the lateral ventricle as well as multiple discrete lesions in the cerebral white matter. (**c**) shows multiple peripheral lesions in the parietal convexity involving white and grey matter

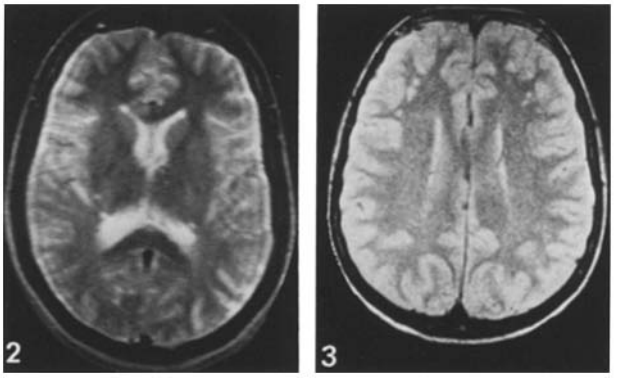

Fig. 2. Behcet's disease (case 11): spin echo sequence ($SE_{2000/120}$). There are small lesions anterior to both trigones

Fig. 3. SLE (case 1): spin echo sequence ($SE_{2000/60}$). There are multiple small discrete lesions in the frontal white matter bilaterally

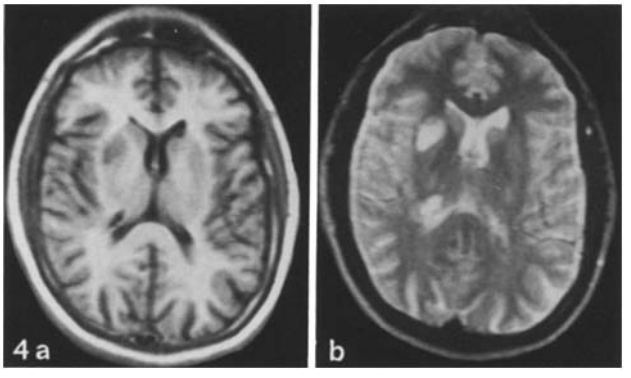

Fig. 4a, b. Behcet's disease (case 6): (**a**) inversion recovery ($IR_{2000/500/40}$) and (**b**) spin echo ($SE_{2000/120}$) sequences at the same level. There are 3 lesions: (i) adjacent to the L frontal horn; (ii) in the R putamen/internal capsule; (iii) in the R posterior internal capsule/optic radiation

seen in multiple sclerosis, although in most of the cases the periventricular changes were less extensive than that seen in established multiple sclerosis (Fig. 2).

3 patients had multiple discrete cerebral lesions alone, a finding most unusual in multiple sclerosis (Fig. 3); 2 patients had a single small periventricular lesion, one of whom had 2 additional discrete lesions (Fig. 4); and finally one patient had the signs of infarction in the territory of the right middle cerebral artery without additional lesions.

Both CT and MRI scans were performed in 6 patients. CT scanning was abnormal in 4 and MRI was abnormal in all 6. As well as showing the abnormalities seen on CT scanning, MRI showed additional abnormalities in these 4 cases.

Illustrative case reports

Case 1. SLE

A 38-year-old female presented with a peripheral symmetrical polyarthritis in 1982. A year later she developed a red maculopapular rash on her upper trunk and face along with confusion and poor memory. Antinuclear antibody was strongly positive at 1 in 2560, and DNA binding was strongly positive at 79.9%. She was treated with prednisolone. In 1986 she had an episode of pneumococcal pneumonia. After recovery she developed a confusional state with auditory and visual hallucinations, myoclonic jerks and an akinetic posture. Psychometry revealed patchy performance of tasks dependent on frontal lobe function. Verbal IQ was 92 and performance IQ 93, both low compared to estimated premorbid levels. EEG showed excess slow wave activity. CT scan was normal. MRI scan revealed several discrete lesions in the frontal white matter (Fig. 3). Her steroid treatment was increased and there was a substantial improvement in her mental state.

Case 6. Behcet's disease

A 42-year-old male presented in 1986 with an acute brainstem syndrome. In 1968 he developed oral and

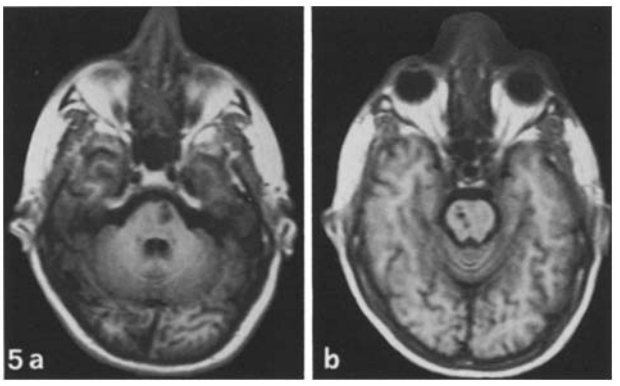

Fig. 5a, b. Behcet's disease (case 6): inversion recovery sequences ($IR_{2000/500/40}$) at the level of the pons (**a**) and midbrain (**b**), show multiple brainstem lesions

genital ulceration and arthralgia. He was diagnosed as having Behcet's disease and his symptoms were controlled by prednisolone which he stopped in 1983. There was no definite history of iritis. In 1983 he complained of tunnel vision, difficulty reading along a line, and frontal headaches. CT scan, EEG and CSF were all normal and the symptoms subsided. He presented in 1986 with a 24-hour history of dysarthria, dysphagia, unsteadiness and clumsiness of the right arm. Examination revealed dysarthria, gait ataxia, a diminished left corneal reflex, mild right facial weakness, and an absent left gag reflex. In the limbs there was a mild right hemiparesis with bilateral ataxia. Tendon reflexes were brisk and plantars flexor. ENT examination revealed several ulcers on the vocal cords. Investigations included an ESR of 40 mm/h, and C-reactive protein 70.7 mg/l (normal <10). CSF revealed 2 red cells/mm^3, 17 white cells/mm^3 (mononuclears) and protein 0.53 g/l. CT brain scan showed a lesion in the right posterior internal capsule/optic radiation. MRI scan showed this lesion plus other lesions in the left frontal horn, right putamen/internal capsule, right midbrain and left pons (Figs. 4, 5). The patient was treated with prednisolone and rapidly improved.

Case 8. Polyarteritis nodosa

A 44-year-old male gave a history of recurrent deep venous thrombosis since 1973. In 1983 he complained of headaches, poor memory and poor vision. Examination revealed nail splinter haemorrhages, a vasculitic ulcer in the right leg, nominal aphasia, constructional apraxia, right sided deafness and a severe bilateral retinal vasculitis. Renal and coeliac axis angiography revealed multiple aneurysms. Polyarteritis nodosa was diagnosed and treatment started with cyclophosphamide and prednisolone.

Two months later he had a cerebrovascular accident with right hemiparesis. Since then his main problem has been severe retinal vasculitis resulting in loss of the left eye, and severe reduction of vision on the right. A recent CT scan is normal, while an MRI scan shows multiple lesions around the lateral ventricles and throughout the cerebral hemispheres, including a number of peripheral/cortical lesions one of which was wedge-shaped (Fig. 1 a–c).

Discussion

Central nervous system manifestations are seen frequently in association with vasculitic disorders. SLE and Behcet's disease in particular often have associated neurological features. CNS involvement was described in approximately 40% of cases in two series of patients with SLE [10, 11] and in 18% of cases of Behcet's disease found in a review of the literature [12]. The clinical features often suggest multifocal central nervous system disease and the course may be relapsing and remitting. Such features occurring typically in the young adult age group suggest a diagnosis of multiple sclerosis, and in practice SLE and Behcets disease are often considered in the differential diagnosis of MS. Usually there are obvious systemic features which lead to the correct diagnosis, but in some cases the neurological features are seen in isolation. One such example is the case of SLE described by Allen et al. [13] who had a 30 year history of relapsing and remitting symptoms affecting the optic nerves, brainstem and spinal cord.

The MRI findings in MS are well described [1, 14]. Most striking are multiple periventricular lesions, which we found in 112 of 114 patients with MS [14]. Similar findings have been seen with cerebrovascular disease [2, 3], but most patients were in an older age group and suffered arteriosclerotic disease. We were therefore particularly interested then to document the MRI findings in our younger group of patients with vasculitis and to compare them with the changes seen in MS.

There have been two reports of MRI findings in SLE [15, 16]. These have reported the presence of large cerebral infarctions, multiple white matter lesions and focal grey matter changes. MRI detected more lesions than CT, though the proportionate increase in yield was less than generally found in MS. Our findings in SLE were similar to those previously reported except that we did not see the focal grey

matter abnormalities described. We know of one previous case report of cerebral MRI findings in Behcet's disease. This case had a focal brain stem lesion [17].

Although 10 patients had evidence of multiple periventricular lesions similar to those seen in MS, there were a number of features which were helpful in distinguishing the two groups. (1) The periventricular changes in vasculitis were often rather mild. In MS the periventricular changes are usually more irregular and extensive. (2) 3 patients had discrete hemisphere lesions without periventricular changes. This was not seen in any of 114 patients with clinically definite MS [14]. (3) The typical appearance of infarction in the territory of a major cerebral artery as seen in 2 of our patients with SLE clearly suggests a vascular disorder. (4) Multiple cortical lesions as seen in case 8 or areas of focal cortical atrophy as seen in case 5 are suggestive of vascular disease.

Lesions are detected on MRI by virtue of their increased water proton density and changes in the macromolecular environment of the protons. There is experimental evidence that cerebral oedema produces an increase in the MRI signal [18]. In multiple sclerosis, oedema is probably an important cause of the increased signal seen in acute plaques. Evidence from experimental and human pathological studies indicates that astrocytic gliosis, by increasing the amount of cytoplasm per unit volume of white matter, will also produce an abnormal MRI signal [14]. Gliosis probably contributes to the abnormal signal seen in chronic multiple sclerosis plaques. Neuropathological changes described in SLE and Behcet's disease include infarction, haemorrhage, loss of myelinated fibres, necrosis and gliosis [19-21]. These changes could produce an increase in tissue water content (and hence an alteration in the MRI signal) by a variety of mechanisms: oedema and cellular infiltration in acute infarction, extravasation of blood in acute haemorrhage and astrocytic gliosis in chronic infarcts.

Although only a small number of our patients had both CT and MRI scans, MRI detected more lesions and there were no lesions visible on CT that were not seen on MRI. MRI would appear to be the method of choice in imaging the brain of patients suspected of having cerebral vasculitis. Serial scanning in the future may provide an opportunity to monitor response to therapy in some cases.

In conclusion, many patients with cerebral vasculitis have white matter lesions on MRI similar to those seen in multiple sclerosis. Additional changes suggesting vascular disease aid the diagnosis in some cases. In others, it is not possible to make the distinction radiologically, and interpretation of the scan appearance must depend on the clinical context.

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