

Multiple sclerosis with clinical and radiological features of cerebral tumour

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SUMMARY Three cases of multiple sclerosis, all confirmed pathologically, are described in whom both the unusual clinical features and the CT scan appearances suggested cerebral tumours. The failure of mass effect reliably to differentiate plaques and tumours on a CT scan is stressed and the literature relating to CT scanning in multiple sclerosis is reviewed.

“Cerebral” features, notably headache, epilepsy and aphasia are recognised but uncommon in multiple sclerosis and may suggest a diagnosis of cerebral tumour.¹ Computed tomography of the head (CT scan) in multiple sclerosis has demonstrated enhancing plaques which have been said to be distinguishable from tumours by their lack of mass effect.²⁻⁶ We present three cases of “cerebral multiple sclerosis” in whom cerebral tumours were suspected

not only clinically but also from the CT scan appearances of enhancing lesions with mass effect. Pathological support for the diagnosis of multiple sclerosis was obtained in all cases.

Case reports

Case 1 A 34-year-old woman developed blurring of vision and pain in her right eye in mid-October 1977 followed, six weeks later, by progressive aphasia, acalculia and severe left temporal headache and then, on the 18 December 1977, a generalised tonic-clonic seizure. The abnormalities on examination were aphasia, acalculia, visual acuity in the right eye limited by a large central scotoma to counting fingers, a swollen right optic disc with

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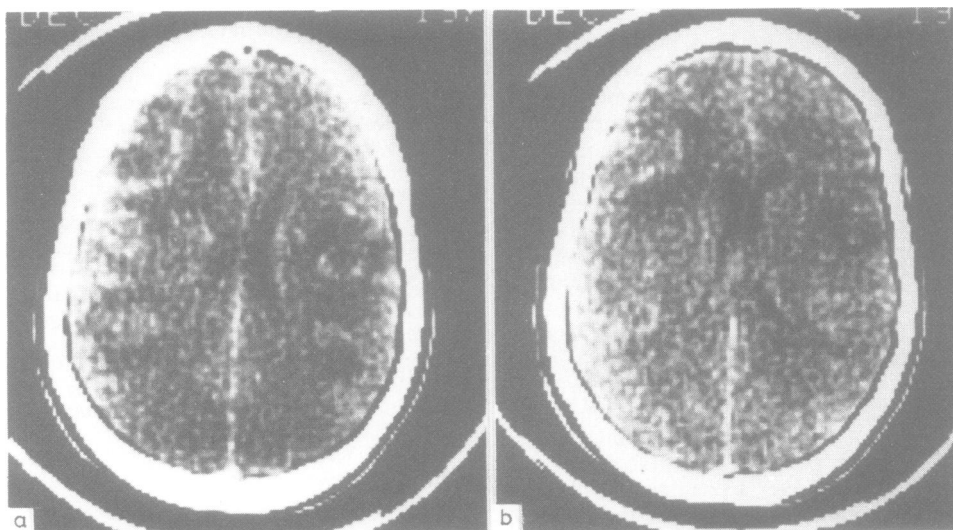


Fig 1 Case 1. 1st CT scan with contrast (December 1977) showing multiple enhancing lesions with compression of the left frontal horn and midline shift.



Fig 2 Case 1. 2nd CT scan with contrast (January 1978) showing normal appearance.

haemorrhages, an equivocal left plantar response and impaired two-point discrimination in the right hand. A CT scan with contrast (fig 1) showed two enhancing lesions in the right parietal area and one in the left frontal area with compression of the left frontal horn. The appearances were thought to represent multiple cerebral metastases. In January 1978, she was re-admitted with a left iliofemoral vein thrombosis. The neurological symptoms and signs had completely resolved and a repeat CT scan with contrast was normal (fig 2).

She remained well until July 1978 when she developed a gradual spread of sensory loss from the right groin through the whole right side of the body and the left abdomen and thigh, associated with a mild right hemiparesis. The right optic disc was pale. A third CT scan at that time showed a small area of high density in the left cerebellum. Her deterioration continued with increasing weakness of all

four limbs, confusion and poor memory. In May 1979, she had a recurrent episode of aphasia and, in July, was re-admitted in status epilepticus following an aura of aphasia. A fourth CT scan (fig 3) showed a ring enhancing low density area in the right frontal region with displacement backwards and downwards of the right frontal horn. There were other hypodense areas scattered throughout both cerebral hemispheres. By December 1979 she was wheelchair bound, depressed and considerably aphasic. She showed bilateral optic pallor and sensory and motor abnormalities in all four limbs. A fifth CT scan showed cerebral atrophy, a residual left frontal low density area and a new diffuse right frontal low density area. Her deterioration continued and she died on 21 July 1980. At necropsy, there was extensive white matter damage throughout both hemispheres with typical punched out perivenous plaques and other more extensive areas of yellowish discoloration of subcortical white matter in which there were areas of necrosis. Such abnormalities were found in both frontal lobes (a large plaque was present in the left frontal area; fig 4a), paracentral lobules, both temporal lobes, the splenium of the corpus callosum, the middle cerebellar peduncle and around the upper end of the fourth ventricle. Far fewer plaques were seen in the spinal cord. Histology of the lesions showed active demyelination with intense cellular glial reactions and perivascular lymphocytic cuffing. There was also evidence of damage to white matter by oedema around plaques resulting in microcyst formation (fig 4b).

Case 2 A 37-year-old man developed blurring of vision and pain in his left eye in July 1977 which recovered over a few weeks. In August 1977, paraesthesiae and weakness spread gradually from his feet to his neck and these also subsequently resolved completely. At the end of January 1979, he gradually developed aphasia, mild difficulty in comprehension and severe early morning throbbing

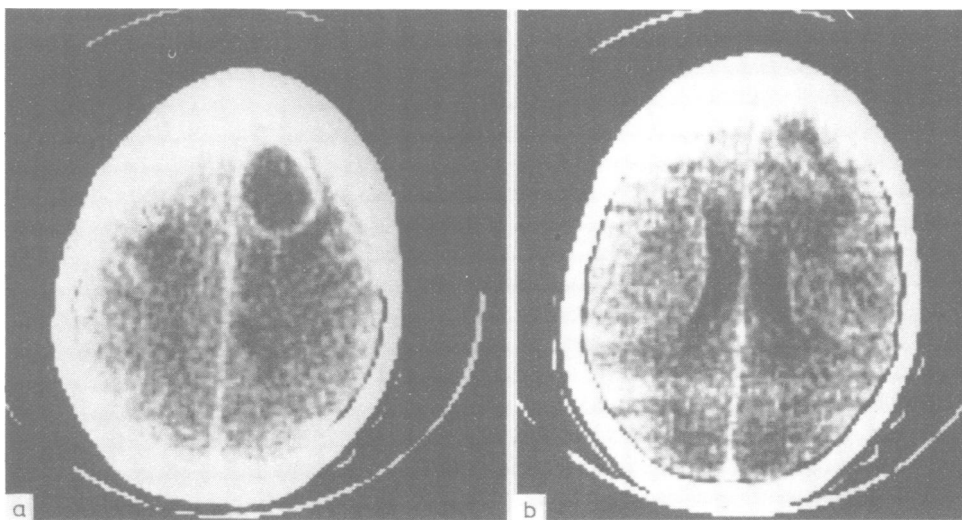


Fig 3 Case 1. 4th CT scan with contrast (July 1979) showing right frontal (a) ring-enhancing lesion with (b) displacement of the right frontal horn.



Fig 4 Case 1. (a) Low view of autopsy specimen showing horizontal section of left frontal horn and surrounding white matter, stained for myelin. There is extensive demyelination at lateral angle of ventricle extending on left (arrow) into white matter of centrum semi-ovale. $\times 1$
 (b) Plaque within subcortical white matter of left parietal lobe, showing small microcysts resulting from oedema. Phosphotungstic acid haematoxylin stain. $\times 13$

headaches and, on the 9 February 1979, had a generalised tonic-clonic seizure. Examination revealed marked non-fluent aphasia with only slight agraphia, slightly impaired corrected visual acuity on the left (6/12) and right sided reflex emphasis. A CT scan with contrast (fig 5) showed a large ring enhancing low density area in the left cerebral hemisphere with mass effect and midline shift.

Despite the previous history, the clinical and radiological findings of this illness strongly suggested a glioma so a brain biopsy was performed. This showed spongy tissue dominated by microglial phagocytes and large gemistocytic astrocytes with possibly some altered oligodendrocytes. There were no myelinated fibres but only scattered myelin debris in the presence of well preserved axons. There was

heavy perivascular cuffing by mononuclear cells. These appearances were thought to be those of an acute severe demyelinating lesion. He improved considerably. Neuropsychological examination on the 26th February, 1979 revealed only mild hesitancy of spontaneous speech but considerable impairment in a test of word fluency, slow naming and reading but normal writing and some acalculia. There was a mild comprehension deficit on the Token test but visuospatial ability and verbal and non-verbal memory were normal.

Between March and August 1979, he had four further relapses, each consisting of aphasia and right hemiparesis. In one of these, he also had recurrent severe headache and three generalised seizures, and, in a second, right focal motor seizures as well as generalised seizures. Each of these relapses was followed by dramatic recovery. Repeat CT scans performed after the onset of each of the first two of these relapses showed persistence of the left frontoparietal low density area but loss, and then some reappearance, of the enhancement. A fourth CT scan performed in the USA in August 1979 was said to show an irregular zone of lucency deep in the white matter of the left midfrontal region without mass effect and non-enhancing.

Case 3 A 24-year-old man with a four week history of dizziness and severe occipital headaches unresponsive to analgesia had two generalised seizures in one day (July 1979). He had had two episodes of enuresis in the preceding twelve months. There were no abnormal signs on examination apart from bilateral extensor plantar responses and an atrophic left optic disc associate with blindness from birth. A focal right hemisphere abnormality was seen on the electroencephalogram. A CT scan with contrast (fig 6) demonstrated a ring-enhancing lesion with mass effect in the right middle fossa which was thought to be neoplastic. Right carotid angiography showed an avascular mass in the right temporal lobe displacing the brain

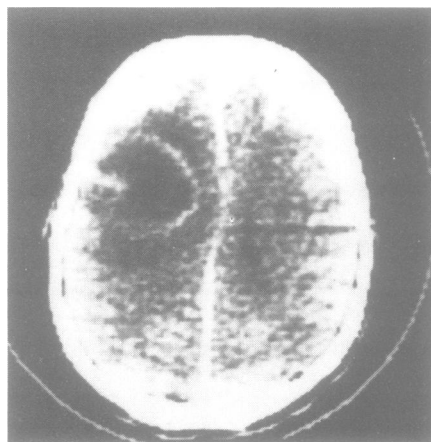


Fig 5 Case 2. 1st CT scan with contrast (February 1979) showing left hemisphere ring-enhancing lesion with midline shift.

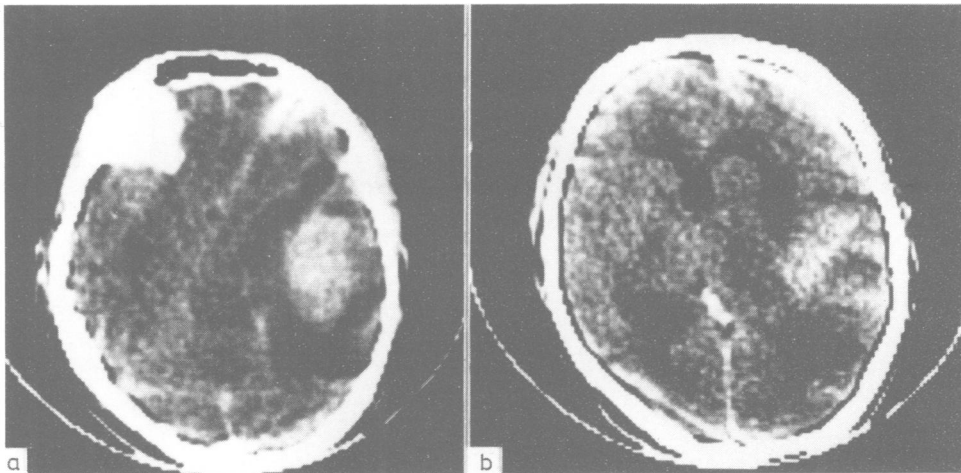


Fig 6 Case 3. 1st CT scan with contrast (July 1979) showing large right temporal enhancing lesion with considerable mass effect.

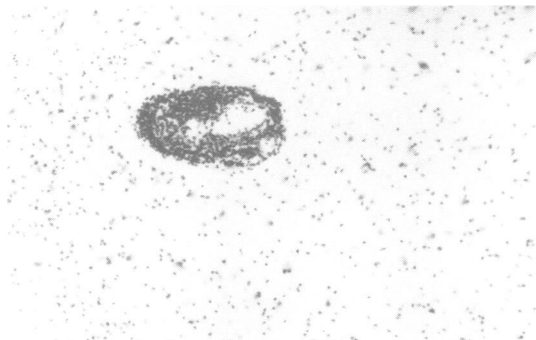


Fig 7 Case 3. Low power view of biopsy specimen stained for myelin and cells. Myelin is absent, a small vein is heavily cuffed with lymphocytes and the surrounding white matter contains reactive astrocytes, microglial cells and probable oligodendrocytes. Luxol fast blue/cresyl violet stain. $\times 60$

stem. Craniotomy and biopsy were performed. The right temporal lobe was found to be pale with widened gyri. The histology of the region showed perivascular lymphocytic cuffing and abundant microglial cells and reactive astrocytes in the white matter. There was an absence of myelin but axons were well preserved and the appearances were considered to be those of a multiple sclerosis plaque (fig 7).

He was treated with phenytoin and dexamethasone. By September 1979, all his symptoms and signs had resolved apart from those associated with his long standing amblyopia. In December 1979, he had a recurrence of tonic-clonic seizures each preceded by a visual aura. They have continued approximately monthly since then, despite anti-convulsant medication, but he has had no further relapses and developed no new neurological signs. Neuropsychological examination in March 1980 demonstrated a normal IQ

and no aphasia, alexia or agraphia. His visual memory was however impaired in the presence of normal visual perception. Further CT scans on 30 August 1979 and 15 February 1980 (fig 8) showed a residual low density area on the right with compensatory dilatation of the right lateral ventricle but the previous mass effect and contrast enhancement had completely resolved.

Discussion

The CT scan of the brain in multiple sclerosis has been reported to show three kinds of abnormality: low density areas, which are often multiple, situated particularly in periventricular areas; diffuse cortical atrophy; and regions which enhance with contrast sometimes without corresponding hypodensity on the unenhanced scan. In large series, the reported prevalence of low density areas varies between 12% and 79% (mean 29%), of atrophy between zero and 79% (mean 45%) and of enhancing lesions between 11% and 30% (mean 17%). Normal scans occur in 15% to 75% of multiple sclerosis patients (mean 37%). (Table).

The prevalence of low density areas and atrophy is highest in the clinically definite cases but a 30–50% frequency of abnormality in the early probable or latent and suspected categories has also been reported in series in which such clinical distinctions have been made.^{7–9} In general, the correlation between the sites of the lesions on the scan and the clinical features is poor and “silent” plaques are well recognised.^{6,9–15} The degree of radiological abnormality, particularly atrophy, does however correlate with the duration of the disease in most series.^{8,9,16–20} Enhancing lesions appear to be particularly associ-

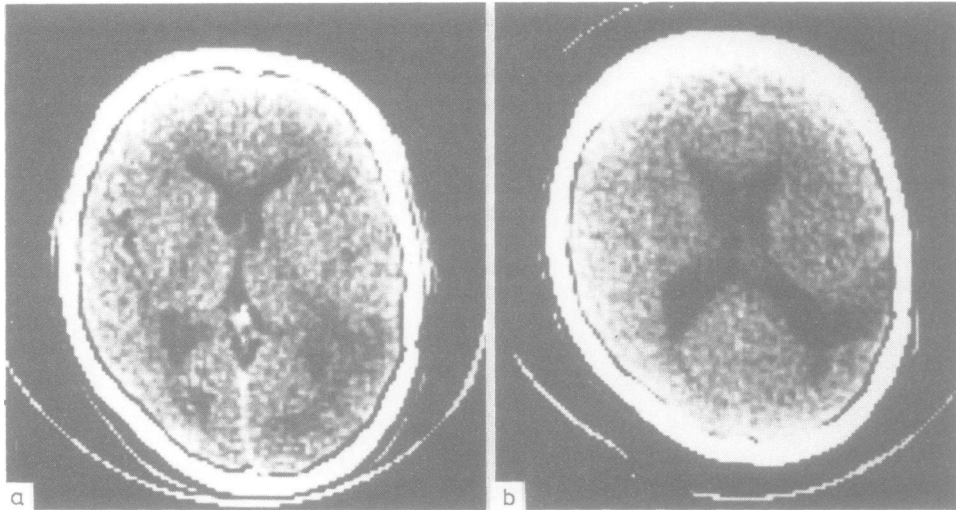


Fig 8 Case 3. 2nd (a) and 3rd (b) CT scans (August 1979 and February 1980) the former with contrast, showing a residual non-enhancing low density area on the right with compensatory dilatation of the right lateral ventricle and no mass effect.

Table Review of the literature on CT scanning in multiple sclerosis

Authors	Clinical grade	No contrast			Contrast		Mass effect	Normal
		No	Low density areas	Atrophy	No	Enhanced		
Davis & Pressman 1974 ³⁰	?	?	+	0	—	—	0	?
Baker <i>et al</i> 1974 ³⁵	Poss	8	25%	13%	?	—	0	63%
Cala & Mastaglia 1976 ¹⁰	Def/prob	19	47%	21%	?	—	0	32%
Jacobs & Kinkel 1976 ¹⁶	?	34	18%	29%	?	—	0	56%
Eyerman <i>et al</i> 1976 ³⁶	Adv/subac	20	+	0	?	—	0	?
Gyldensted 1976 ^{37,38}	Def/prob	110	36%	79%	20	0	0	18%
Wütrich <i>et al</i> 1976 ¹⁷	Prob/poss	60	25%	42%	8	13%	0	50%
Huckman <i>et al</i> 1977 ²¹	?	?	+	+	?	+	0	?
De Weerd 1977 ¹⁸	Def	23	43%	57%	6	0	0	35%
Mastaglia <i>et al</i> 1977 [*]	Def	23	61%	0	?	—	0	53%
	EP/L	25	52%	0				
	S	14	14%	0				
Cala & Mastaglia 1977 [*]	Def	45	56%	62%	0	0	0	29%
	EP/L	25	44%	28%				
	S	23	52%	26%				
	CP	2	0	100%				
Lane <i>et al</i> 1978 ²⁵	Def	18	28%	0	18	11%	0	56%
Radue & Kendall 1978 ⁴	?	49	23%	35%	16	13%	0	43%
Weinstein <i>et al</i> 1978 ¹¹	Prob	57	25%	11%	57	16%	0	75%
Cala <i>et al</i> 1978 ⁹	Def	46	57%	61%	2	100%	0	28%
	EP/L	26	35%	27%				
	S	26	46%	27%				
	CP	2	0	100%				
Hershey <i>et al</i> 1979 ¹⁹	Mixed	66	21%	23%	44	14%	0	71%
Paty <i>et al</i> 1979 ^{12*}	CPM	72	4%	50%	?	"2 cases"	0	47%
Tritschler <i>et al</i> 1979 ¹³	Mixed	33	79%	73%	33	30%	0	15%
Mikol <i>et al</i> 1980 ⁶	Mixed	60	17%	60%	48	21%	0	25%
Quattrini <i>et al</i> 1981 ²⁰	Mixed	100	12%	58%	31	19%	"some"	24%
Total		757	29%	45%	283	17%		37%

* omitted (^{7,8} included in ⁹; ¹² not all multiple sclerosis)

Small series† (^{2,3,14,26,32,39,40,41})	24	17‡	4‡	19	13‡	3	1‡
Single cases (^{3,15,22-24,27-29,31,33,42,43})	12	10‡	3‡	8	8‡	2	0

† 2-3 cases

‡ number of cases (not percentages)

CPM = chronic progressive myelopathy

Def = definite

prob = probable

poss = possible

Adv = advanced

subac = subacute

EP/L = early probably or latent

S = suspected

CP = chronic progressive

+ = presence reported but frequency not stated

ated with acute disease.^{3,5,11,14,15,21-24} Serial scanning has shown regression of enhancing lesions both to normal and to low density areas without enhancement;^{2-4,6,11,14,15,24-29} appearance of new lesions, both enhancing and non-enhancing;^{2,4,8,9,13,15,22,24,27} and even the subacute development of atrophy.^{8,9,23,26}

In most reports, the diagnosis has been established clinically but the clinically definite cases have seldom been distinguished from the others. Pathological confirmation of the disease has seldom been obtained but biopsy evidence of multiple sclerosis has been obtained in some cases^{22,26,30,31} and necropsies in a few others.^{13,17,23,25,26,29,32,33} The latter have shown good correlation between the radiological and pathological findings and confirmed that enhancing plaques represent areas of recent demyelination.^{17,23} The biopsy findings in cases 2 and 3 of our series are in agreement with this.

It has been said²⁻⁶ that the characteristic of the enhancing lesions in multiple sclerosis is the lack of mass effect but five pathologically verified cases in three recent reports show this to be untrue.^{26,29,31} Our report adds a further three cases of pathologically proven multiple sclerosis all showing enhancing lesions with mass effect on their CT scans.

The headache, seizures and aphasia seen in our three cases are unusual in multiple sclerosis and a diagnosis of cerebral tumour was strongly suspected clinically as well as radiologically. This "cerebral" form was also a clear feature of four of the other five cases reported in the literature and even the fifth patient was said to be "confused".³¹ Of all the eight cases, five had headaches, four had seizures and three had aphasia. Confusion, somnolence, poor memory, frontal signs, fever and a visual field defect were also seen. This cerebral form of multiple sclerosis is not common. Aphasia in particular is rare, being reported in only 1% of cases during the whole course of the disease.¹ Similarly, seizures occur in only about 1-3% of cases.^{1,34} The CT scan evidence suggests that this form of the disease is a particularly severe one pathologically, the large plaques, breakdown of the blood-brain barrier and surrounding oedema formation causing space occupation and impingement on the cerebral cortex.

The cases reported here in conjunction with those in the literature suggest that multiple sclerosis should be considered in the differential diagnosis of patients presenting with an acute higher cerebral disturbance in whom the CT scan appearances suggest a cerebral tumour.

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