

Short report

Multiple sclerosis: correlation of magnetic resonance imaging with cerebrospinal fluid findings

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SUMMARY MRI examination of 41 patients with clinical definite multiple sclerosis showed white matter lesions of high proton T₂ signal consistent with demyelination in 76% and CSF abnormalities present in 76%. Of patients with CSF abnormalities, 26% had normal MRI scans; conversely 26% of patients with MRI abnormalities had negative CSF studies. Thus a significant number of multiple sclerosis patients had negative results on either MRI or CSF examination, while only 5% had normal results on both tests.

Diagnosis of multiple sclerosis depends primarily on clinical history and neurological examination. Signs and symptoms attributable to at least two central nervous system lesions must occur in two or more separate attacks of remitting neurological dysfunction (or, a progressive course of at least 6 months' duration).¹ Explanations other than demyelinating disease must be ruled out.^{1,2} Advantage may be made of "para-clinical" studies² such as contrast-enhanced computed tomography (CT),³⁻⁷ magnetic resonance imaging (MRI),⁶⁻²² or cerebrospinal fluid (CSF) analysis,²³⁻²⁹ as well as evoked responses,²⁹⁻³¹ urodynamic³² or neuropsychologic evaluations.^{33,34}

MRI of the brain is superior to CT in demonstrating the white matter lesions of multiple sclerosis.⁶⁻²² Sensitivity of MRI is greatest when using T₂ weighted images acquired by spin-echo sequences with relatively long repetition (TR) and echo (TE) times,^{11-13,17,22} although images with extreme T₂ weighting decrease parenchymal contrast and obscure periventricular white matter involvement because of intense signal from ventricular CSF. Multiple sclerosis lesions consist most frequently of areas of high T₂ signal in the periventricular and supraventricular white matter, often in the atria, or genu of the occipi-

tal and frontal horns; involved other regions include internal capsule, centrum semiovale, cerebellum, and brainstem (notably pons). Several MRI grading scales for multiple sclerosis have been developed.^{1,3,20,22} We use that of Runge et al¹³ with score 0 to 4 according to the extent and distributions of the lesions. We report here dual examination by both MRI and CSF analysis of patients with definite multiple sclerosis of varying disability and disease duration, to determine the relative usefulness of these two tests.

Materials and methods

Our study group consisted of 41 patients (30F/11M) from the University of Miami Multiple Sclerosis Clinic with average age 39.4 ± 10 (SD) yr (range 22-62). Diagnosis of clinically definite multiple sclerosis was established by the criteria of Schumacher et al.¹ Mean duration of disease was 7.4 ± 6.5 yr (range 1-24). Each patient was evaluated by the Kurtzke Disability Status Scale³⁵ (DSS, mean 3.8 ± 2.6, range 1-8), and by lumbar puncture. The presence of CSF oligoclonal banding,^{24,28} increased IgG (> 5.5 mg/dl), IgG percentage of total protein (> 10.5%), or increased myelin basic protein (> 6 ng/ml) was interpreted as abnormal.²³⁻²⁹ CSF IgG Index and IgG SYN were determined²⁵⁻²⁷ when possible; these derived results did not change any CSF diagnosis.

MRI was performed with a Siemens Magnetom (0.35 Tesla), using a spin-echo acquisition sequence of TR = 1500 ms with dual echo delays of TE = 35 and 70 ms and a 256 × 256 matrix. Axial images were obtained in two interlaced sets of seven slices, 10 mm thick with 10 mm inter-spacing.¹⁶ Films were reviewed without knowledge of the

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patients' clinical classification and graded on a scale of 0 (normal scan), or 1 to 4 using the Vanderbilt criteria of Runge et al.¹³

Results

MRI Examination Periventricular and white matter lesions were visualised by MRI in 76% (31/41) of patients (table 1). There was a significant trend ($p = 0.006$ by Mann-Whitney test) for positive MRI to be found in patients of longer duration illness: only 45% (5/11) of patients with less than 3 years illness had abnormal MRI while 87% (26/30) of those with duration of multiple sclerosis greater than 3 years showed positive MRI findings (table 1). Mean duration of disease in patients with negative MRI findings (3.4 ± 2.8 yr) differed significantly ($F[1,39] = 5.6$; $p < 0.02$) from patients with positive MRI findings (8.7 ± 6.9 yr). Comparison of those 24% of patients with normal MRI with those showing abnormal imaging exams did not however show any significant differences in age (36 ± 10 vs 41 ± 10), sex (80%F vs 71%F), age of onset (33 ± 9 vs 32 ± 10), or DSS (3.8 ± 2.7 vs 3.8 ± 2.6). In addition, there was poor correlation ($r = 0.11$; $p > 0.05$) between Vanderbilt grade of brain MRI and DSS.

CSF Analysis An increase in CSF IgG, MBP and/or oligoclonal CSF banding was noted in 76% (31/41) of patients (table 1). Of these patients with abnormal CSF, 80% (25/31) had elevated IgG as percentage of total protein, while 10% (3) were classified as abnormal only on the basis of increased MBP, and another 10% (3) only by the presence of oligoclonal banding. There was no significant (all $p > 0.05$) correlation of CSF abnormalities to patient age, sex, age at multiple sclerosis onset, MRI grade, duration of illness, or DSS score, although there was a slight trend with the latter two.

Comparison of CSF and MRI findings The paired MRI and CSF results were examined for each patient, and summarised in table 2. Among patients with abnormal MRI examinations, 26% were without demonstrable CSF abnormalities. Conversely, of patients with CSF abnormalities, 26% had negative MRI studies. The CSF study and MRI examination results were *both abnormal* in 56% (23/41) of patients. Only 5% (2/41) of study patients with clinically

Table 2 Correlation of paired MRI and CSF findings in multiple sclerosis patients

	MRI		Total
	[-]	[+]	
C	2 (5%)	8 (20%)	10 (24%)
S	8 (20%)	23 (56%)	31 (76%)
F	10 (24%)	31 (76%)	41 (100%)

[-]: no abnormalities present

[+]: abnormalities present

definite multiple sclerosis had MRI and CSF examinations *both normal*.

Discussion

Magnetic resonance imaging detected abnormal areas of increased proton T₂ signal in a high proportion (76%) of our multiple sclerosis patients. While some initial reports of MRI in selected patients indicated aberrant findings in nearly 100% of patients with clinically definite multiple sclerosis^{8 10 11 13 18} the patients in such studies mostly had florid disease of long duration. More recent studies^{7 16 19} suggested 76–85% of clinically definite multiple sclerosis patients have abnormal MRI findings.

MRI of the brain showed no abnormalities in a significant proportion (24%) of our patient group, mostly those early in the course of disease. The absence of cerebral findings by MRI, despite clinical disease (and abnormal CSF in eight of these 10 patients) might be due to mild, diffuse infiltration, limited disturbances of the blood-brain barrier or small lesions below present spatial resolution limits (several mm). Technical improvements in signal/noise ratio and resolution should increase MRI image quality, and the use of paramagnetic contrasting agents may allow MRI evaluation of barrier dysfunction.³⁶ However, some normal brain MRI examinations probably accurately reflect an absence of cerebral involvement. A number of clinically definite multiple sclerosis patients are without cerebral pathology at necropsy,³⁷ or by MRI (Honig and Sheremata, in preparation), the result of demyelination exclusively in the spinal cord, for which MRI surface coil tech-

Table 1 Abnormal MRI and CSF findings in relation to duration of disease

MS duration (years)	VGS average	Abnormal MRI No. (%)	Abnormal CSF No. (%)	Total No. patients
0-3	1.7 ± 2.0	5 (45)	7 (64)	11
3-6	2.5 ± 1.6	11 (79)	13 (93)	14
6-12	2.3 ± 1.4	6 (86)	5 (71)	7
12-30	3.0 ± 0.7	9 (100)	6 (67)	9
0-30	2.4 ± 1.6	31 (76)	31 (76)	41

VGS = Vanderbilt MRI Grading Scale; means ± standard deviations.

nology is providing higher sensitivity. The poor correlation between MRI grade and DSS also probably reflects that most DSS disability is a function of spinal cord rather than cerebral involvement.

We observed a correlation of the frequency of high T₂ signal MRI lesions with duration of multiple sclerosis. Of our 30 patients with multiple sclerosis of longer than 3 years duration, 87% had positive brain MRI examinations, while negative findings on MRI were significantly related to shorter duration of disease (although not to DSS, age of onset, or sex). Of the 10 patients with normal MRI exams, eight (80%) had duration of illness of less than 4 years, compared with 29% of the 31 patients with positive, abnormal scans ($\chi^2 = 6.13$, $p < 0.02$). The increasing incidence of positive MRI findings with duration of disease is consistent with our observations (unpublished results) and others that while lesions of multiple sclerosis seen by MRI may fluctuate in size they do not disappear.^{15 38}

Cerebrospinal fluid was abnormal in 76% of our patient group. Prior reports identify increased IgG in 73–90% of definite multiple sclerosis cases.^{24 26 28 29} Different CSF indices are of comparable sensitivity, but of varied advantage in specificity, variability and relevance to blood-brain barrier dysfunction.^{24–27} Normalised CSF IgG in the form of the dimensionless IgG index,^{24–27} or the quantitative IgG SYN^{16 23} correct for loss of barrier integrity. However, in our patient group neither of these computed values increased CSF exam sensitivity. Oligoclonal bands in CSF are not as specific for multiple sclerosis, but have been reported present in 85–95% of cases and may be present in the face of normal CSF IgG.²³ Reports conflict on relation of CSF findings to the timing of lumbar puncture with respect to disease exacerbation.^{24 28 29} CSF results probably vary more with clinical status than MRI results.

Brain MRI and CSF examinations showed approximately equal sensitivity (76%) in detecting disease in our group of patients with definite multiple sclerosis. MRI may be valuable in providing objective anatomical evidence of disease activity, by monitoring lesion number or size.^{13 15 16 38} However, some 20% of the patients had normal examinations by MRI but had abnormal findings on CSF study. Significant numbers of patients diagnosed as having definite multiple sclerosis may lack confirmatory laboratory findings if only MRI imaging, or CSF analysis, is performed. The frequency of negative findings on MRI examination may be greatest early in the course of disease.

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