Eur. Radiol. 10, 368–376 (2000)

Neuroradiology European Radiology

Original article

Spinal cord magnetic resonance imaging in suspected multiple sclerosis

G.J. Lycklama à Nijeholt[1], B.M.J. Uitdehaag[2], E. Bergers[1], J.A. Castelijns[1], C.H. Polman[2], F. Barkhof[1]

[1] Department of Radiology, Dutch MS-MRI Center, Vrije Universiteit Hospital, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands
[2] Department of Neurology, Dutch MS-MRI Center, Vrije Universiteit Hospital, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands

Received: 21 April 1999; Revised: 3 August 1999; Accepted: 7 August 1999

Abstract. We examined the value of spinal cord magnetic resonance imaging (MRI) in the diagnostic work-up of multiple sclerosis (MS). Forty patients suspected of having MS were examined within 24 months after the start of symptoms. Disability was assessed, and symptoms were categorized as either brain or spinal cord. Work-up further included cerebrospinal fluid analysis and standard proton-density, T2-, and T1-weighted gadolinium-enhanced brain and spinal cord MRI. Patients were categorized as either clinically definite MS ($n = 13$), laboratory-supported definite MS ($n = 14$), or clinically probable MS ($n = 4$); four patients had clinically probable MS, and in nine MS was suspected. Spinal cord abnormalities were found in 35 of 40 patients (87.5 %), consisting of focal lesions in 31, only diffuse abnormalities in two, and both in two. Asymptomatic spinal cord lesions occurred in six patients. All patients with diffuse spinal cord abnormality had clear spinal cord symptoms and a primary progressive disease course. In clinically definite MS, the inclusion of spinal imaging increased the sensitivity of MRI to 100 %. Seven patients without a definite diagnosis had clinically isolated syndromes involving the spinal cord. Brain MRI was inconclusive, while all had focal spinal cord lesions which explained symptoms and ruled out other causes. Two other patients had atypical brain abnormalities suggesting ischemic/vascular disease. No spinal cord abnormalities were found, and during follow-up MS was ruled out. Spinal cord abnormalities are common in suspected MS, and may occur asymptomatic. Although diagnostic classification is seldom changed, spinal cord imaging increases diagnostic sensitivity of MRI in patients with suspected MS. In addition, patients with primary progressive MS may possibly be earlier diagnosed. Finally, differentiation with atypical lesions may be improved.

Correspondence to: G.J. Lycklama à Nijeholt

Key words: Multiple sclerosis – Magnetic resonance imaging – Spinal imaging – Diagnosis

Introduction

Multiple sclerosis (MS) is the most common chronically disabling disease of the central nervous system (CNS) in young adults, affecting up to 1 per 1000 persons in the Western world [1]. The diagnosis is based primarily on clinical findings; however, laboratory and paraclinical tests are also included in the most recent and widely used diagnostic criteria [2]. Of the paraclinical tests, brain magnetic resonance imaging (MRI) is most commonly applied, being highly sensitive for MS abnormalities while having a high negative predictive value [3].

About 80 % of MS patients present with spinal cord symptoms, suggesting frequent spinal cord involvement in MS. Recent improvements in spinal cord MRI enable reliable visualization of the spinal cord in MS [4]. Several MRI studies have described spinal cord abnormalties in MS patients as consisting primarily of focal lesions, located mostly in the lateral and posterior white matter columns and generally shorter than two segments [5, 6]. Diffuse abnormalities have recently been reported to be visualized on cardiac gated proton-density (PD) weighted MRI [7], with the cerebrospinal fluid (CSF) appearing isointense with normal spinal cord tissue, which means that even subtle changes in the spinal cord are readily visualized. Diffuse abnormalities are associated with severe disease and a primary progressive disease course [8].

Adding spinal cord MRI in the work-up of suspected MS cases is conceptually attractive as it depicts the entire central nervous system (CNS), in a disease in which histopathology typically reveals lesions in the spinal cord. Only a few studies have so far evaluated the value of spinal cord MRI findings in the diagnostic setting of MS [9, 10, 11]. In the study of Thorpe et al. [11] spinal

cord MRI findings changed the diagnosis laboratory supported to clinically definite MS in 3 of 20 cases. However, the patients were selected on the basis of having negative brain MRI findings, and therefore the group was not representative of the general MS population. The occurrence of diffuse spinal cord abnormalities in early or suspected MS has not yet been studied.

We present a series of patients referred to our department for diagnostic purposes. Our purpose was to study the brain and spinal cord appearance of patients suspected of having MS on clinical criteria. In addition, we evaluated the added value of spinal cord MRI in the work-up of such patients.

Methods and materials

Patients

Our series included 40 patients (28 women, 12 men; median age 37 years, range 19–61) referred to our outpatient department with symptoms suggestive of MS. Of these, 65 % presented with pyramidal and/or sensory symptoms attributable to spinal cord involvement. Five patients had brainstem symptoms, seven visual disturbances, and five cerebellar symptoms, and one sphincter disturbances. All patients were evaluated in the setting of routine diagnostic work-up within 24 months (median of 3.5) after the initial symptoms. Each gave informed consent to the study. The following clinical parameters were recorded: age, sex, date of initial symptoms, type of symptoms, and concomitant diseases. Most patients were mildly disabled, with a median score on the Expanded Disability Status Scale (EDSS) of 3.5 (range 0–6.5). Further, the neurologist recorded whether there was clinical evidence of dissociation in space, i. e., whether symptoms could be associated with abnormalities in more than one CNS region. CSF was analyzed for the presence of oligoclonal bands. Other diseases were ruled out by appropriate tests when necessary.

MRI

MRI of the brain and spinal cord was performed in one session at 1.0 T, and imaging of the brain consisted of PD- and T2-weighted conventional spin echo (SE; TR/TE 2300/45, 90/1 excitations), and T1-weighted conventional SE (600/15, 2), after the administration of gadolinium-DTPA (0.1 mmol/kg). Twenty-one axial slices were obtained, with a pixel size of 1 mm^2, 5-mm slice thickness, and an interslice gap of 0.5 mm. Acquisition time was approximately 20 min. MRI of the spinal cord was performed using a spinal phased array coil. Twelve sagittal slices, depicting the spinal cord over its entire length (3-mm slice thickness, 0.3-mm interslice gap, pixel size 0.94 mm^2), were acquired using cardiac triggered conventional SE (2200/20, 80/1; PD and T2-weighted) and T1-weighted SE (550/15, 2). Acquisition time for spinal cord imaging was approximately 20 min. Total acquisition time was approximately 1 h; including changing the MRI coils between brain and spinal cord imaging.

Hardcopy images of brain and spinal cord were scored by two observers by consensus, unaware of clinical data, for the number of focal lesions, both on T1- and on PD/T2-weighted images. Further, spinal cord images were scored for the presence of diffuse abnormality, which was defined as diffuse signal increase on both the PD and T2-weighted MRI, regardless of presence of focal lesions [10]. Finally, the number of enhancing lesions was scored in brain and spinal cord. According to previously described brain MRI criteria for MS, the brain images were judged as to whether they were compatible with a radiological diagnosis of MS. According to these criteria, which were designed to differentiate MS lesions from atypical ("ischemic vascular") white matter lesions in the elderly [12], patients were judged to have brain MRI findings compatible with MS if they had at least threelesions fulfilling two of the following criteria: (a) a lesion larger than 6 mm, (b) a lesion abutting the ventricles, and (c) an infratentorial lesion. Brain lesions were considered to be ischemic vascular in origin when they were confluent, nonovoid, and spared the U-fibers.

Diagnostic classification

After evaluation of clinical, MRI, and laboratory data (CSF) patients were categorized according to the diagnostic criteria of Poser et al. [2] as having either clinically definite MS (CDMS), laboratory-supported definite MS (LSDMS), or clinically probable MS (Table 1). For this categorization only brain MRI was included. Only upon fulfilling the Fazekas et al. [12] criteria was the brain MRI considered to be positive as paraclinical evidence. After diagnostic work-up, patients were followed up for a median of 17 months (range 6–33). Table 2 summarizes the diagnostic work-up in patients not fulfilling the Poser et al. criteria for CDMS. Statistical comparisons between groups were made using the Mann-Whitney *U* test.

Results

Clinical and MRI data are summarized in Table 3. After evaluating clinical, laboratory, and brain MRI data, 13 of 40 patients fulfilled the Poser et al. criteria for CDMS, 14 for LSDMS, and 4 for clinically probable MS. In the remaining 9 patients MS could not be ruled out, nor could another diagnosis be made.

Clinically definite MS

The median duration between appearance of the initial symptoms and examination in the 13 patients with CDMS was somewhat longer than that in the other 27 patients (Table 2), although not significantly so. Eleven

Table 1. Diagnostic criteria for multiple sclerosis according to Poser et al. [2]

Category	Attacks[a]	Clinical evidence[b]		Paraclinical evidence of dissocation in space[c]	CSF: oligoclonal banding/IgG
Clinically definite MS	2	2		–	–
	2	1	and	1	–
Laboratory-supported definite MS	2	1	or	1	Positive
	1	2		–	Positive
	1	1	and	1	Positive
Clinically probable MS	2	1		–	–
	1	2		–	–
	1	1	and	1	–
Laboratory-supported probable MS	2	–		–	Positive

[a] Having at least two attacks suggests dissociation in time
[b] Clinical evidence of dissociation (1, only one CNS area affected; 2, dissociation in space)
[c] Paraclinical evidence of dissociation in space using brain MRI

Table 2. Diagnostic work-up and result of 27 patients not fulfilling the criteria for clinically definite MS (*CDMS* clinically definite multiple sclerosis, *SUSP* suspected MS, *PROB* clinically probable MS, *LSDMS* laboratory-supported definite MS, *PPMS* primary progressive MS, *RRMS* relapsing-remitting MS, *VASC* vascular-ischemic brain abnormalities)

Presentation	*n*	CSF[a]	Brain MRI[b]	Spinal cord[c]	Initial diagnosis	Clinical course during follow-up	Final diagnosis
One attack, > 1 × clinical evidence	6	5 Pos	5 Pos	2 Pos	2 LSDMS	1 Progressive	1 PPMS
				3 Neg	3 LSDMS	1 Stable	1 LSDMS
						2 Stable	2 LSDMS
						1 new attack	1 RRMS
		1 Neg	1 Pos	1 Pos	1 PROB	1 Stable	1 PROB
		14 Pos	9 Pos	8 Pos	8 LSDMS	3 Progressive	3 PPMS[d]
						1 relapse	1 RRMS
						4 Stable	4 LSDMS
				1 Neg	1 LSDMS	1 Stable	1 LSDMS
			5 Pos	3 Pos	3 SUSP	3 Stable	3 SUSP
				2 Neg	2 SUSP	2 Stable	2 SUSP
			2 Pos	2 Neg	2 PROB	2 Stable	2 PROB
One attack, 1 × clinical evidence	20	6 Neg	4 Neg	2 Pos	2 SUSP	1 Progressive	1 PPMS[e]
						1 Stable	1 SUSP
				2 VASC	2 SUSP	2 Stable	2 VASC
Two attacks, 1 × clinical evidence	1	1 Neg	1 Neg	1 Pos	1 PROB	1 Stable	1 PROB

[a] Pos, oligoclonal bands in CSF; suggestive of MS
[b] Pos, brain MRI examination positive for the Fazekas et al. [12] criteria for MS
[c] Pos, focal and/or diffuse abnormalitie on spinal cord MRI examination
[d] Two of three patients showed diffuse spinal cord abnormalities
[e] Spinal cord MRI showed diffuse abnormality

patients had at least two separate clinical attacks (dissociation in time), and had clinical evidence of abnormalities in two different areas of the CNS (dissociation in space). Brain MRI showed abnormalities (positive for the Fazekas et al. [12] criteria) in 10 of 11 patients, while spinal cord MRI showed focal lesions in all 11 patients. The other two patients with CDMS had experienced two separate attacks, but confined to a single CNS area. However, brain MRI findings provided *paraclinical* evidence of dissociation in space in these patients. Again, spinal cord MRI also showed focal lesions; thus sensitivity of combined brain and spinal cord MRI was 100 % in the patients with CDMS. Gadolinium enhancement was seen on brain MRI in 8 of 13 patients with CDMS. In 3 of these the spinal cord also showed gadolinium enhancement. Furthermore, 8 of 13 CDMS patients showed hypointense lesions on the T1-weighted brain MRI. Such hypointense lesions were not found in the spinal cord (nor in the spinal cord of any other subgroup). Median EDSS was higher in these patients (median 3, range 1.5–5.5) than in patients who did not have hypointense lesions (median EDSS 1, range 0 –2, $P < .01$). None of the 13 patients with CDMS had diffuse spinal cord abnormalities. During follow-up all patients with CDMS were classified as having relapsing-remitting MS.

Laboratory supported definite MS

The diagnosis LSDMS was made in 14 patients (Table 2). In 5 of these an isolated clinical attack in combi-

Table 3. Summary of clinical and MRI data on 40 patients suspected of having MS

	Overall series (n = 40)	Clinically definite (n = 13)	Laboratory-supported definite (n = 14)	Clinically probable (n = 4)	Remaining (n = 9)
Clinical presentation					
Duration of symptoms (months)	4 (0–20)	6 (0–20)	4.5 (0–25)	1 (0–3)	3 (1–18)
EDSS	2 (0–6.5)	2 (0–5.5)	2 (0–6.5)	1.5 (0–3)	2 (0–5.5)
Oligoclonal banding in CSF	27 (67%)	9 (70%)	14 (100%)	–	5 (56%)
Brain symptoms	15 (38%)	6 (46%)	9 (64%)	1 (25%)	1 (11%)
Spinal cord symptoms	26 (65%)	8 (62%)	7 (50%)	3 (75%)	8 (89%)
Duration of follow-up (months)	17 (6–33)	17 (7–33)	15 (6–30)	26 (10–30)	21 (8–33)
Course during follow-up					
Relapsing-remitting MS	13 (33%)	13 (100%)	2 (14%)	–	–
Primary progressive MS	5 (12%)	–	4 (28%)	–	1 (11%)
Ischemic vascular disease	2 (5%)	–	–	–	2 (22%)
Definite diagnosis	6 (15%)	–	–	–	6 (67%)
Brain MRI					
PD/T2 lesions	9.5 (0– > 60)	16 (3– > 60)	11 (5– > 60)	7 (2–15)	2 (0–30)
T1 lesions	0 (0–23)	1 (0–14)	0 (0–23)	0 (0–1)	–
Gadolinium-positive scans	15 (38%)	8 (62%)	6 (43%)	1 (25%)	–
Positive brain MRI scans[a]	30 (75%)	12 (92%)	14 (100%)	3 (75%)	1 (11%)
„Vascular“ brain lesions	3 (8%)	–	1 (7%)	–	2 (22%)
Spinal cord MRI					
PD/T2 lesions	1 (0–7.5)	4.5 (1–7.5)	1 (0–6.5)	1 (0–1)	0.5 (0–2)
Gadolinium-positive scans	4 (10%)	3 (23%)	–	–	1 (11%)
Scans showing diffuse abnormality	4 (10%)	–	3 (21%)	–	1 (11%)
Abnormal spinal cord scans[b]	33 (82%)	13 (100%)	10 (71%)	4 (100%)	7 (78%)

[a] According to the Fazekas et al. [12] criteria
[b] Either focal spinal cord lesions, or diffuse abnormalities or both

nation with clinical evidence of dissociation in space, together with CSF findings suggestive of MS, led to a diagnosis of LSDMS (Table 2). The remaining 9 patients with LSDSM had also experienced only a single clinical episode, but neurological evaluation revealed only one affected system (“clinically isolated syndrome”). In these patients positive brain MRI findings provided paraclinical evidence of dissociation in space, and CSF findings were suggestive of MS, thus leading to a diagnosis of LSDMS (Table 2).

All patients with LSDMS had brain MRI findings suggestive of MS (positive for the Offenbacher et al. [12] criteria). In ten patients there wer also spinal cord abnormalities. These consisted of only focal lesions in seven, focal and diffuse abnormalities in two, and only diffuse abnormalities in one patient. Six of the ten LSDMS patients with spinal cord abnormalities had spinal cord symptoms, while only one patient without spinal cord abnormalities had spinal cord symptoms. The LSDMS patients with spinal cord abnormalities had higher EDSS (median 2.5, range 0–6.5) than those without (median 2, range 1–2.5). The four LSDMS patients without spinal cord abnormalities tended to have more brain lesions (median 19, range 6–25) than those with (median 9, range 5–53).

During follow-up eight patients with LSDMS experienced no new symptoms. Four patients experienced gradual worsening, and a diagnosis of primary progressive MS was made (Table 3). Interestingly, all three LSDMS patients with diffuse spinal cord abnormalities developed primary progressive disease course (Fig. 1). Two patients with LSDMS had a clinical relapse during follow-up demonstrating dissemination in time and space, enabling a diagnosis of relapsing-remitting MS. In one of these patients (61 years old) brain MRI was inconclusive, since in addition to typical MS lesions there were also multiple lesions suggestive for ischemic-vascular white matter involvement. However, spinal cord MRI revealed several focal lesions suggestive for MS (Fig. 2).

Remaining patients (no definite MS)

In 13 patients MS could neither be confirmed nor ruled out after evaluation of clinical, CSF, and MRI data. In four patients the Poser et al. criteria led to a diagnosis of clinically probable MS. Two of these patients had experienced one clinical episode consisting of spinal cord symptoms. Spinal cord MRI ruled out cord compression, and a focal spinal cord lesion was found in one of the two. In addition, brain MRI provided paraclinical evidence or dissociation in space in both patients. However, CSF findings were negative, and the diagnosis therefore remained clinically probable MS (Tables 1, 2). Of the other two patients with clinically probable MS, one had experienced two separate clinical attacks, both consisting of identical spinal cord symptoms, thus not demonstrating dissociation in space. Spinal cord MRI revealed a single spinal cord lesion, and spinal cord compression was ruled out. Since the focal lesion was most likely the cause of symptoms, dissociation in space was not verified, and brain MRI was negative. Because CSF findings were also negative, the diagnosis thus remained probable MS. The last of the four pa-

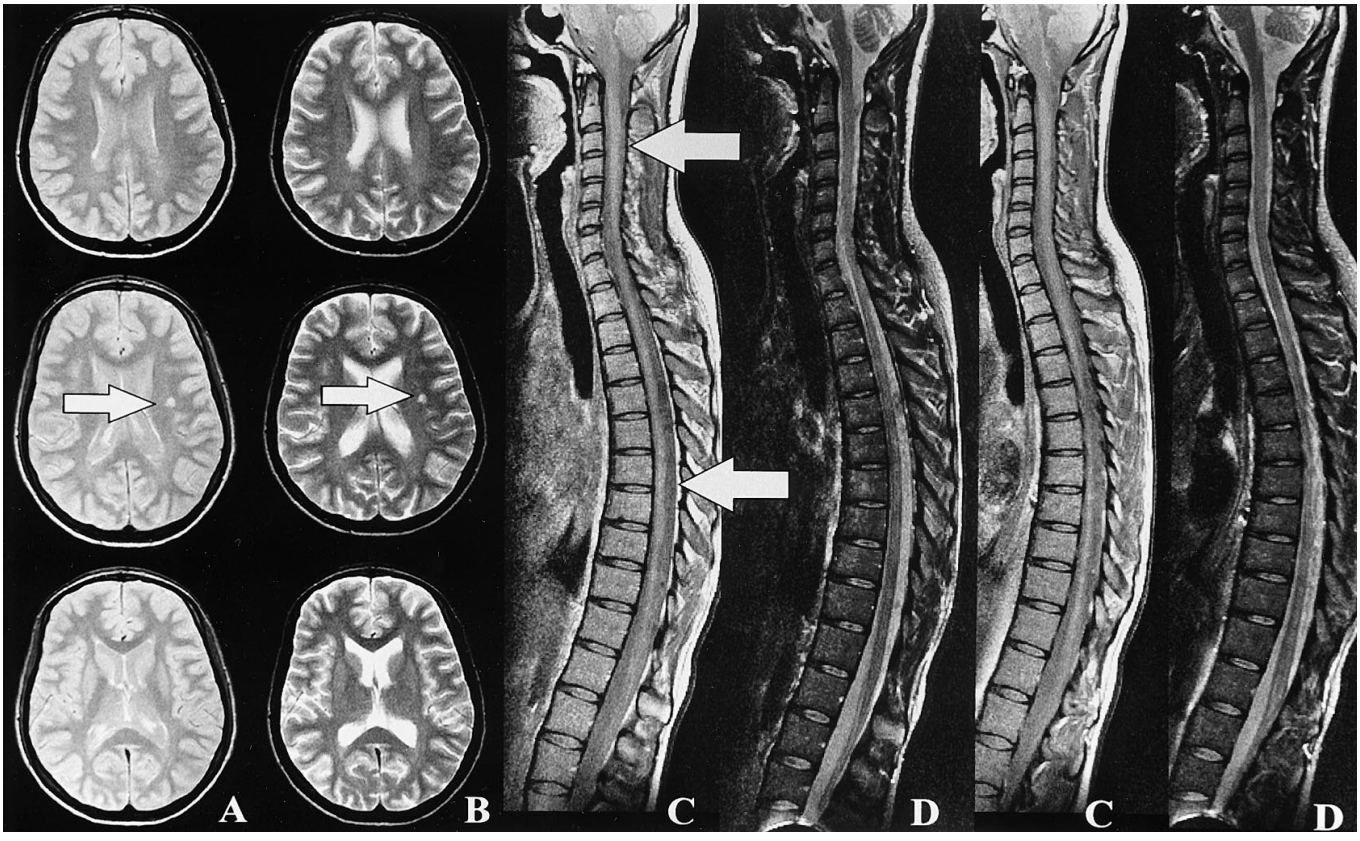

Fig. 1A–D. A 28-year-old woman with progressive pyramidal symptoms. At the time of examination her EDSS was 6.5, indicating severe impairment. CSF findings suggested MS. Because she had experienced only one clinical attack, with no clinical evidence of dissociation in space, the diagnosis was LSDMS. **A**,**B** PD- **(A)** and T2-weighted **(B)** brain MRI revealed small periventricular white matter lesions and one isolated white matter lesion *(arrow)*. The Fazekas et al. [12] MRI criteria for MS were not fulfilled. Gadolinium-enhanced T1-weighted MRI revealed no enhancing or hypointense lesion, and the brain MRI examination was inconclusive. **C**,**D** PD-weighted spinal cord MRI revealed diffuse abnormality of the spinal cord without focal lesions *(arrows)*. During follow-up, while the patient's symptoms further deteriorated, a diagnosis of primary progressive MS was made

tients with probable MS had experienced one attack involving both visual and sensory symptoms (dissociation in space). Spinal cord imaging revealed a single lesion, explaining the sensory symptoms. Also, brain MRI was compatible with MS. However, because CSF findings were negative, the diagnosis remained probable MS. During follow-up, none of the four patients with probable MS experienced new symptoms.

In another two patients (44 and 43 years old), the location and shape of the brain MRI lesions suggested ischemic vascular lesions. One of these patients, who had experienced sensory symptoms, showed a total of 30 focal brain lesions on T2-weighted MRI. No gadolinium enhancement was seen, and none of the lesions appeared as hypointense on T1-weighted images. Nevertheless, the MRI criteria for MS were fulfilled. However, no spinal cord abnormalities were detected in this patient, and CSF examination showed no abnormalities (Fig. 3). The other patient had 13 focal brain lesions, without gadolinium enhancement or hypointensity on T1-weighted images. Because of location and size of the lesions the MRI criteria were not fulfilled. Again, spinal cord showed no abnormalities, and CSF findings were negative. During follow-up no new symptoms developed in either patient, and the final diagnosis was probable ischemic vascular disease.

The remaining seven patients all presented with symptoms attributable to spinal cord abnormalities. MRI ruled out spinal cord compression in all. While none of the patients had brain abnormalities, spinal cord MRI showed abnormalities in all seven, consisting of focal lesions in six and diffuse abnormalities in one. Regarding the patients with focal spinal cord lesions, dissociation in space could not be established because clinical symptoms were correlated well with spinal cord imaging findings, and additional asymptomatic spinal cord lesions were not found. CSF examination revealed oligoclonal bands in five of six patients. During follow-up none of the six patients experienced new symptoms, and the diagnosis remained clinically isolated syndrome (Fig. 4). The last patient, showing diffuse spinal cord abnormality, showed disease progression during follow-up, and eventually a final diagnosis of primary progressive MS was made.

Correlation between clinical findings and MRI data: overall series

Of 24 patients with symptoms clinically attributable to spinal cord localization (Table 2), 22 showed spinal

Fig. 2A–D. A 61-year-old women presenting with motor symptoms. Clinical examination revealed no evidence of dissociation in space, and her EDSS was 2.0. CSF findings suggested MS. **A**, **B** Brain MRI revealed numerous hyper-intense lesions on the T2-weighted images, and the Fazekas et al. [12] criteria were fulfilled. However, the appearance of the lesions suggested an ischemic-vascular origin of at least part of the lesions. Based on clinical, laboratory, and brain MRI findings, a diagnosis of LSDMS was made. **C**,**D** Spinal cord MRI revealed several focal lesions suggestive of MS. During follow-up she developed a clinical relapse, and eventually a diagnosis of relapsing-remitting MS was made

cord abnormalities. Spinal cord abnormalities were also found in 3 additional patients with symptoms judged as possibly related to spinal cord abnormalities. In 13 patients the neurologist found no clinical evidence of spinal cord dysfunction. However, 6 patients (46%), showed focal spinal cord lesions, mostly involving one segment, but in two patients involving more than two vertebral segments. As to the patients with diffuse spinal cord abnormalities, all had spinal cord symptoms, and EDSS was higher (median 4.5, range 3–6.5) than in patients with no or only focal lesions (median EDSS 2, range 0–6, $P < 0.01$). Duration of symptoms was longer in patients with diffuse abnormalities (median 16, range 10–18 months) than in the other patients (median 5.5, range 0 –24 months, $P < 0.05$). Four of five patients with a primary progressive disease course showed diffuse spinal cord abnormalities. By contrast, none of the other 35 patients showed diffuse spinal cord abnormalities.

Discussion

The findings of this study show that abnormalities on spinal cord MRI are very common in patients with suspected MS or early definite MS. Spinal cord imaging increased the overall sensitivity of MRI since we found spinal cord abnormalities in most patients with negative or inconclusive brain MRI findings. Furthermore, spinal cord abnormalities were not restricted to patients with spinal cord symptoms. Asymptomatic spinal cord lesions were found in about 50% of all patients, which is in agreement with a recent study in clinically isolated syndromes [13].

We evaluated the effect of including spinal MRI findings as paraclinical evidence of MS in our group of patients. In this respect it is important to realize that our patients were not selected on basis of brain MRI findings and are therefore representative of patients who are encountered in clinical routine. The impact of including spinal MRI findings in the final diagnostic classification in these patients was minimal. Even when considering only a single focal lesion and/or the presence of diffuse spinal cord abnormalities suggestive of MS, the final diagnosis was not altered in the vast majority of our patients. To some extent this may reflect the design of the criteria, which were developed when imaging of the spinal cord was not possible. However, the value of spinal cord MRI went beyond influencing diagnostic classification, which is illustrated in our study in several ways (Table 4).

Firstly, in the patients with primary progressive MS a previous study of ours suggested that diffuse spinal cord

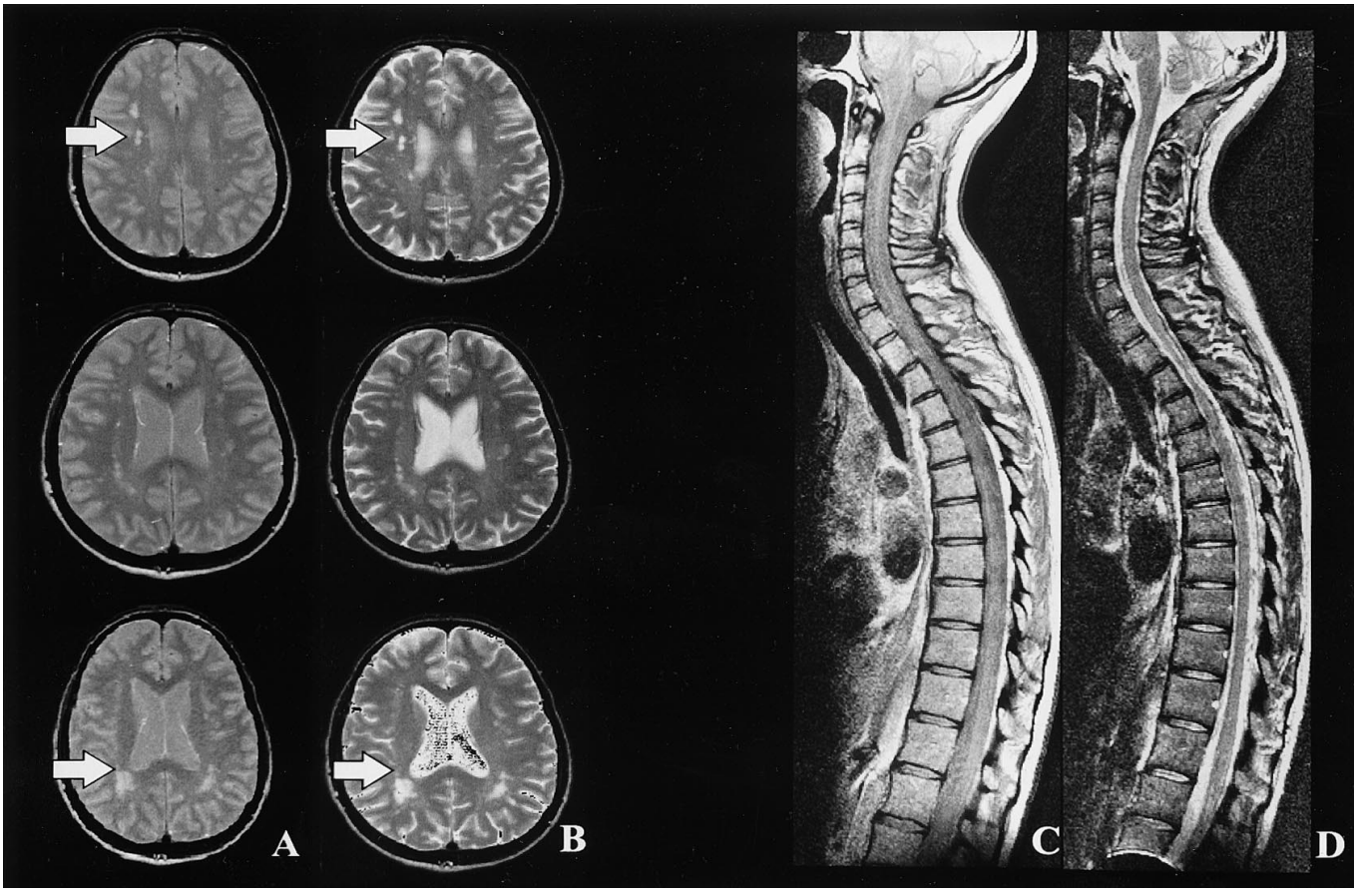

Fig. 3A–D. A 44-year-old woman presenting with one period of sensory symptoms. Clinical examination revealed no evidence of dissociation in space, and her EDSS was 1.0. No CSF abnormalities were found. **A**,**B** Brain MRI showed several focal lesions on the PD- and T2-weighted MRI images. Note that the thoracic spinal cord appears to be narrowed due to slight scoliosis during positioning. The adjacent images showed that the spinal cord had normal thickness at thoracic level. No gadolinium enhancement was seen, and none of the lesions appeared as hypointense on T1-weighted images. Nevertheless, the MRI criteria for MS were fulfilled. However, the appearance of lesions suggested an ischemic-vascular origin. **C**,**D** No spinal cord abnormalities were detected in this patient. During follow-up no new symptoms developed, and the patient was diagnosed as probably having ischemic-vascular disease of the brain

Table 4. Situations with a possible role for spinal cord MRI in suspected MS

Situation	Value of spinal cord imaging
Clinically definite MS	Explaining spinal cord symptoms
Primary progressive disease course	Demonstrating diffuse spinal cord involvement
Suspected MS; no spinal cord symptoms	Demonstrating dissociation in space
Suspected MS, spinal cord symptoms	Ruling out other causes Explaining spinal cord symptoms Prognostic value for future clinical course?
Suspected MS, older hypertensive patient (brain MRI atypical)	Ruling out MS (if no spinal cord abnormalities)

abnormalities found in primary progressive MS patients are typical for advanced disease [7, 8]. In the present study we encountered four patients with diffuse spinal cord abnormalities at presentation, all of whom later developed clinically definite primary progressive MS. The diagnostic problems involving a primary progressive disease course are well known, because the Poser et al. criteria are more difficult to apply in these cases [14]. Therefore spinal cord MRI may provide important clues for the diagnosis of primary progressive MS, as diffuse spinal cord abnormalities may be the only finding in these patients.

Secondly, in patients with isolated spinal cord symptoms. when confronted with an isolated spinal cord syndrome, the differential diagnosis is extensive. In such patients spinal cord MRI is of great importance since this may both rule out spinal cord compression and demonstrate abnormalities suggestive of MS [15]. Of course, finding spinal cord abnormalities in patients with a clinically isolated syndrome involving the spinal cord is not likely to demonstrate dissociation in space, thus altering the diagnostic classification, unless lesions at several spinal levels are present. It would be interesting to determine whether the patients with isolated spinal cord involvement eventually develop clinically definite MS over time. If so, the finding of spinal cord abnormalities in patients suspected of having MS could be of prognostic value. On the other hand, it is conceivable that some of these patients never develop definite MS, as in isoloated optic neuritis. Nevertheless, both

Fig. 4A–D. A 20-year-old man, presenting with one period of motor symptoms. Clinical examination revealed no evidence of dissociation in space, and his EDSS was 0. CSF examination suggested MS. **A**,**B** Brain MRI showed only one periventricular lesion, and the MRI criteria for MS were not fulfilled. **C**,**D** Spinal cord MRI showed two focal lesions, explaining symptoms and ruling out compressive causes. During follow-up no new symptoms developed, and the diagnosis remained clinically isolated syndrome

for explaining symptoms and for ruling out other causes spinal cord MRI clearly is useful in patients with clinically isolated syndromes involving the spinal cord.

Thirdly, in patients with nonspecific symptoms possibly related to vascular disease brain abnormalities are often present [16], sometimes indistinguishable from MS lesions. Spinal MRI may be useful in discriminating between the two conditions. In the two patients who were finally diagnosed as having vascular disease, no abnormalities were found in the spinal cord, despite the fact that both had many brain lesions (one fulfilled the MRI criteria for MS). This finding is in accord with previous reports that atypical hypoxic/ischemic lesions probably are not to be found in the spinal cord of healthy subjects [4]. However, large population studies, including those of elderly subjects with cerebrovascular risk factors, are needed to confirm this.

Adding spinal cord MRI to the diagnostic work-up of suspected MS patients comes at the price of increased imaging time. Further, the MRI coil may have to changed during the MRI examination. In the future, permanent MRI coils and faster acquisition times may resolve this problem. However, in our opinion, the clear advantages of imaging the spinal cord in such patients warrants the acquisition time disadvantage.

We conclude that spinal cord MRI should be considered more frequently in the diagnostic work-up of patients suspected of having MS. In several instances, summarized in Table 4, it may increase sensitivity and/or specificity of the examination, although this is not reflected in current clinical classification schemes.

Acknowledgement. Dr. Lycklama à Nijeholt is supported by a grant from the Dutch MS Society (92–131).

References

1. Matthews WB, Compston A, Allen IV. Matthews WB, Compston A, Allen IV, editors (1991) McAlpine's multiple sclerosis, 2nd edn. Churchill Livingstone, New York
2. Poser CM, Paty DW, Scheinberg L, et al (1983) New diagnostic criteria for multiple sclerosis: guidelines for research protocols. Ann Neurol 13: 227–231
3. Barkhof F, Filippi M, Miller DH, et al (1997) Comparison of MRI criteria at first presentation to predict conversion to clinically definite multiple sclerosis. Brain 120: 2059–2069
4. Thorpe JW, Kidd D, Kendall BE, et al (1993) Spinal cord MRI using multi-array coils and fast spin echo. I. Technical aspects and findings in healthy adults. Neurology 43: 2625–2631
5. Tartaglino LM, Friedman DP, Flanders AE, Lublin FD, Knobler RL, Liem M (1995) Multiple sclerosis in the spinal cord: MR appearance and correlation with clinical parameters. Radiology 195: 725–732
6. Kidd D, Thorpe JW, Thompson AJ, et al (1993) Spinal cord MRI using multi-array coils and fast spin echo. II. Findings in multiple sclerosis. Neurology 43: 2632–2637

7. Lycklama à Nijeholt GJ, Barkhof F, Scheltens P, et al (1997) MR of the spinal cord in multiple sclerosis: relation to clinical subtype and disability. AJNR Am J Neuroradiol 18: 1041–1048
8. Lycklama à Nijeholt GJ, Vanwalderveen MA, Castelijns JA, et al (1998) Brain and spinal cord abnormalities in multiple sclerosis – correlation between MRI parameters, clinical subtypes and symptoms. Brain 121: 687–697
9. Larsson EM, Holtas S, Nilsson O (1989) Gd-DTPA-enhanced MR of suspected spinal multiple sclerosis. AJNR Am J Neuroradiol 10: 1071–1076
10. Aichner F, Poewe W, Rogalsky W, Wallnofer K, Willeit J, Gerstenbrand F (1985) Magnetic resonance imaging in the diagnosis of spinal cord diseases. J Neurol Neurosurg Psychiatry 48: 1220–1229
11. Thorpe JW, Kidd D, Moseley IF, et al (1996) Spinal MRI in patients with suspected multiple sclerosis and negative brain MRI. Brain 119: 709–714
12. Fazekas F, Offenbacher H, Fuchs S, et al. (1988) Chriteria for an increased specificity of MRI interpretation in elderly subjects with suspected multiple sclerosis. Neurology 38: 1822–1825
13. O'Riordan JI, Losseff NA, Phatouros C, et al (1998) Asymptomatic spinal cord lesions in clinically isolated optic nerve, brain stem, and spinal cord syndromes suggestive of demyelination. J Neurol Neurosurg Psychiatry 64: 353–357
14. Thompson AJ, Polman CH, Miller DH, et al (1997) Primary progressive multiple sclerosis. Brain 120: 1085–1096
15. Miller DH, McDonald WI, Blumhardt LD, et al (1987) Magnetic resonance imaging in isolated noncompressive spinal cord syndromes. Ann Neurol 22: 714–723
16. Fazekas F (1989) Magnetic resonance signal abnormalities in asymptomatic individuals: their incidence and functional correlates. Eur Neurol 29: 164–168