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BACKGROUND AND PURPOSE: **Improving the sensitivity of MR imaging for the detection of multiple sclerosis (MS) lesions in the cord might be useful in the diagnostic workup and could lead to a better understanding of the evolution of the disease. The purpose of this study was to compare fast spin-echo (FSE) with magnetization transfer–prepared gradient-echo (MT-GE) and fast short-inversion-time inversion recovery (fast-STIR) MR sequences to determine which is best for imaging cervical cord lesions in MS patients.**

METHODS: **FSE, MT-GE, and fast-STIR MR images were obtained in 56 MS patients and 10 healthy control subjects with a 1.5-T MR system and a phased-array coil. Cord lesions seen on images obtained with each sequence were counted by two observers in two stages (stage 1: random review of the complete sets of images from each technique; stage 2: side-by-side review with a retrospective count of lesions).**

RESULTS: **At the end of stage 1, a mean of 1.16 cord lesions per patient were seen on FSE images, 1.57 on MT-GE images (35% more than on FSE), and 1.92 on fast-STIR images (66% more than on FSE). Two or more cervical cord lesions were found on 16 FSE images (29%), 23 on MT-GE images (46%), and 30 on fast-STIR images (54%). Differences were reduced after stage 2: MT-GE detected 22% more lesions and fast-STIR 36% more lesions than FSE. Considering the three sequences together, 113 cervical cord lesions were seen in 50 patients (89%).**

CONCLUSION: **Both MT-GE and fast-STIR sequences depict more cervical cord MS lesions than the FSE sequence, with fast-STIR having the best sensitivity. Fast-STIR MR images may be useful for the diagnostic workup of patients with suspected MS and for improving our understanding of the evolution of MS.**

The spinal cord is frequently involved in multiple sclerosis (MS), with one postmortem study disclosing cord lesions in 86% of randomly selected MS patients (1) and other investigators reporting MR cord abnormalities in 47% to 90% of patients studied (2–11). The different generations of MR technology used (particularly the introduction of phased-array coils), the use of different pulse sequences, and the differences in patient subgroups studied may explain the disparate sensitivities reported in the detection of cord lesions. In two studies (7, 12), the sensitivity of fast spin-echo (FSE) sequences in detecting spinal MS lesions was similar to that of conventional spin-echo (CSE) imaging; however, the use of FSE may sometimes cause subtle abnormalities to be missed (7). Nevertheless, this limitation would seem to be overcome when the FSE sequence is adapted to 3D acquisition (13). While the good sensitivity of FSE sequences, coupled with their short acquisition time, has made the use of FSE routine for detecting MS abnormalities in the cord (7), other pulse sequences might prove equally useful. Even though four independent studies (3, 14–16) found that fast fluid-attenuated inversion recovery (fast-FLAIR) has a lower sensitivity than FSE for detecting spinal MS lesions, the roles of fast short-inversion-time inversion recovery (fast-STIR) and magnetization transfer-prepared gradient-echo (MT-GE) sequences have still to be fully examined. Hittmair et al (3), in a study of 20 MS patients, showed that fast-STIR produced better lesion contrast in the cervical cord than did both CSE and FSE; but Thorpe et al (17) found that fast-STIR and FSE

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revealed similar numbers of cervical cord lesions in 17 MS patients. Similarly, Finelli et al (18) showed that in six MS patients, MT-GE provided better cervical cord lesion delineation than CSE, but Lycklama à Nijeholt et al (5) found more cervical cord lesions with CSE in a study of 20 MS patients. The present study was carried out in a large cohort of patients to compare the sensitivities of these two pulse sequences with that of FSE for detecting MS lesions in the cervical spinal cord.

Methods

Patients

We studied 56 patients with clinically definite MS (19) (37 women and 19 men). Their mean age (SD) was 37 (12.5) years, the median disease duration was 6 years (range, 1 to 28 years), and the median Expanded Disability Status Scale (EDSS) score (20) was 2.5 (range, 0.0 to 7.5). According to the Lublin and Reingold criteria (21), 32 patients had relapsing-remitting MS, 20 had secondary-progressive MS, two had primary-progressive MS, and two had benign MS. Ten age- and sex-matched healthy individuals served as control subjects. Approval was obtained from the local ethics committee, and written informed consent was obtained from all the subjects included in the study.

Cervical Cord MR Imaging

MR imaging was performed in all patients and control subjects on a 1.5-T system. With a tailored cervical spine phased-array coil for signal reception, the following pulse sequences were used: a) T2-weighted FSE (4700/112/3 [TR/TE/excitations]; echo train length, 15; field of view [FOV], 280 × 280 mm; matrix size, 360 × 512; acquisition time, 5 minutes 43 seconds); b) gradient-echo (fast low-angle shot [FLASH]) (600/10/2; flip angle, 20°; FOV, 280 × 280 mm; matrix size, 224 × 256; acquisition time, 4 minutes 31 seconds). This sequence, henceforth referred to as MT-GE, was performed twice, once with and once without a magnetization transfer saturation pulse (the saturation pulse was an off-resonance radio-frequency pulse centered 1.5 kHz below the water frequency, with a gaussian envelope of 7.68 milliseconds' duration and a flip angle of 500°); and c) fast-STIR (2288/60/4; echo train length, 11; FOV, 280 × 280 mm; matrix size, 264 × 512; acquisition time, 7 minutes 21 seconds).

The acquisition parameters for the MT-GE and the fast-STIR sequences were chosen to match, within the machine's constraints, those suggested as optimal by previous studies (3, 6).

In addition to these sequences, and only in the patients, we obtained contrast-enhanced T1-weighted CSE studies 5 minutes after the injection of gadopentetate dimeglumine (0.1 mmol/kg). Parameters for this sequence were 500/12/2; FOV, 245 × 280 mm; matrix size, 192 × 256; acquisition time, 3 minutes 15 seconds. This sequence was performed to ascertain how many of the lesions seen with the other sequences could be classified as T1 hypointense or contrast-enhancing.

For all the images, eight contiguous interleaved 3-mm-thick sagittal sections were obtained with an intersection gap of 0.3 mm. All images were printed on film by a single technician, who was asked to use a different window setting for each sequence that provided optimal visibility of the spinal cord lesions for that sequence.

Image Review

A review of all the images was performed in two stages by two experienced observers who examined the hard copies side-by-side and came to an agreement about the presence and number of lesions. Since there were obvious contrast differences, the observers could not be blinded to the type of sequence. At stage 1, each of the sequences from each subject was evaluated randomly, and lesions were marked on the hard copies. At this stage, the observers did not know to whom the images belonged. When the MT-GE images were considered, both images (ie, with and without the MT pulse) were viewed side-by-side in order to increase confidence in lesion identification. At stage 2 of image analysis, which occurred 1 month after stage 1 was completed, the two observers met again and reviewed all sequences from the same subject simultaneously in order to clarify the reasons for any differences in the sensitivities of the three sequences. In addition, ghost artifacts from subject motion or CSF flow, and truncation-type artifacts were classified as absent, not affecting or reducing the confidence of the reading. During this second review, a retrospective count of lesions was performed for each sequence: when the observers agreed that a lesion not previously seen on one of the three sequences could be identified using the information from one or both of the other two, this lesion was added to the count. Conversely, when a hyperintense area, which was counted as a lesion at stage 1, was, on reflection, considered not to be a lesion using the information coming from the other sequences, it was removed from the previous count. The reasons that might explain these discrepancies were recorded. Once the lesions were identified, they were classified according to their location in the cervical cord and their length relative to the spacing of the vertebral bodies. They were also classified as lesions that either occupied or did not occupy the entire cord cross-sectional area; the latter were then divided into mainly anterior, central, or posterior lesions. It was also noted whether the cord morphology was altered by the presence of lesions (ie, whether there was cord swelling or atrophy). Using contrast-enhanced T1-weighted images, the lesions that appeared hypointense or enhancing were also counted.

Table 1: Number of cervical cord lesions seen using each technique at stages 1 and 2 of image review

	Stage 1	Stage 2
FSE	65	83
MT-GE	88	101
Fast-STIR	108	113

Note.—FSE indicates fast spin-echo; MT-GE, magnetization transfer-prepared gradient-echo; fast-STIR, fast short inversion-time inversion recovery.

Statistical Analysis

The number of lesions detected at the end of stages 1 and 2 of the image review process for each technique was entered into the analysis. Differences in the number of lesions detected by the three sequences at the end of each stage were evaluated by fitting the raw data into a Poisson model, considering the patients in blocks. Then, the likelihood ratio test was used to assess heterogeneity. The differences between the three techniques in the number of abnormal findings, in the prevalence of images with artifacts, and in the number of false-positive and false-negative findings were tested using the χ^2-test.

Results

No abnormalities were found in the healthy control subjects on any of the sequences. The numbers of lesions detected by each of the three techniques at the end of stage 1 and stage 2 of image analysis are shown in Table 1. In Tables 2 and 3, the reasons for false-negative and false-positive findings and

Table 2: Number, reason for misinterpretation, and location of lesions considered to be false negative at stage 2 of image analysis for each technique

	No.	Reason for Misinterpretation (No.)	Location (No.)
FSE	18	Slight hyperintensity (10)	C2 (5)
		Movement artifacts (5)	C2–C3 (4)
		Flow artifacts (3)	C3–C4 (1)
			C4–C5 (1)
			C5 (1)
			C5–C6 (3)
			C6 (1)
			C7 (2)
MT-GE	14	Slight hyperintensity (10)	C2 (4)
		Movement artifacts (2)	C3–C4 (1)
		Flow artifacts (2)	C2–C3 (1)
			C4 (1)
			C4–C5 (1)
			C6 (2)
			C6–C7 (1)
			C7 (3)
Fast-STIR	6	Slight hyperintensity (2)	C2 (2)
		Movement artifacts (1)	C3 (1)
		Flow artifacts (3)	C4–C5 (1)
			C6 (1)
			C7 (1)

Note.—FSE indicates fast spin-echo; MT-GE; magnetization transfer–prepared gradient-echo; fast-STIR; fast short-inversion-time inversion recovery.

Table 3: Number, reason for misinterpretation, and location of lesions considered to be false positive at stage 2 of image analysis for each technique

	No.	Reason for Misinterpretation	Location
FSE	0	…	…
MT-GE	1	Movement artifacts	C2–C3
Fast-STIR	1	Movement artifacts	C4–C6

Note.—FSE indicates fast spin-echo; MT-GE; magnetization transfer–prepared gradient-echo; fast-STIR; fast short-inversion-time inversion recovery.

their locations are reported for each of the three techniques.

At the end of stage 1 of image analysis, a mean of 1.16 cord lesions per patient (95% confidence interval [CI] = 0.91 to 1.48) were seen on the FSE images, 1.57 (95% CI = 1.28 to 1.94) on the MT-GE images, and 1.92 (95% CI = 1.60 to 2.33) on the fast-STIR images. Taking FSE as the reference technique, MT-GE showed on average 35% more (95% CI = −2% to +86%) and fast-STIR 66% more (95% CI = +22% to +126%) lesions (χ^2-test for heterogeneity = 10.8 [df = 2], P = .005).

No lesions were seen on 17 FSE images, seven MT-GE images, and seven fast-STIR images. Thus, 70% of the FSE images and 87% of the MT-GE and fast-STIR images showed abnormal findings. A single cervical cord lesion was found on 23 FSE images (41%), on 26 MT-GE images (46%), and on 19 fast-STIR images (34%); and two or more lesions were found on 16 FSE images (29%), on 23 MT-GE images (46%), and on 30 fast-STIR (54%) images. These differences were statistically significant (P = .02).

At the end of stage 2 (ie, after the retrospective count of lesions), 1.48 cord lesions per patient (95% CI = 1.20 to 1.84) were detected on FSE images, 1.80 (95% CI = 1.48 to 2.19) on MT-GE images, and 2.02 (95% CI = 1.48 to 2.19) on fast-STIR images. Taking FSE as the reference technique, MT-GE detected on average 22% more (95% CI = −9% to +63%) and fast-STIR 36% more (95% CI = +3% to +81%) lesions (χ^2-test for heterogeneity = 4.7 [df = 2], P = .09). The percentages of false-positive and false-negative lesions were 22% for FSE, 16% for MT-GE, and 6% for fast-STIR (P = .006). No lesions were seen on 12 FSE images (21%) or on six (11%) of the MT-GE and fast-STIR images.

Considering the three sequences together, no lesions were seen on the images from six patients. In the remaining 50 patients (89%), 113 lesions were seen. Seventy-two lesions were seen on all three sequences, 25 were seen on MT-GE and fast-STIR images only (Figs 1 and 2), six on FSE and fast-STIR images only (Fig 2), one on FSE and MT-GE images only, seven on fast-STIR images only, and two on MT-GE images only. Four lesions were seen as discrete abnormalities on FSE images: they were not counted as individual lesions on MT-GE and fast-STIR images, since they were included in larger abnormalities. Another three lesions were discrete on fast-STIR images, whereas they were part of larger areas of abnormalities on FSE and MT-GE images. One lesion counted separately on MT-GE images was included with larger abnormalities on the other two images.

The length of 55 lesions (49%) was equal to or shorter than one vertebral segment; 47 lesions (42%) were equal to or shorter than two vertebral segments; and the remaining 11 lesions (9%) were longer than two vertebral segments. Lesion location in the cervical cord was as follows: C1 = 1, C2 = 24, C2–C3 = 17, C2–C4 = 7, C2–C6 = 1, C3 = 7, C3–C4 = 16, C3–C5 = 1, C4 = 4; C4–C5 = 5, C5 = 3, C5–C6 = 7, C5–C7 = 2, C6 = 8, C6–C7 = 1, C7 = 8, and C7–T1 = 1. Thus, 83 lesions (73%) involved the upper cervical cord (ie, C1–C4) either alone or in association with part of the lower cervical cord. Thirty-four lesions (30%) occupied the whole cross-sectional area of the cord; 46 (41%) were posterior, 26 (23%) were anterior, and seven (6%) were central. The majority of lesions did not alter cord morphology; atrophy of the cord was identified in association with two lesions (2%) and swelling of the cord was identified in association with 13 lesions (11%). Eight lesions (7%) were enhancing and nine (8%) were hypointense on postcontrast T1-weighted images.

In Table 4, the prevalence of images with or without artifacts is reported for each of the three

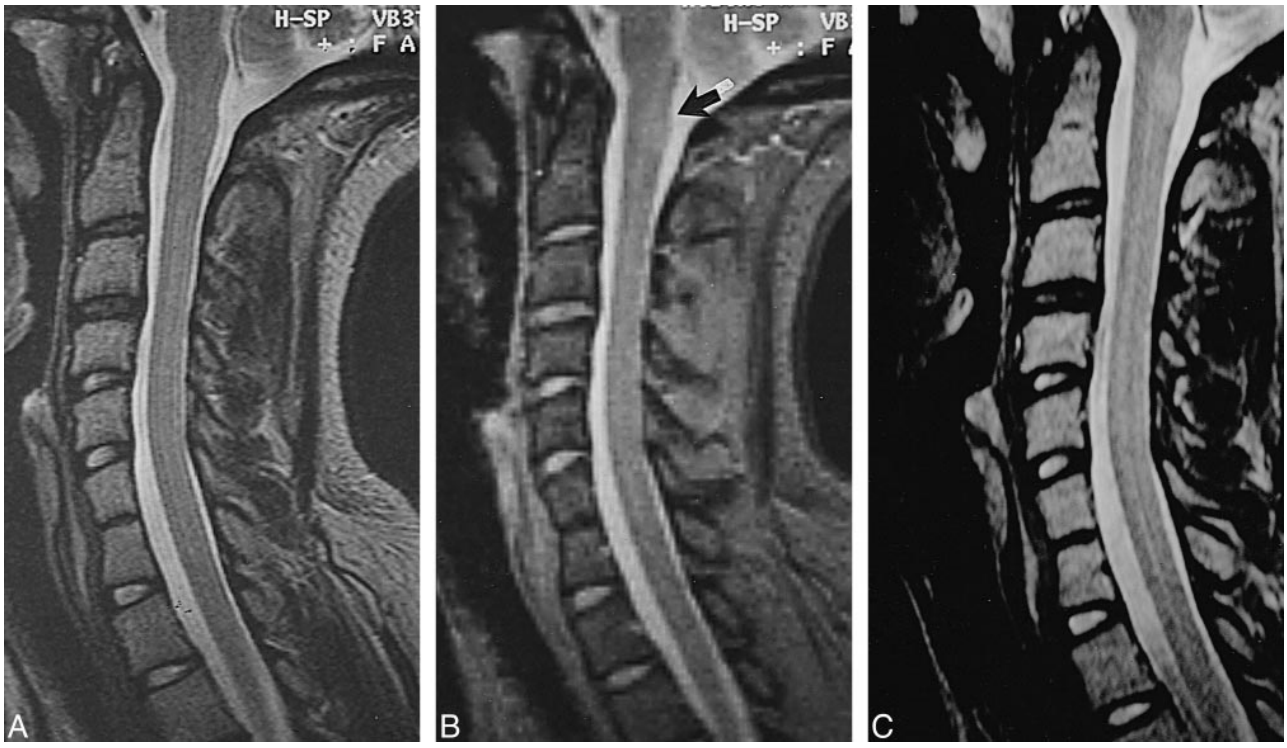

FIG 1. Sagittal 3-mm-thick sections of the cervical cord in a patient with relapsing-remitting MS.
A, FSE (4700/112/3) sequence.
B, MT-GE (600/10/2) sequence.
C, Fast-STIR (2288/60/4; TI = 110) sequence.
One lesion is seen at the C1 level in *B* (*arrow*) and *C.*

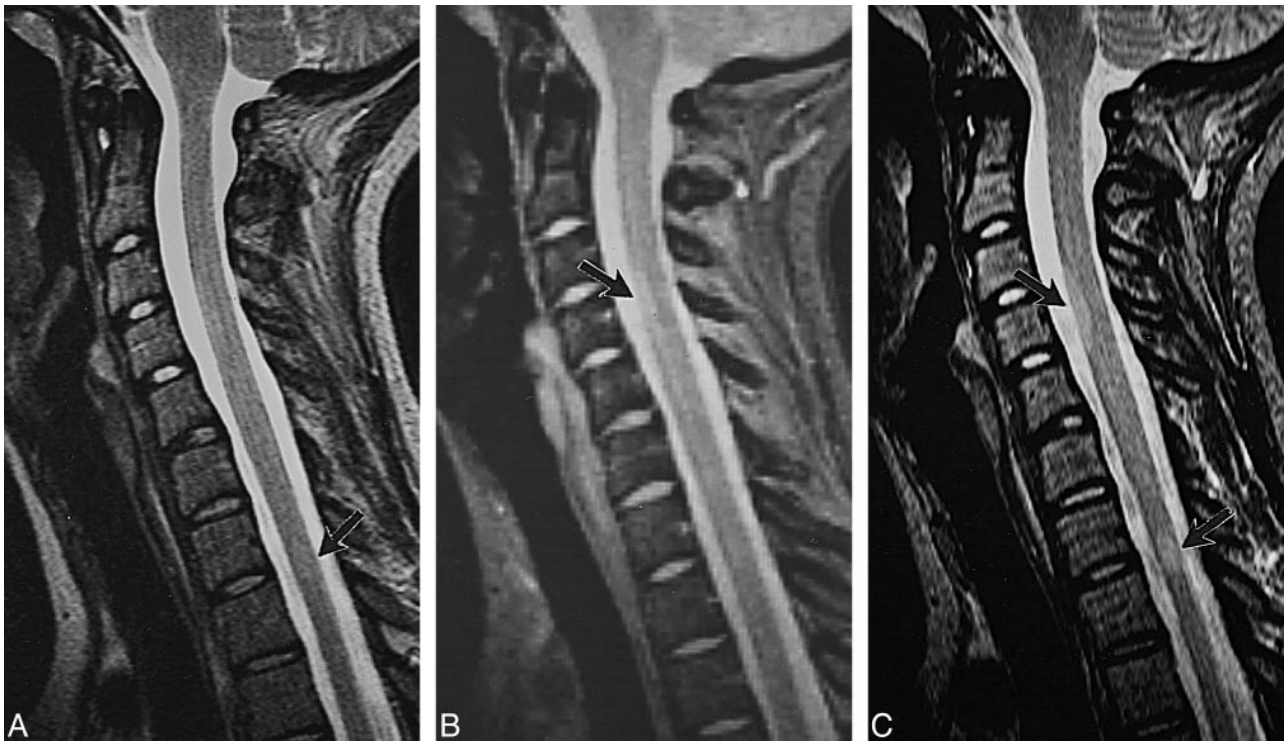

FIG 2. Sagittal 3-mm-thick sections of the cervical cord in a patient with relapsing-remitting MS.
A, FSE (4700/112/3) sequence.
B, MT-GE (600/10/2) sequence.
C, Fast-STIR (2288/60/4; TI = 110) sequence.
Two lesions, one anterior at C4 and one central at C7–T1, are visible in *C* (*arrow*). Only the C4 lesion is visible in *B* (*arrow*), and only the C7–T1 lesion is visible in *A* (*arrow*).

Table 4: Number of images with and without artifacts classified according to the severity

Score for Artifacts	FSE	MT-GE	Fast-STIR
0	38	31	36
1	11	20	14
2	7	5	6

Note.—Score for artifacts: 0 = absent, 1 = not affecting the reading confidence, 2 = reducing the reading confidence.

sequences. Although the number of MT-GE and fast-STIR images with artifacts that did not reduce confidence in the reading were higher than the corresponding number of FSE images, no statistically significant difference was found between the three sequences regarding the frequency and severity of artifacts.

Discussion

Improving MS lesion detection in the spinal cord on MR images is important for two reasons. First, the presence of cord lesions may increase confidence when making a diagnosis of MS, since cord lesions do not develop with aging per se (4) and are therefore more specific to MS than are cerebral white matter lesions. In addition, cord lesions may be seen in patients presenting with a clinical picture suggestive of MS but with normal findings on brain MR images (22, 23), and have been reported in 30% of patients presenting with clinically isolated syndromes suggestive of MS but not involving the cord (24). High-quality cord MR images may also reveal other conditions that clinically mimic MS (25). Second, acute MS symptoms are more often caused by cord lesions than by brain lesions (4, 26, 27), and a recent study (6) found that cord abnormalities correlate well with fixed spinal symptoms and degree of physical disability. Thus, improving the sensitivity of cord MR imaging may lead to a better understanding of disease evolution.

Previous studies have shown that the sensitivity of FSE is similar to that of CSE for detecting spinal cord lesions in MS (7, 12), while some preliminary studies, but not all (5, 17), have found that MT-GE (18) and fast-STIR (3) sequences may offer improved sensitivity. In the present study, we compared the sensitivities of an MT-GE and a fast-STIR sequence with that of FSE in a large sample of MS patients. Although we recognize that several factors limit the ability of T2-weighted FSE sequences to show subtle spinal cord abnormalities (3, 7), we chose FSE instead of CSE as the reference technique for imaging the cord because FSE is increasingly being used in routine neuroradiologic practice for its short acquisition time. In addition, we chose not to include a fast-FLAIR sequence in this study because four previous studies (3, 14–16) have shown fast-FLAIR to be much less sensitive than FSE in the detection of cord abnormalities in MS.

Our study indicates that both MT-GE and fast-STIR sequences reveal more cervical cord MS lesions than FSE, and that fast-STIR has the best sensitivity of the three sequences. At the end of stage 1 of image analysis, which most closely resembles routine radiologic practice, our fast-STIR sequence showed more than double the number of lesions seen with FSE, and about 30% more lesions than the MT-GE sequence. MT-GE and fast-STIR images were more frequently abnormal than FSE images and (particularly for fast-STIR) more frequently showed two or more cervical cord lesions. The demonstration of multiple abnormalities (spatial dissemination of lesions) in the cord is essential for diagnosing MS (19) and might be of particular value in patients with few or no brain abnormalities, such as can occur in cases of primary progressive MS (28).

The better performance of the fast-STIR sequence may be attributable to the synergistic effect of prolonged T1 and T2 relaxation times (29); this is particularly advantageous in lesions with only slightly increased T2, as might be the case for chronic MS lesions. Thus, although the sensitivity of the FSE sequence might be improved by using a dual-echo sequence or by acquiring it with shorter TEs and echo train lengths (12), we believe that it is unlikely that such refinements would change the situation a great deal. Admittedly, the fast-STIR sequence had a slightly longer acquisition time, although increasing the number of averages in the FSE image is unlikely to change the sensitivity dramatically. The same applies to CSE imaging, which has been shown to detect only slightly more cord lesions than FSE (3, 7).

As expected, the retrospective analysis smoothed out the differences among sequences. However, another aspect that favors the fast-STIR sequence is that the number of false-positive and false-negative lesions seen during the retrospective phase of the image analysis was much smaller than those of the other sequences, although a standard of reference for defining false-positive and false-negative rates of these sequences is not available, and definite conclusions cannot be reached. Nevertheless, the reduced number of false-positive and false-negative findings on fast-STIR images is important because it suggests that reporting of cervical cord abnormalities in MS may be more reliable when using fast-STIR and, as a consequence, the diagnostic certainty increased.

The prevalence of spinal cord abnormalities found in this study of randomly selected patients with clinically definite MS was 90%, a figure that is very similar to those found in a postmortem study (1) and in more recent MR studies (3–6, 10). This is of interest because not only was our sample large but it was representative of the range of clinical phenotypes, disabilities, and disease durations found in MS. In addition, our patients were not selected because of spinal cord symptoms or because they had a progressive disease evolution, and

it is therefore unlikely that our 90% prevalence of cord lesions is an overestimate. This study also confirms, as shown in previous studies (4, 10, 30, 31), that spinal lesions in MS have the following typical characteristics: they are shorter than two vertebral segments in length, they do not occupy the entire cord cross-sectional area, they are located in the upper cervical cord, they do not alter cord morphology, and they are not hypointense on T1-weighted images. These characteristics suggest a role for cervical cord imaging in diagnosing MS, particularly in cases with few or no lesions in the brain (22, 23), as is often seen in patients with primary progressive MS (28), in elderly patients who may have multiple nonspecific hyperintense abnormalities in the brain, or in patients who present with clinically isolated syndromes. Here it is necessary to demonstrate a spatial dissemination of the lesions within the CNS. On the other hand, atypical features of spinal cord lesions (eg, long lesions or severe atrophy or swelling) should alert the clinician to other possible conditions.

Consistent with previous studies, we found that few cord lesions enhanced after contrast administration, since, in MS, enhancement is much less frequent in the cord than in the brain (26, 32). In our study, patients were included regardless of spinal cord symptoms, but they were outside phases of clinically manifested exacerbation. Thus, it is likely that the true frequency of enhancement is higher in these patients (27). Enhancement might become more apparent when scanning the entire cord (26, 27) or when using higher doses of contrast medium (33).

Conclusion

The fast-STIR sequence we used is a sensitive technique for detecting cervical cord lesions in patients with clinically definite MS and may have a role in the diagnosis of this disease. Longitudinal studies are needed to determine whether this sequence is useful for detecting changes in cord lesions over time and, as a consequence, whether it can contribute to our understanding of MS evolution.

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