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Gd-DTPA–Enhanced MR of Suspected Spinal Multiple Sclerosis

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A prospective study was undertaken to evaluate the potential of Gd-DTPA–enhanced MR to differentiate active from inactive demyelinating lesions of the cervical spinal cord. Five patients with elongated high-signal-intensity lesions in the cervical cord on long TR/TE spin-echo MR images and a clinical suspicion of demyelinating disease had MR before and after IV Gd-DTPA. Delayed contrast enhancement (after 45–60 min) of the lesions was seen on short TR/TE images in two patients with clinically active disease, but no enhancement could be detected in three patients with stable disease. The patients with active disease underwent repeated MR examinations until the enhancement disappeared. The decrease in Gd-DTPA enhancement paralleled a decrease in clinical signs and symptoms of cervical myelopathy.

MR is useful in evaluating patients suspected of having demyelinating disease. The MR finding of asymptomatic lesions in the brain lends support to the diagnosis of multiple sclerosis. Other possible causes of myelopathy, such as spinal cord compression and intramedullary tumor, can be excluded with the use of MR.

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MR is the only technique that allows direct visualization of demyelinating lesions in the spinal cord [1–3]. Such lesions are usually elongated and have a high signal intensity on long TR/TE spin-echo images. No abnormality is seen on short TR/TE images unless the cord is enlarged because of focal edema accompanying an acute lesion or is atrophic in chronic disease [2, 3]. Acute demyelinating lesions are indistinguishable from older, chronic lesions on long TR/TE images [4, 5]. In patients with clinically definite or suspected multiple sclerosis (MS), a correlation has been described between recent clinical exacerbation of the disease and contrast enhancement of lesions in the brain on CT [6–8] as well as on MR [4, 9]. A similar correlation might be expected for demyelinating lesions in the spinal cord, but none has, to our knowledge, been reported. The aim of this prospective investigation was to evaluate the potential of Gd-DTPA–enhanced MR in differentiating acute, active demyelinating lesions from inactive lesions in the cervical spinal cord.

Subjects and Methods

Five patients with elongated high-signal-intensity lesions in the cervical spinal cord on long TR/TE images and a clinical suspicion of demyelinating disease were included in the study. Clinical data on the patients are summarized in Table 1. None of the patients had a definite MS diagnosis since all had isolated myelopathy without clinical evidence of lesions in any other part of the CNS.

In all patients, visual evoked potentials (VEPs) were recorded and CSF was examined for oligoclonal bands and immunoglobulin G (IgG)/albumin ratio.

MR was performed with a 0.3-T imaging system with a vertical magnetic field (Fonar β-3000 M). A solenoid surface coil wrapped around the neck was used for examination of the

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TABLE 1: Clinical, Laboratory, and MR Findings in Patients with Suspected Demyelinating Disease

Type of Finding	Case 1	Case 2	Case 3	Case 4	Case 5
Clinical					
Age (years)	43	40	44	49	44
Gender	F	M	F	F	M
Duration of disease	1 mo	1.5 mo	4 mo	9 yr	21 yr
Clinical course	One attack	One attack	One attack	Progressive	Attacks, progressive
Laboratory					
Intrathecal IgG synthesis	Pathologic	Normal	Pathologic	Pathologic	Pathologic
Visual evoked potentials	Pathologic	Pathologic	Normal	Pathologic	Pathologic
MR					
Clinically active or stable	Active	Active	Stable	Stable	Stable
Cervical cord (long TR/TE)	Lesion	Lesion	Lesion	Lesion	Lesion
Cord enlargement or atrophy (short TR/TE)	Enlargement	Normal	Normal	Atrophy	Atrophy
Contrast enhancement of cervical cord (short TR/TE)	Yes	Yes	No	No	No
Brain (long TR/TE)	One lesion	Normal	Multiple lesions	Normal	Multiple lesions

Note.—F = female; M = male; mo = month(s); yr = year(s); IgG = immunoglobulin G.

cervical spine. Sagittal images were obtained using spin-echo pulse sequences with a short TR/TE, 500/16/3 (TR/TE/excitations) in four patients and 300/16/5 in one, as well as a long TR/TE, 2000/84/1. A 256 × 256 matrix was used and the pixel size was 1.0 mm. The slice thickness was 5 mm with a 2.1-mm gap between slices. Gd-DTPA was administered IV at a dose of 0.1 mmol/kg body weight. Imaging protocols consisted of short TR/TE images before and 10, 45, and 60 min and in one case also 24 hr after the patient received Gd-DTPA. Long TR/TE images were obtained before and 30 min after Gd-DTPA injection. In two patients with contrast enhancement on the primary MR examination (cases 1 and 2), MR before and after Gd-DTPA was repeated 3 months later. In case 1 a second follow-up examination was performed 5½ months after the first MR study.

Signal-intensity measurements were performed to estimate the degree of contrast between lesion and normal cord on short TR/TE images before and after IV administration of Gd-DTPA. The signal intensity was determined in a region of interest in the lesion and was compared with the signal intensity in the cord cranial and caudad to the lesion.

MR of the brain without Gd-DTPA was performed using a head coil. Axial long TR/TE images (2000/60/1) with a 7-mm slice thickness and 3-mm interslice gap were obtained.

Three patients (cases 1–3) who had had their first attack of cervical myelopathy (Table 1) underwent a neurologic examination within 1 week before the primary MR study. One patient (case 1) was examined with MR 4 weeks and another (case 2) 6 weeks after the onset of the attack; at that time none of the patients showed clinical signs of remission of the attack. In case 3, MR was performed 4 months after the onset of the attack when the patient was in a clinically stable phase of the disease. Cases 4 and 5, with a slowly progressing myelopathy (Table 1), did not show any notable worsening of disease during the weeks before and after the MR examination. Cases 1 and 2 were categorized as clinically active and cases 3–5 as clinically stable at the time of the primary MR examination.

In cases 1 and 2, repeated neurologic examinations were performed during the course of the attack and one neurologic examination was performed after the last follow-up MR study.

Results

The laboratory tests for intrathecal synthesis of IgG were positive in all patients except case 2. VEPs showed a pathologic response in all except case 3 (Table 1). All patients had elongated high-signal-intensity lesions in the cervical spinal cord on long TR/TE images before injection of Gd-DTPA (Figs. 1A, 2A, and 3A).

Clinically Stable Patients

On short TR/TE images, general atrophy of the cervical cord was seen in case 5 and local atrophy at the level of the lesion in case 4 (Fig. 1B). These two patients had a long duration of disease (Table 1). In case 3, with a shorter duration of the disease, the cord had a normal sagittal diameter. No Gd-DTPA enhancement was observed in these three patients. Two of the patients had multiple asymptomatic high-signal-intensity lesions compatible with MS plaques in the brain on long TR/TE images, whereas MR of the brain was normal in the third patient.

Clinically Active Patients

The cervical cord was enlarged at the level of the lesion on short TR/TE images in case 1 (Fig. 2B) and had a normal configuration in case 2 (Fig. 3B).

Contrast enhancement of the lesion was observed in both patients on short TR/TE images. The enhancement was best seen on images obtained 45 and 60 min after Gd-DTPA injection (Figs. 2 and 3). Signal-intensity measurements revealed a 25% contrast enhancement 60 min after Gd-DTPA in both cases, but the two studies could not be fully compared quantitatively owing to differences in TR (300 msec in case 1 and 500 msec in case 2). A slight enhancement was already present 10 min after injection but was not as obvious as after 45 and 60 min (Figs. 2 and 3). No remaining enhancement was detected after 24 hr (case 1) (Fig. 2). A slight enhancement was also discerned on long TR/TE images 30 min after Gd-DTPA injection.

In case 1 a follow-up MR examination 3 months after the first MR study showed that the enlargement of the cord had

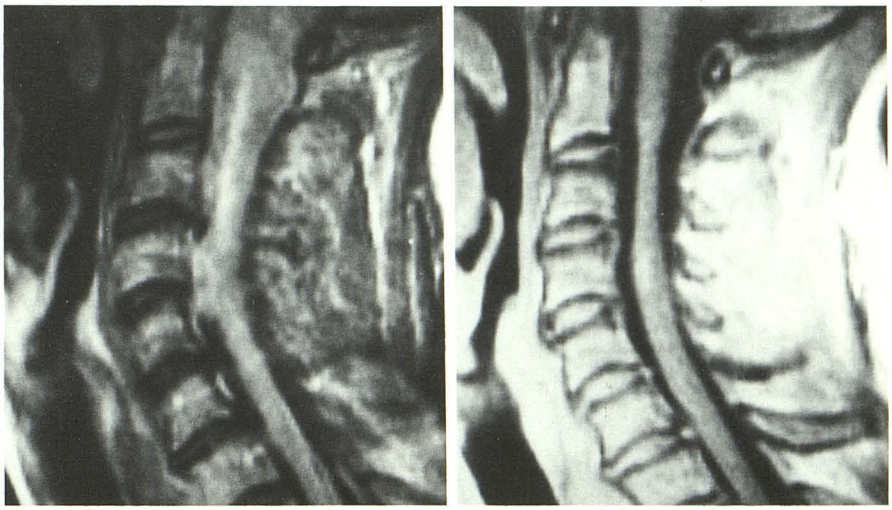

Fig. 1.—Case 4: 49-year-old woman with slowly progressing myelopathy, clinically stable at time of MR.

***A*, Long TR/TE image (2000/84) shows elongated high-signal-intensity lesion in cord at C2–C3.**

***B*, Short TR/TE image (500/16) after Gd-DTPA shows local atrophy of cervical cord at C2–C3 and no contrast enhancement. Area of increased signal in cord at level of vertebral body of C4 is considered an artifact since it was present also on corresponding image before Gd-DTPA injection.**

decreased and the contrast enhancement on short TR/TE images appeared less intense 10 as well as 60 min after Gd-DTPA (Fig. 2G). In a third MR examination 5½ months after the first, the width of the cord was normal and no contrast enhancement was present (Fig. 2H). The lesion could not be identified on long TR/TE images without Gd-DTPA after 3 and 5½ months. In case 2 the contrast enhancement on short TR/TE images had disappeared completely after 3 months and the lesion could not be detected on long TR/TE images without Gd-DTPA. In both patients the decrease in contrast enhancement paralleled a decrease in clinical signs and symptoms of cervical myelopathy.

MR of the brain showed one small high-signal-intensity lesion in case 1 and was normal in case 2 (Table 1).

No adverse reactions to IV administration of Gd-DTPA were observed in the five patients.

Discussion

In this investigation we found delayed Gd-DTPA enhancement of suspected demyelinating lesions in the cervical cord in two patients with active disease but no enhancement in three patients with clinically stable disease (Table 1; Figs. 1–3). The two patients with active disease underwent repeated MR examinations until the enhancement had disappeared (Fig. 2), and the decrease in enhancement could be correlated with a decrease in clinical signs and symptoms.

The possibility of differentiating active demyelinating lesions from inactive lesions in the brain has been investigated by iodinated contrast-enhanced CT [6–8] and Gd-DTPA–enhanced MR [4, 5, 9, 10]. The inflammatory process of an active demyelinating lesion is associated with a transient breakdown of the blood-brain barrier, which is responsible for the contrast enhancement seen on CT and MR [4, 7]. The enhancement of active but not of inactive lesions in the cervical cord in our study is in agreement with the previous CT and MR investigations of lesions in the brain, in which a correlation between contrast enhancement and clinical activity has been found in most patients [4–9]. Recently, suspected Gd-DTPA enhancement of a clinically active lesion in the cervical cord on MR was reported in a patient with definite MS, whereas another patient with clinically active suspected MS did not exhibit any enhancement of a lesion in the cord [11]. In the same study, a third patient with definite MS without acute symptoms showed no enhancement of a cervical lesion. Because inactive lesions are not depicted on Gd-DTPA–enhanced short TR/TE images, a long TR/TE scan without Gd-DTPA should always be obtained first to detect both active and inactive lesions. Most acute demyelinating lesions are accompanied by edema as the increased permeability of the blood-brain barrier allows a leakage of water [3, 6]. This may cause transient local enlargement of the cord at the level of the lesion [2, 3], as was seen in one of our patients. With resolution of edema, the T2 relaxation time frequently shortens and the lesion diminishes, which may make detection more difficult on long TR/TE images [3].

The delayed enhancement, best seen about 45–60 min after IV injection of Gd-DTPA in our study, correlates with previously reported delayed iodinated contrast enhancement of MS plaques in the brain on CT [6–8]. Gd-DTPA enhancement of MS plaques in the brain was reported to be visualized on short TR/TE images obtained only 3 min after contrast injection in most patients, whereas a few lesions were better seen on delayed (55-min) images [4]. In the same investigation, initial enhancement displayed on a 3-min image was absent on the 55-min image in two patients [4]. Enhancement of intracranial and intraspinal tumors usually is most marked immediately after injection of contrast material [11–15], but delayed scans have recently been reported to show a further increase in signal intensity in some tumors, especially small ones [15, 16]. A delay in enhancement has been observed also in necrotic tumor tissue [11, 13]. It is presumed that demyelinating lesions produce a minor blood-brain barrier disruption compared with the disruption associated with malignant tumors [8]. An increased dose of contrast medium and a delay before CT scanning allow a larger amount of contrast medium to leak from the intravascular to the extra-

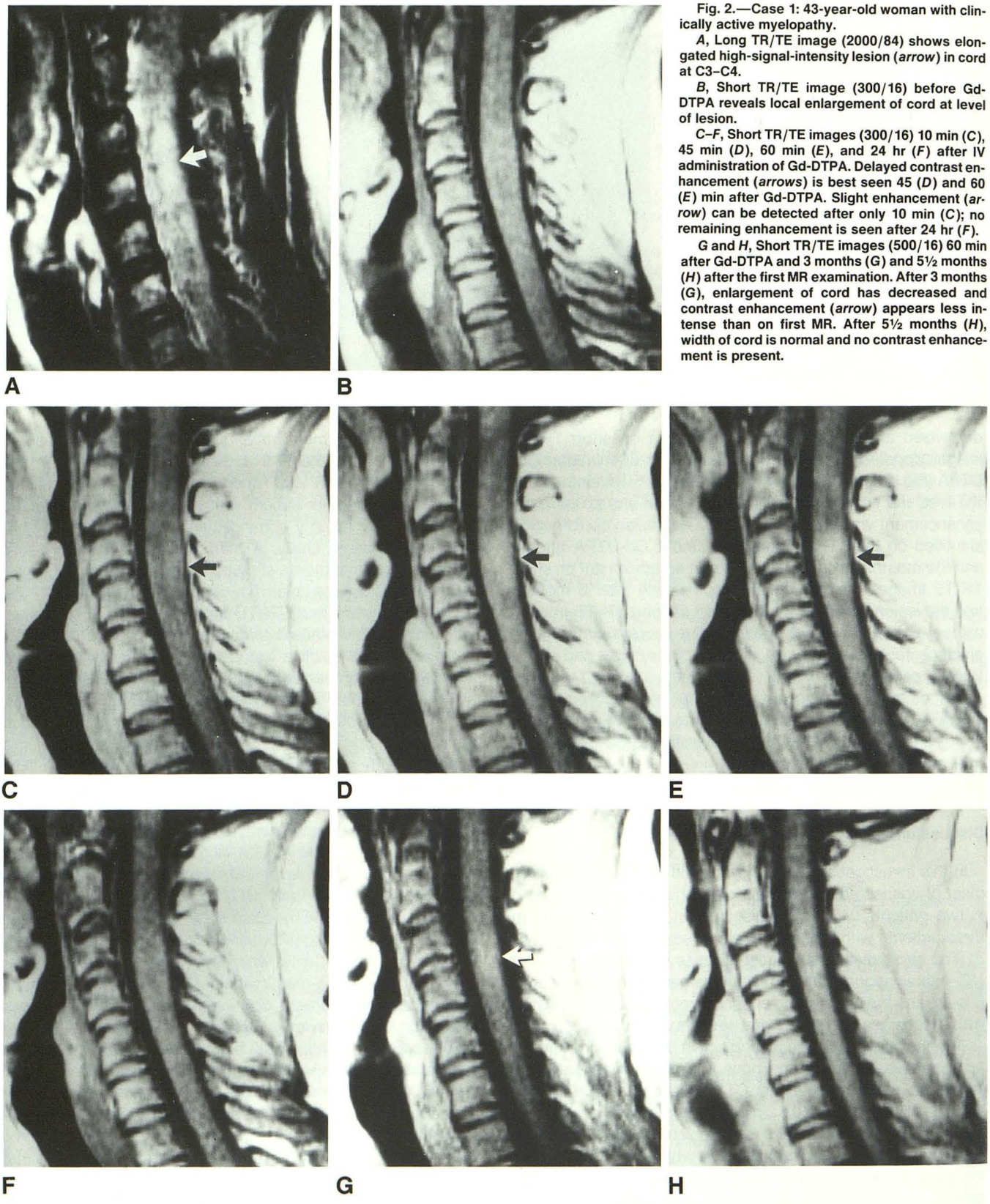

Fig. 2.—Case 1: 43-year-old woman with clinically active myelopathy.

A, Long TR/TE image (2000/84) shows elongated high-signal-intensity lesion (*arrow*) in cord at C3–C4.

B, Short TR/TE image (300/16) before Gd-DTPA reveals local enlargement of cord at level of lesion.

C–F, Short TR/TE images (300/16) 10 min (*C*), 45 min (*D*), 60 min (*E*), and 24 hr (*F*) after IV administration of Gd-DTPA. Delayed contrast enhancement (*arrows*) is best seen 45 (*D*) and 60 (*E*) min after Gd-DTPA. Slight enhancement (*arrow*) can be detected after only 10 min (*C*); no remaining enhancement is seen after 24 hr (*F*).

G and *H*, Short TR/TE images (500/16) 60 min after Gd-DTPA and 3 months (*G*) and 5½ months (*H*) after the first MR examination. After 3 months (*G*), enlargement of cord has decreased and contrast enhancement (*arrow*) appears less intense than on first MR. After 5½ months (*H*), width of cord is normal and no contrast enhancement is present.

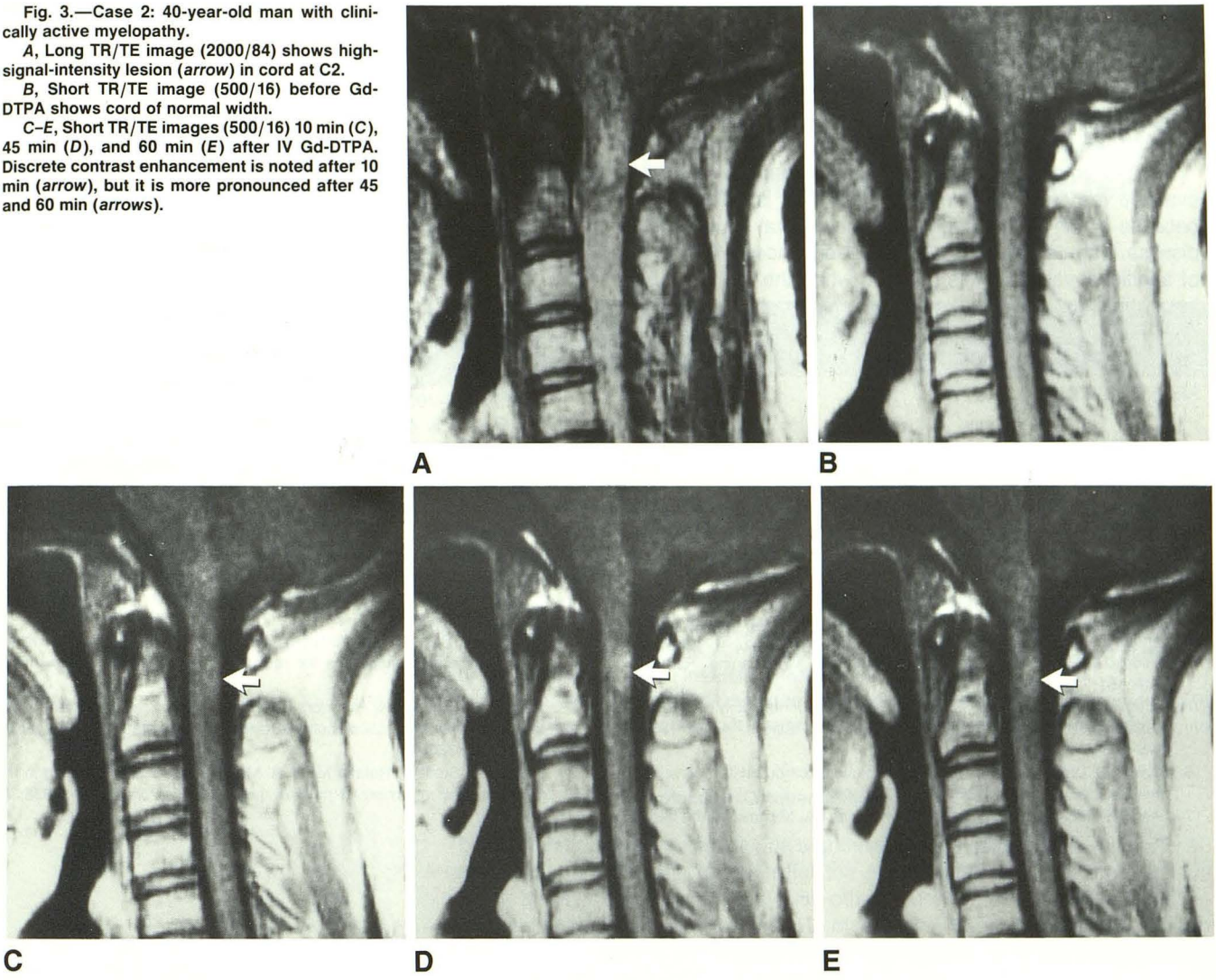

Fig. 3.—Case 2: 40-year-old man with clinically active myelopathy.

***A*, Long TR/TE image (2000/84) shows high-signal-intensity lesion (*arrow*) in cord at C2.**

***B*, Short TR/TE image (500/16) before Gd-DTPA shows cord of normal width.**

***C–E*, Short TR/TE images (500/16) 10 min (*C*), 45 min (*D*), and 60 min (*E*) after IV Gd-DTPA. Discrete contrast enhancement is noted after 10 min (*arrow*), but it is more pronounced after 45 and 60 min (*arrows*).**

cellular space and thereby improve the detection of demyelinating lesions in the brain [7, 8]. The same mechanism is probably responsible for the marked increase in signal intensity on delayed scans compared with the early postinjection scans of the spinal cord in our study. Because the Gd-DTPA enhancement pattern of lesions in the brain does not seem to be identical in all patients [4] and our myelopathy material is small, we suggest that early as well as delayed scans of suspected demyelinating lesions should be obtained after Gd-DTPA. If delayed scans had not been obtained in our investigation, the discrete contrast enhancement 10 min after Gd-DTPA would probably have been interpreted as equivocal.

The evolution of acute Gd-DTPA–enhancing cerebral demyelinating lesions to inactive nonenhancing lesions over time has been demonstrated on MR in a dog with experimental allergic encephalomyelitis [5]. The decrease in the Gd-DTPA enhancement of the lesions in the spinal cord over the course of the disease in two of our patients is in agreement with these findings. Presumably, the duration of the contrast enhancement is variable, correlating with the variable course of the disease in different patients.

MR is not required for confirmation when a definite diagnosis of MS has been made on clinical grounds. Clinically, dissemination of the lesions in space and time is included in the diagnostic criteria of MS [17]. In patients with isolated myelopathy and a clinical suspicion of demyelinating disease, as in our investigation, MR is useful for demonstrating asymptomatic lesions in the brain, lending further support to the diagnosis of MS. In patients with a normal MR scan of the brain, an MR examination of the spinal cord can provide support for the diagnosis of MS if elongated high-signal-intensity lesions are detected on long TR/TE images, especially if they are associated with local or general atrophy of the cord on short TR/TE images. In addition, other potential causes of myelopathy, such as spinal cord compression and intramedullary tumor, can be excluded [2, 3]. It should be emphasized that no MR findings are specific for MS and that neither CSF examination nor evoked potential recordings can be used as specific tests for MS [2, 18, 19]. MR can be used to support the diagnosis of MS by revealing dissemination in space, as mentioned above. In addition, Gd-DTPA–enhanced MR imaging may, in the future, be used as indirect support

of dissemination in time when contrast-enhancing active lesions and nonenhancing inactive lesions are observed in the same examination. This requires, however, further studies of the enhancement pattern of demyelinating lesions and a development of the technique to reliably detect enhancement of all active lesions.

Another potential use of MR in demyelinating disease is to evaluate the effect of treatment [20]. This is often difficult because of the great variability in the natural course of the disease. The use of serial Gd-DTPA–enhanced MR may be of additional value for this purpose when the technique has been improved.

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