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Magnetic Resonance Demonstration of Multiple Sclerosis Plaques in the Cervical Cord

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Magnetic resonance imaging (MRI) has been shown to be far more sensitive than computed tomography (CT) in the detection of multiple sclerosis plaques within the brain. Unlike CT, MRI is also able to detect multiple sclerosis in the brainstem and cerebellum. This report is the first description of MRI of multiple sclerosis plaques within the cervical spinal cord. Twenty-one patients with clinically typical multiple sclerosis had characteristic plaques within the brain. In 10 patients one or more plaques were identified in the cervical spinal cord. Plaques in the spinal cord were detected only in the upper cervical region using the 30-cm head radiofrequency coil. No lesions were identified using the larger-diameter body coil because of poorer signal-to-noise ratio. Further improvement in visualization of plaques in the lower cervical and thoracic spinal cord may depend on development of high-quality surface coils.

Multiple sclerosis (MS) is a widespread demyelinating disease of the central nervous system consisting of lesions widely separated in location as well as time of onset. MS has traditionally been a diagnosis of exclusion that has required evaluation of patients with multiple imaging studies including computed tomography (CT) of the head and myelography whenever symptoms attributable to a spinal cord lesion are present.

In recent years, an improved battery of nonimaging studies has been developed that greatly aids in establishing the clinical diagnosis of MS [1, 2]. These tests include visual, auditory, and somatosensory-evoked potentials. Cervical cerebrospinal fluid (CSF) analysis, including measurement of IgG and CSF electrophoresis for the detection of oligoclonal bands, is also extremely helpful. However, while these sophisticated tests increase the sensitivity and accuracy for diagnosing MS, they have several limitations. They are not positive in 100% of patients with MS, and patients with other diseases may have elevated IgG and oligoclonal bands within the CSF leading to false-positive diagnoses. In addition, even though the diagnosis of MS can be implied using a comprehensive battery of nonimaging studies, these tests do not provide the information needed for localizing MS lesions, determining the number and size of lesions, and determining their sites of distribution. This is important not only for diagnosis but also for determination of extent of the disease and subsequent prognosis. Moreover, this type of information is crucial in following patients, determining their response to therapy, and in evaluating the efficacy of proposed new treatment regimens. Efforts to obtain this information have been greatly hampered by the inability to reliably image MS plaques.

CT of the brain, especially with high-dose intravenous contrast enhancement, has been used to detect some MS plaques [3–5], but CT also has serious limitations. Small, low-density plaques often are not visualized on the CT study, and even large periventricular plaques may not be seen since their density may approximate that of CSF within the ventricles, and they may be inseparable from the outline of the ventricular wall [6]. Partial-volume effects between CSF and the periventricular plaques further diminish the sensitivity of CT. Some demyelinating

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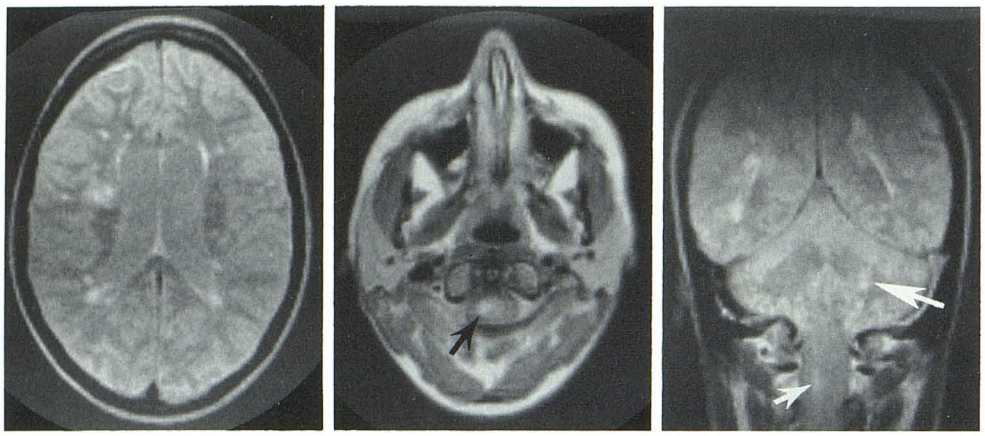


Fig. 1.—**A,** Characteristic changes of MS plaques. Abnormal areas of relative increased RF signal intensity in periventricular regions and within white matter of centrum semiovale. **B,** Transaxial MR image at level of C2. MS plaque in right side of spinal cord (*arrow*). Pathologically, spinal cord plaques often involve large cross-sectional areas and do not respect gray-white matter boundaries or fiber tracts. **C,** Coronal view confirms demyelinating plaque within upper cervical spinal cord at C2 (*small arrow*). Periventricular plaques around atrial trigones and prominent demyelinating plaque within left corpus medullare of cerebellum (*large arrow*).

plaques enhance after intravenous injection of iodinated contrast material, but this occurs only during an acute exacerbation when injury to the blood-brain barrier is present. After this acute phase, the enhancement resolves [7] and the plaques usually are no longer visible on CT, thus limiting the usefulness of the contrast-enhanced CT study even when using double-dose delayed technique. Furthermore, CT is not able to depict MS lesions within the optic nerves, brainstem, cerebellum, or spinal cord.

Several reports have indicated that magnetic resonance imaging (MRI) is extremely sensitive for the detection of MS plaques. When compared with CT, far more MS plaques are detected with MRI [8–11]. In addition, MRI studies have enabled detection of MS plaques in the brainstem and cerebellum [8].

Recently, we have been able to detect MS lesions in the cervical spinal cord in a number of patients. We believe this to be the first MRI description of MS plaques in the spinal cord. The implications of this capability for diagnosis, treatment, and follow-up of patients with MS are extremely important.

Subjects and Methods

All 21 patients in this study had strong clinical and laboratory evidence of MS. Each patient was given a detailed explanation of the MRI technique and was informed of the research nature of MRI. A signed informed consent was obtained in each case.

MRI studies were performed with a Diasonics MRI imager. This unit uses a superconducting magnet operating at a field strength of 0.35 T. The details of the system have been described [10, 12].

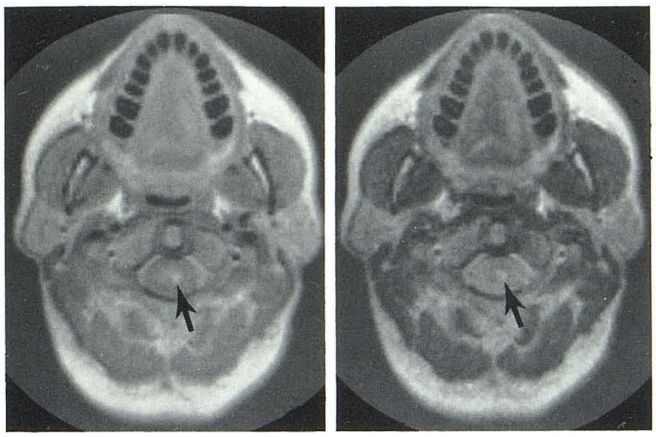
All images in the study were obtained using spin-echo (SE) technique with a pulse repetition rate (TR) of 1.5 or 2 sec. Two SEs were obtained routinely from each image using echo delay times (TEs) of 28 and 56 msec. Multislice technique was used enabling simultaneous acquisition of 15 images with a TR of 1.5 sec or 20 images with a TR of 2 sec. Slice thickness in each case was 7 mm with a center-to-center slice interval of 10 mm, resulting in a gap of 3 mm between adjacent slices.

The imaging protocol consisted of SE transaxial acquisition with a 2.0 sec TR followed by a coronal view using a TR of 1.5 sec. Orthogonal imaging planes minimize the "skip areas" that result from a single transaxial sequence due to the 3 mm gap between slices. While this same result can be obtained by using two imaging sequences in the transaxial plane and moving the patient table 5 mm between acquisitions, we prefer the former method since it also enables us to obtain two different views of the head. We find this useful whenever questionable lesions are present, since the second view provides confirmatory evidence in a different image plane. Furthermore, the second image plane provides additional information regarding the three-dimensional localization and extent of lesions. Using this protocol, we image from the top of the head to the lower cervical spine in two views and routinely visualize the cervical spinal cord to about the C4 or C5 level. All imaging is performed with the head radiofrequency (RF) receiver coil, which has an aperture of 30 cm.

Results

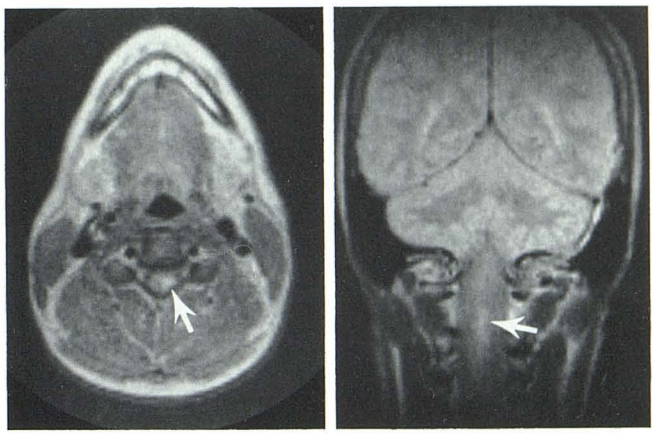
In all 21 patients with characteristic clinical and laboratory criteria of MS, typical MS plaques were demonstrated within the brain on MRI. The intracranial lesions were found in widely scattered locations, including the periventricular regions, the deep white matter of the centrum semiovale, the temporal lobes, the pons and midbrain, the middle cerebellar peduncles, and the corpus medullare of the cerebellar hemispheres.

Among the 21 patients, 10 (47.6%) also had findings characteristic of MS plaques within the cervical spinal cord (fig. 1). Six of the 10 patients with spinal cord lesions displayed a single cervical spinal cord lesion. In four patients, multiple lesions were demonstrated; two patients displayed two lesions, and two patients showed three lesions within the cervical spinal cord. The spinal cord plaques all had MRI signal characteristics similar to those in the brain with prolonged T1 and prolonged T2 relaxation times [11]. They were best shown on the second SE scan (i.e., 56 msec TE) as focal areas of high relative signal intensity (fig. 2). Although plaques were best seen on the 56 msec TE image using the 2 sec TR interval, in all cases plaques were also well shown on the SE scan, 56 msec TE, using 1.5 sec TR. In four patients, the MS plaques within the spinal cord correlated with localized neurologic symptoms. In the other six patients, the spinal cord plaques were seen as part of a widely disseminated demye-



A B

Fig. 2.—**A,** Demyelinating plaque within left side of cervical spinal cord (*arrow*) is area of slightly increased signal intensity on 28 msec TE image. **B,** 56 msec TE image. MS plaque (*arrow*) with greater contrast difference between relatively high-signal-intensity plaque and spinal cord, which now demonstrates decreased signal intensity relative to plaque and surrounding CSF. This indicates prolonged T2 relaxation time of MS plaque.



A B

Fig. 3.—**A,** Transaxial view. Prominent MS plaque in cervical cord (*arrow*), **B,** Coronal view. Demyelinating plaque within central part of spinal cord (*arrow*) extending from C2 to C3 corresponds well in position and appearance to transaxial view.

linating process, but did not directly correlate with the patient's presenting signs and symptoms. All patients in our series who had spinal cord lesions also had multiple intracranial MS plaques.

The possibility was considered that the cervical cord lesions could be artifacts. For several reasons, we concluded that they were indeed real findings. First, whenever the region of abnormality was imaged in more than one plane, the lesion was shown on both the transaxial and coronal images (fig. 3). Second, the lesions demonstrated high signal intensity on the SE scan, 56 msec TE. This precludes partial-volume artifact as a potential source of false-positive diagnosis for the spinal cord lesions. Finally, a review of 100 patients imaged with similar scanning techniques but who were undergoing examination of the head and neck for reasons other than MS or possible cervical spinal cord abnormalities revealed no findings within the cervical spinal cord similar to those demonstrated in the MS patients.

All of the cervical spinal cord plaques were detected in the upper half of the cervical spinal cord during routine evaluation of the head and neck using the head RF coil. No spinal cord demyelinating lesions were identified within the cervical or thoracic spinal cord when imaged with the larger-bore body RF coil.

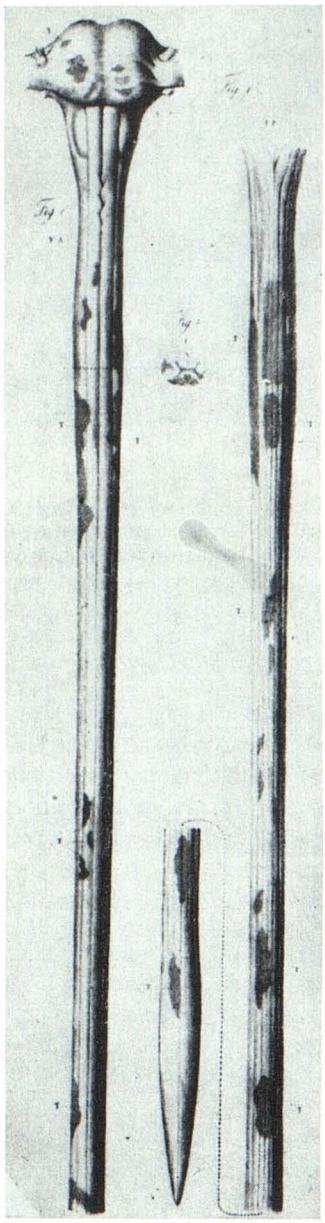
Discussion

The first descriptions of the pathology of MS by Cruveilhier [13] in about 1835 and Carswell [14] in 1838 both placed emphasis on the spinal cord lesions. Pathologically, spinal cord plaques are characterized by their elongated configuration, and they may extend longitudinally along the cord a distance of several centimeters. Cord lesions do not correspond to specific fiber tracts and do not respect gray-white matter boundaries. Plaques within the cord preferentially occur in the dorsal and lateral segments [15]. The initial drawing of Cruveilhier (fig. 4) illustrates the lesions of the spinal cord extremely well and shows their elongated configuration along the long axis of the spinal cord. This same appearance corresponds well to the coronal MR images of the MS plaques in our study.

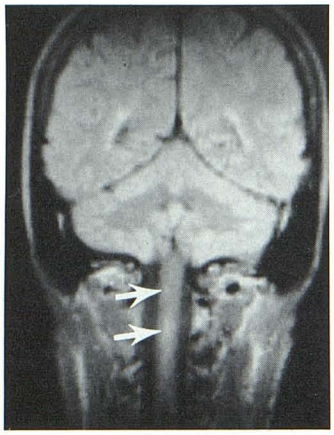
While early researchers considered MS predominantly a disease of the spinal cord, it was only later when it was recognized that pathologic diagnosis could be made routinely by detection of lesions within the brain that less emphasis was placed on careful removal and scrutiny of the entire spinal cord and more emphasis was placed on the brain. Nevertheless, it is well recognized pathologically and clinically that the spinal cord is one of the sites of predilection for MS plaques. Until now, however, visualization of these lesions using various imaging techniques including CT and myelography has not been possible. Although a single case report by Coin and Hucks-Folliss [16] described probable CT visualization of spinal cord enhancement in a patient with MS, this is not a reliable or reproducible method for detection of spinal cord demyelinating plaques.

For the first time MRI provides reproducible direct visualization of demyelinating plaques within the central nervous system. MRI is far more sensitive than CT in the detection of MS plaques within the brain [8–10], and previous reports have indicated that plaques can be easily visualized within the brainstem and cerebellum. In our present series, we have demonstrated for the first time the ability of MRI to detect plaques within the cervical spinal cord. Such lesions were present in nearly one-half of our patients with known MS. This provides further evidence for the extreme sensitivity of the MRI method for detection of demyelinating plaques.

It should be pointed out that there are several unresolved issues regarding the use of MRI for the evaluation and follow-up of MS patients. First is the question of whether or not MRI



A



B

Fig. 4.—**A,** Gross pathology of spinal cord MS. Multiple lesions are shown together with elongated configuration of demyelinating plaques along axis of cord. (Reprinted from [13].) **B,** Coronal view of MS patient. Multiple lesions (*arrows*) in upper cervical spinal cord, larger of which shows typical elongated configuration of spinal cord plaques. Good correlation with gross appearance of cord lesions in **A.**

will be able to separate acute MS lesions from the more chronic lesions. Additional experience will be needed in characterizing the MRI appearance of demyelinating lesions in an attempt to define criteria for acute and chronic plaques. Early experience suggests that T1 and T2 contrast alone may not be sufficient to separate acute from chronic lesions. The problem might be resolved with longitudinal studies using serial follow-up scans of these patients. An additional method that may prove useful in separating acute and chronic lesions is the use of intravenous MR contrast agents to detect increased permeability of the blood-brain barrier surrounding acute lesions. While these contrast agents are not clinically available at the present time, this is a fertile area of research [17–19] and should soon result in useful agents that are safe for use in patients.

The second important question to answer is how sensitive the MRI technique is in the detection of MS plaques and in what percentage of patients can we make the diagnosis by MRI. It is obvious that all of the lesions will not be visualized since many are extremely small, approaching microscopic size at postmortem examination.

Finally, the question as to how specific MRI will be in the diagnosis of MS remains to be resolved. Further elucidation of the MRI characteristics of MS plaques, as well as a more thorough understanding of the comprehensive differential diagnosis of lesions having appearances similar to those attributed to demyelinating plaques, remains to be worked out. Unquestionably, clinical correlation and correlation with the various nonimaging tests will remain critical in establishing the diagnosis of MS.

It should be emphasized that we have only been able to detect spinal cord lesions when using the 30 cm head coil to evaluate the upper cervical spinal cord. We have not been able to detect demyelinating plaques within the spinal cord in either the cervical or thoracic cord when using the body coil to evaluate the patient's spine. The reason for this is not related to a limitation of spatial resolution since the pixel size and slice thickness of the images obtained in the body coil ($1.7 \times 1.7 \times 7$ mm) are identical to those for images obtained using the head coil. The main problem appears to be secondary to a lower signal-to-noise ratio in the body coil due to a poorer filling factor when compared with the head coil. In addition, cardiac and respiratory motion cause further degradation of cervical and thoracic spinal cord images obtained in the body coil.

With further developments in technology, no doubt we will improve our sensitivity for the detection of small MS plaques. Thinner sections are needed to diminish partial-volume effects. These must be obtained at a very high signal-to-noise ratio, which may be made possible through the use of better coil design and/or the use of surface coils for imaging the orbits and spine [20–22]. Finally, intravenous contrast agents are needed to detect increased permeability of the blood-brain barrier.

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