Dorsal Midbrain Syndrome in Multiple Sclerosis with Magnetic Resonance Imaging Correlation

A. Costantino, S.E. Black, T. Carr, R.L. Nicholson and J.H. Noseworthy

ABSTRACT: We describe the clinical characteristics and a series of magnetic resonance imaging (MRI) studies in a patient with the features of dorsal midbrain syndrome occurring in the setting of multiple sclerosis. A T2-weighted MRI study revealed a discrete abnormality in the tectum of the midbrain whereas a high volume delayed computed tomography (CT) scan was uninformative. In parallel with remission of the clinical findings, the MRI abnormality diminished over time and was no longer visible at one year suggesting that some MRI detected MS lesions can completely disappear with time. This report demonstrates the use of MRI to detect and to follow sequentially sites of known disease activity in MS.

RÉSUMÉ: Les syndrome mésencéphalique dorsal dans la sclérose en plaques et ses corrélations avec les données obtenues par résonance magnétique Nous décrivons les caractéristiques cliniques et une série d'images obtenues par résonance magnétique (RM) chez un patient présentant un syndrome mésencéphalique dorsal dans le contexte d'une sclérose en plaques (SEP). Une étude du RM-T2 révéla une anomalie discrète dans le toit du mésencéphale alors qu'une tomodensitométrie à haut volume était négative. Cette image au RM diminua avec le temps, parallèlement à l'évolution clinique et disparut complètement après un an. Le présent rapport indique donc l'utilité du RM pour détecter et suivre les lésions dans la SEP.

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The dorsal midbrain syndrome (DMS) also called Parinaud's,[1] Koeber-Salus-Elschnig,[2] and the Sylvian Aqueduct Syndrome,[3] consists of impaired vertical gaze, retraction nystagmus, pupillary abnormalities, convergence nystagmus, convergence spasm, vertical nystagmus and extra-ocular palsies.[2] The first three signs are most commonly present; the constellation seen in a particular patient may reflect the extent of disease.[3] Pineal gland tumours and midbrain infarction are the most common etiologies, but multiple sclerosis (MS) can be a rare cause of the DMS.[4,5]

We present a patient with the DMS as an isolated manifestation of clinically definite multiple sclerosis (CDMS), who demonstrated an appropriate lesion on magnetic resonance imaging (MRI) in the acute phase and resolution of both the clinical syndrome and MRI abnormality at subsequent follow-up.

Case Report

A 45-year-old right-handed housewife experienced sudden total loss of vision in her right eye at age 29 (1967). This recovered within one month but she then lost vision in her left eye. Her vision gradually returned to normal over the next month. She remained well until November, 1983 when she experienced an acute onset of vertical diplopia accompanied by postural vertigo and nausea. This persisted for one week after which her dizziness and diplopia improved and could only be precipitated by upward gaze.

Examination at this time revealed optic atrophy of the right eye with a corrected visual acuity of 20/30. Visual acuity was normal in the left eye. On attempted upward gaze she had upgaze paralysis, vertical nystagmus, convergence spasm, and convergence-retraction nystagmus affecting both eyes. Bell's phenomenon could not be elicited but the oculovestibular response was present. No pupillary or other extra-ocular movement abnormalities were detected and the remainder of her neurological examination was normal.

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CSF examination revealed normal glucose and protein with 17 white blood cells/per mm^3 (100% mononuclear cells). Oligoclonal banding was present in the CSF and absent in serum. Brain stem auditory evoked responses and somatosensory evoked potentials were normal but the pattern visual evoked responses (PVER) of the right eye were prolonged to 116 msec (normal < 106 msec).[6,7] High volume delayed computerized tomography[8,9] (GE8800) prior to steroid treatment revealed no definite lesions.

The patient was treated for 10 days with 60 mg of delta-cortisone and this was then tapered over several weeks. She made a gradual recovery over the next three months. When seen nine months later she complained of diplopia on upward gaze only when very fatigued and exhibited a few beats of nystagmus on upward gaze. This had resolved by one year and no residual signs of the DMS could be clinically detected at that time.

Magnetic Resonance Imaging (MRI)

MRI was performed on a prototype 0.15T resistive magnet (Technicare Inc., Solon OH) which acquired data using a 256 × 128 matrix (pixel size of 1.1 × 2.2 mm) displayed as a 256 × 256 image. In the MRI examination immediately prior to steroid therapy, within a few days of her CT scan, and subsequently at three months, single sagittal slices (1.5 cm full width half maximum) were obtained near the midline by both spin echo (SE) (TE = 60 msec, TR = 1000 msec) and inversion recovery (IR) techniques (TI = 450, TE = 30, TR = 1500). The brain was also surveyed using an anisotropic SE (TE = 60, TR = 1000) collection of 32 transverse slices (1.7 cm thick FWHM) and two SE single slices at the upper ventricular levels (TE = 120, TR = 1000). The patient was re-examined one year later with a multiple slice, multiecho technique that produced 15 1.0 cm thick transverse slices (TE = 60, 120, TR = 2040) and two series of 0.75 cm sagittal slices (15 sagittal slices at TE = 60, 120, TR = 2040; 5 slices at TE = 60, 120, TR = 1000). Five IR sagittal slices were also obtained near the midline (TI = 400, TE = 30, TR = 1600).

The initial scan showed a small area of increased signal intensity compatible with an MS plaque in the dorsal midbrain on the midsagittal spin echo slice (Figure 1). A small area of increased signal was also seen in the left periatrial region on an axial spin echo slice (TE = 60, TR = 1000) in the transverse plane. In parallel with her clinical improvement a follow-up scan at three months showed diminution of the tectal lesion, but it could still be discerned. This lesion was no longer visible at one year in spite of improved image quality and a survey which included more slices and the application of additional echo delays and repetition rates that have been reported to be sensitive in the detection of MS lesions[10,11,12] (Figure 2a). In the axial spin echo images focal areas of increased signal were detected in the periventricular and supraventricular regions (Figure 2b). These lesions were typical for MS and were clinically asymptomatic. Some of them may have been new, although improved image quality and increased sensitivity in the later series made comparison with the earlier scans difficult.

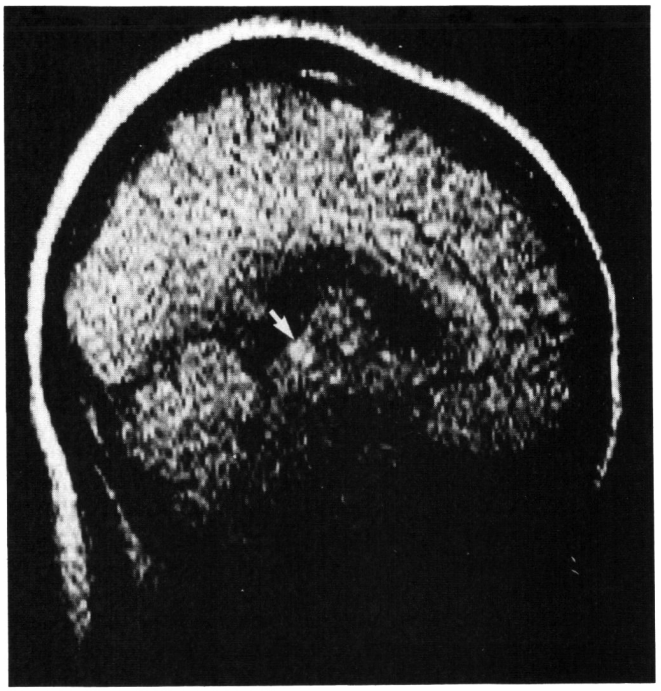

Figure 1 — Midsagittal MRI using a single slice spin echo (SE) technique (TE = 60, TR = 1000) 2 weeks after the acute onset of the dorsal midbrain syndrome. A discrete round area of increased signal intensity (prolonged T2) can be seen in the dorsal midbrain (arrow). An inversion-recovery (IR) image (not shown) of the same slice showed signal void in the same location but this could not be reliably distinguished from the low signal of the adjacent quadrigeminal cistern.

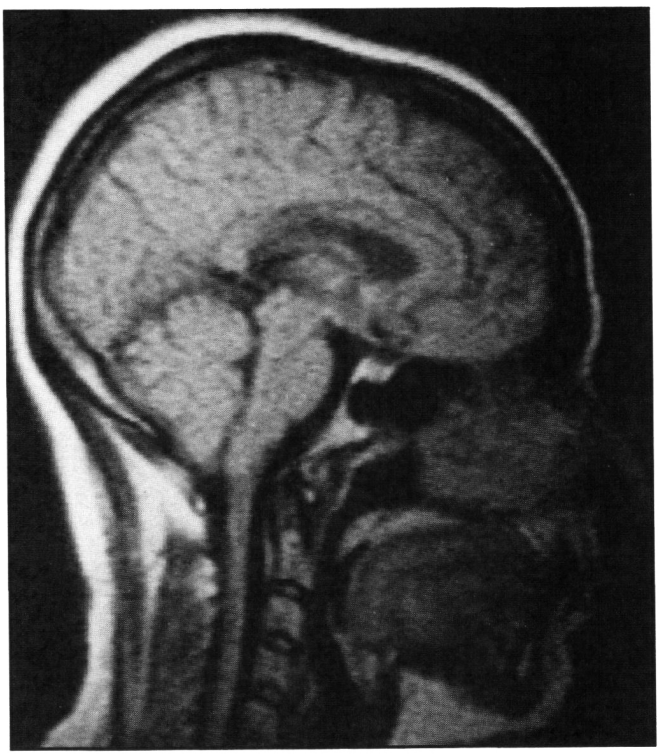

Figure 2a — Midsagittal slices obtained one year later by a multislice multiecho SE technique. The dorsal midbrain lesion could no longer be seen despite the obvious improved image quality using the same pulse sequence (TE = 60, TR = 1000) as a year earlier. Images (not shown) using a longer repetition rate (TR = 2000) and longer echoes (TE = 120, TR = 1000 and 2000) likewise did not reveal any brainstem lesions.

Discussion

This patient meets the criteria for clinically definite multiple sclerosis (CDMS) recently outlined by Poser et al.[13] Optic nerve involvement was confirmed by optic atrophy and an abnormal PVER. The presence of oligoclonal bands in the CSF provided laboratory confirmation of the diagnosis.[14]

The Dorsal Midbrain Syndrome was first comprehensively defined in 1946 by Kestenbaum[2] and included the following

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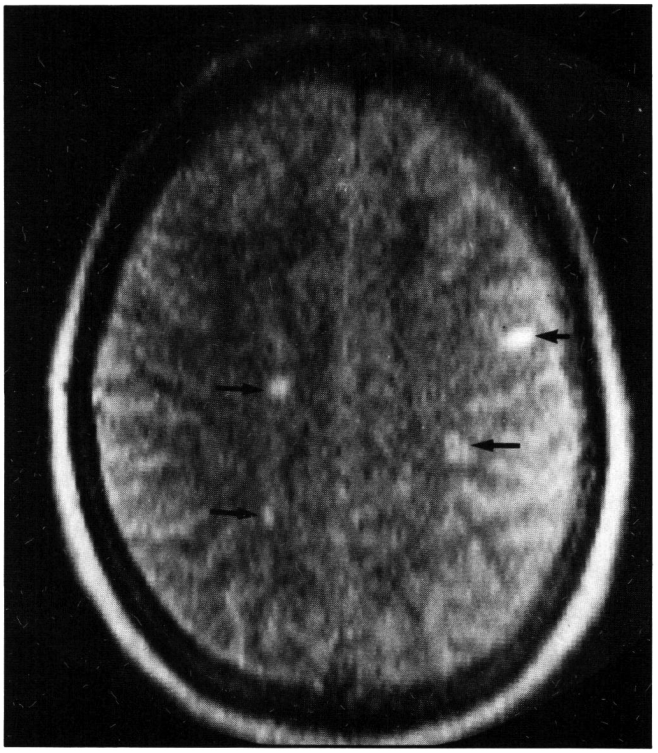

Figure 2b — Transverse supraventricular MR image obtained by the multislice multiecho SE technique (TE = 60, 120; TR = 2040) at one year revealed four foci of increased signal intensity in the white matter (arrows). These changes are consistent with the diagnosis of multiple sclerosis.

signs: (1) impaired vertical gaze, (2) retraction nystagmus, (3) pupillary abnormalities, (4) convergence spasm, (5) convergence nystagmus, (6) vertical nystagmus, and (7) extra-ocular palsies. Five of the seven criteria (1, 2, 4, 5 and 6) could be elicited in our patient in the acute phase of her exacerbation.

The control of vertical eye movements is thought to be located in the dorsal midbrain in the region of the posterior commissure and mesencephalic tegmentum.[15,16,17] Convergence and retraction nystagmus, described respectively as intermittent quick jerking movements of the eyes toward each other and retraction of the globes, are believed to be closely related.[18,19] The mechanism of convergence-retraction nystagmus is not clear, but it may represent a release phenomenon of the supranuclear cortical inhibitory fibres which results in a loss of the normal pattern of reciprocal innervation and an anomalous co-firing of the rectus muscles.[20] Upgaze paralysis and convergence-retraction nystagmus are both associated with lesions of the dorsal midbrain and, therefore, often occur together clinically.

It is quickly becoming established that MRI is the most sensitive neuroimaging technique for the detection of MS plaques, not only in the posterior fossa but also in the cerebral hemispheres.[10,12,21-26] Although there are few studies published to date comparing MRI to high volume delayed CT scanning, it appears that MRI is the more sensitive imaging modality in patients with MS.[25,26] Typically the lesions of MS have longer T1 and T2 relaxation times than normal white matter and, therefore, appear as areas of decreased signal intensity on T1 weighted images and of increased signal intensity on T2 weighted images.[10,21,24,25,27] Recent studies have suggested that the spin echo technique, using echo delays of 60-120 msec and repetition times greater than 1000 msec, is the most sensitive pulse sequence in detecting MS lesions,[10,11,12,28] although earlier studies reported greater sensitivity with inversion-recovery pulse sequences (IR).[24,25] One group has reported that SE (120/1000) was the most useful screening procedure, although IR may be more revealing in the brainstem and a repetition time around 2000 msec may provide more contrast in lesions of the white matter remote from the ventricular system.[10]

It remains to be clarified how these MRI abnormalities relate to the age of the plaques and the pathological changes within them. It is known that contrast enhancement on CT correlates with sites of active inflammation and demyelination in MS.[29] Failure of the high volume delayed CT study to identify an abnormality in our patient does not permit us to infer that the blood-brain barrier was intact at the site of the midbrain lesion as the lack of enhancement may have been due to the known insensitivity of CT studies in the posterior fossa. The single autopsy-MRI correlation that has been published reported that areas of demyelination corresponded to areas of increased signal intensity on T2 weighted MRI images.[30] Preliminary studies designed to correlate the pathological findings in the experimental allergic encephalomyelitis animal model of MS with the changes in MRI relaxation times have suggested that the T1 and T2 abnormalities seen with inflammation and demyelination may normalize in the presence of extensive cellular infiltration.[31] These studies imply that apparent improvement in an MRI image may not always mean resolution of disease activity but rather may reflect changes in the degree of cellular infiltration, tissue protein content or the amount of free water locally in an MS plaque.

There have been few studies of serial magnetic resonance imaging in MS patients, but the limited evidence available suggests that lesions may remain unchanged, may diminish or enlarge and that new lesions can appear.[25,26,29] Many lesions, especially in the hemispheric periventricular white matter, are clinically asymptomatic and it is not possible to determine whether they represent acute or chronic sites of activity. In lesions of uncertain age quantitative sequential studies have shown unpredictable changes in T1 and T2 values.[25] The actual disappearance of MRI-detected abnormalities has been noted only infrequently and this is felt to be uncommon.[29] Our patient is of particular interest because she had a discrete lesion in the dorsal midbrain which corresponded to her clinical signs during an acute exacerbation. This suggested that the midbrain MRI lesion represented an active and, presumably, acute MS plaque. She improved substantially and at three months the MRI lesion had correspondingly diminished. By one year she had fully recovered and the lesion was no longer visible on MRI despite technical improvements which allowed a more comprehensive survey with better resolution. This suggests that the alterations in T1 and T2 properties (especially T2 prolongation), which occurred during the acute exacerbation were no longer great enough to cause visible contrast with normal white matter and to permit detection by MRI. In a lesion of this size, accurate T1 and T2 measurement is impossible due to partial volume averaging. At the time of the final MRI study several previously undetected small areas of increased signal were seen in the hemispheric white matter. Because of the intervening technical improvements it cannot be determined if these foci represented new plaques or simply reflected the increased sensitivity of the imaging technique.

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