Meningeal Gd-DTPA Enhancement in Multiple Sclerosis

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Summary: We demonstrate meningeal enhancement in a 42-year-old man with multiple sclerosis, an MR finding that—with further confirmation—may shed light on the pathology of multiple sclerosis.

Index terms: Scelerosis, multiple; Demyelinating disease; Contrast media, paramagnetic; Meninges

Although the cause of demyelination in multiple sclerosis (MS) remains obscure, inflammation invariably is present. Demyelination in MS is accompanied by lymphoplasmocytic infiltration of retinal veins (1), cerebral white matter, and meninges (2–4).

In vivo demonstration of infiltration of the retina can be observed on ophthalmoscopy and by means of fluorescein angiography (1). In vivo demonstration of inflammation of the cerebrum can be achieved by means of gadopentate dimeglumine (Gd-DTPA)-enhanced magnetic resonance (MR) imaging (5–7). We had the opportunity to demonstrate meningeal enhancement in MS by means of Gd-DTPA-enhanced MR imaging.

Case Report

A 42-year-old man suffered from rapidly progressive, clinically definite MS (8) for 2 years. In the course of the disease he developed spinal, cerebellar, brainstem, and ocular symptoms and signs. For 2 months he complained of urinary urge-incontinence and for 1 month noticed paraesthesias in both arms.

On examination there were no signs of meningeal irritation. A bilateral internuclear ophthalmoplegia was noted. He had dysarthia and dysphagia. Furthermore, mild quadriparesis with intact sensory function was present. Deep tendon reflexes were decreased and symmetrical, and plantar reflexes were extensor. Severe dysdiadochokinesis and intention tremor were observed. The expanded disability status scale score (EDSS) was 8 (9).

The erythrocyte sedimentation rate was 15 mm/hr (Westergren), and blood count showed 398,000/mm^3 erythrocytes, 880/mm^3 white cells with a normal differentiation. In the cerebral spinal fluid, there were seven white cells per mm^3, glucose of 3.2 mmol/L (blood glucose 5.1 mmol/L), the intrathecal IgG-synthesis was 0.53 (normal: <0.56), no oligoclonal bands, myelin basic protein was 2.0 μg/L (normal <1.5). No tumor cells were seen. MR imaging was performed on a 0.6 T machine (Teslacon II, Technicare USA), using a standard head-coil, and three consecutive scout images for positioning errors (7). Axial 5-mm images (gap 1.25 mm and in-plane resolution of 1.0 × 1.3 mm) consisted of unenhanced long TR spin echo (SE) sequences (2755/60,120/2, TR/TE/excitations) and enhanced short TR SE sequences (400/28/4) obtained 5–15 min after intravenous administration of Gd-DTPA (Magnevist, Schering AG, Germany) (0.2 mmol/kg). On the unenhanced long TR images, increased signal intensity was seen around the ventricular system. The meninges were partly visible (Fig. 1A). On the enhanced short TR images, one small enhancing parenchymal lesion was seen in the temporal lobe. Enhancement of the meninges was seen around the whole brain, including the falx (Fig. 1B), but was most conspicuous around the frontal (Fig. 1C), and temporal (Fig. 1D) lobe, due to chemical shift artifact (10). There was no enhancement of the ventricular ependyma. The patient was treated with intravenous methylprednisolone 1 g daily for 10 consecutive days. No subjective clinical improvement was seen and the EDSS remained 8 after treatment. A second MR scan (14 days later with an identical scan protocol) no longer revealed enhancement of the parenchymal lesion or the meninges (Figs. 1E–G).

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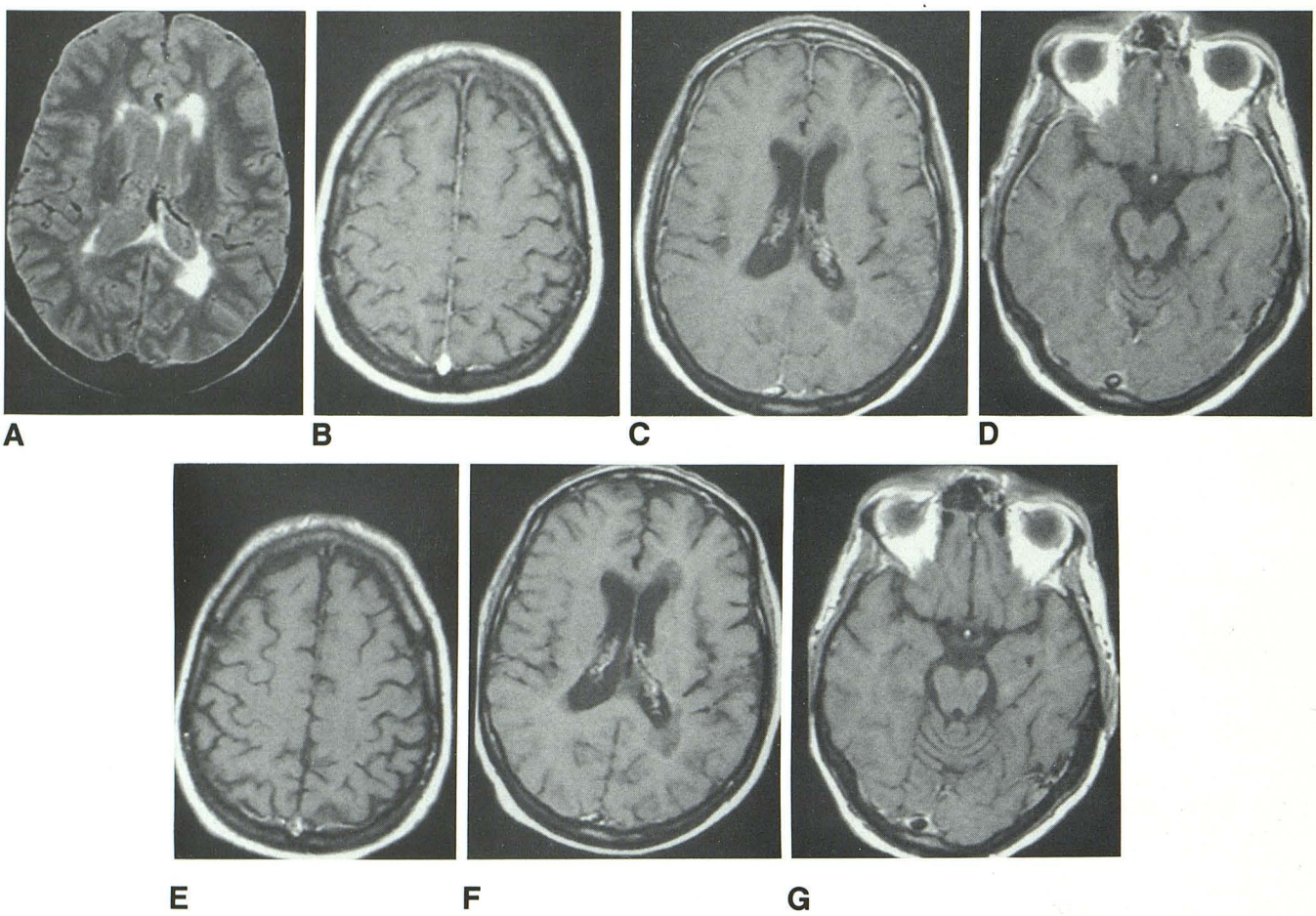

Fig. 1 *A*, Long TR/long TE image shows multiple confluent periventricular white matter lesions and partly visible meninges.
B, Short TR/short TE images at three selected levels, obtained 5–15 min after Gd-DTPA injection in a patient with definite multiple sclerosis: note the abnormal continuous enhancement of the (thickened) falx (*B*) and meninges of especially the frontal (*C*) and temporal (*D*) lobe before treatment with high-dose intravenous methylprednisolone and its subsequent disappearance after treatment (*E-G*).

Discussion

Increased signal intensity on short TR SE images of certain cranial tissues after Gd-DTPA is a common observation in controls and can invariably be observed in the choroid plexus, the cavernous sinus, the pituitary gland, and the infundibulum, and is sometimes observed in the falx and the tentorium (11). Physiologic meningeal enhancement can be observed parasagittally near the midline at the dural reflections around the superior sagittal sinus and in short segments around the tip of the temporal lobe (11). In none of the patients in the latter study (10) could enhancement be followed around the brain on the axial sections without primary meningeal or systemic disease, including patients with MS. Meningeal enhancement can be observed in carcinomatous meningitis (12), bacterial meningitis (13), neurosarcoidosis (14), in the vicinity of a meningeoma (15), in postoperative states (16), and in rheumatoid disease (17). In our patient, such diseases were ruled out by clinical, cerebral spinal fluid, and MR findings.

Gd-DTPA enhancement in MS (18) and chronic relapsing experimental allergic encephalomyelitis (19) has been found to correlate with the site of inflammation. We hypothesize that the meningeal enhancement observed in our patient indicates meningeal infiltration, such as is frequently found at autopsy in MS patients (2–4).

In a study of 143 autopsy cases (4), a mild to moderate perivascular lymphoplasmocytic infil-

tration was found in 60% of the cases, and was associated with active demyelination in 74%. Lymphoplasmocytic infiltration in the leptomeninges was found in 41% of the cases, and in 80% of them was associated with active demyelination. Leptomeningeal infiltration thus is associated with disease activity in MS. Our patient experienced an acute relapse at the time of the initial MR scan. Although it has been suggested that meningeal involvement could explain why headache is frequently associated with an acute relapse of MS (2), our patient had neither symptoms of meningeal involvement such as headache nor signs of meningeal irritation.

The occurrence of meningeal involvement has implications for the concept of pathogenesis in MS. As it occurs in a region free of myelin, this might indicate that perivascular infiltration is not triggered by myelin, but by disruption of the blood-brain barrier. This is also suggested by the finding of gray matter lesions in MS (20, 21) and by the ophthalmologic findings (1) in patients with optic neuritis, which include fluorescein leakage, perivenous sheathing and cells in the vitrous and the anterior chamber, regions free of myelin. In the latter study (1), no MR imaging was performed. It would be of particular interest to know whether abnormal ophthalmologic findings (especially fluorescein leakage) correspond to gadolinium-enhancing lesions of the brain or the optic nerve. Using a short inversion recovery imaging sequence, Gd-DTPA "enhancement" (leading to a decrease in signal intensity) has been shown to occur in the acute stage of lesions in neuromyelitis optica (22). Future studies should concentrate on the relation of fluorescein leakage to Gd-DTPA enhancement of optic nerve lesions. Such a correlation might be informative about the origin of inflammation in regions free of myelin, such as the retina and the meninges. In 23 cases of MS treated with steroids (4), leptomeningeal infiltration was found in only 40% of the cases (as compared to 60% of the untreated cases), which were less severe then in untreated cases. In our patient Gd-DTPA enhancement resolved after treatment with steroids. It has been shown that high-dose intravenous methylprednisolone improves blood-brain barrier integrity in parenchymal lesions (7) as well. If disruption of the blood-brain barrier is indeed the initiating factor of disease activity, then our finding underlines the capabilities of steroids in the treatment of MS. Demonstration of meningeal enhancement in MS by means of Gd-DTPA enhanced MR is an interesting finding, which may shed light on the basic concept of MS pathology, but needs further confirmation.

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