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# The value of magnetic resonance imaging in diagnosis and monitoring of treatment in multiple sclerosis

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**Abstract.** We analysed MR examinations of 277 patients with multiple sclerosis. White matter hyperintensities in brain were found in 270 of them. The most frequently they were found in periventricular white matter (in 100% of cases), in subcortical localization (52.2%) and in the corpus callosum (44.4%). MR examination allows to estimate the activity of the disease on the basis of the presence of oedema around the plaques and their contrast enhancement with gadopentetate dimeglumine (Gd-DTPA). 17.8% of all cases showed the signs of the acute phase of MS. About one-third of all cases were accompanied by cortical brain atrophy (the most often seen in the frontal lobes), subcortical brain atrophy was less frequent (one-sixth). In about two-third of all cases the corpus callosum atrophy was found. The analysis of follow-up MR examinations of 83 patients taking part in a double-blind placebo-controlled trial of a new immunosupressive drug cladribine showed that patients from the placebo group were more compliant to any changes of the plaques. Decrease of the plaques size was found mainly in women. No correlation between the patients age and the plaques changes was established.

**Key words:** magnetic resonance (MR), multiple sclerosis (MS), white matter hyperintensisties, plaques, brain atrophy, cladribine (2-CDA)

## INTRODUCTION

More than 400 persons with a mean age of 30 years fall ill with multiple sclerosis in Poland every year. Demyelination of nerve fibres causes the multifocal damage of the CNS. The etiopathogenesis of MS has not been established so far. The most probable theories assume the influence of viral, genetic and autoimmunological factors. Considering varied clinical picture and difficulties in differential diagnosis it seems to be quite obvious that these patients are often referred to magnetic resonance examinations, sometimes with omission of computerized tomography (CT) which in majority of cases reveals no specific abnormalities. The MR method improves diagnostic possibilities in MS and allows to detect plaques in the spinal cord as well as in brain.

The purpose of this study was to establish MR symptomatology of MS and to estimate its value in monitoring of treatment of MS.

## METHODS

### Subjects

Magnetic resonance examinations of 277 patients (171 women, 106 men) were evaluated for the distribution of MS lesions. The mean age was 37.59 years (range 11-66 years). Eighty three patients (51 women, 32 men) took part in a double-blind placebo-controlled trial of cladribine. Their mean age was 36.5 (range 22-55 years).

### Apparatus

Magnetic resonance imaging was performed on a 0.5 T machine (Toshiba MRT50A) and on a 1.5 T machine (Magnetom Siemens) with a standard head coil.

### Procedure

MR imaging was performed according to the following protocol: slices in two planes (axial and sagittal) with slice thickness of 7.5 and 5 mm using spin echo (SE) technique including T1-weighted images (TR 500 or 600 ms, TE 20 or 15 ms), PD-weighted (TR 3,000 or 2,500 ms, TE 30 or 15 ms) and T2-weighted (TR 3,000 or 2,500 ms, TE 120 or 90 ms). 81 patients were examined twice: before and after 6 courses of treatment. Cladribine and placebo were administered subcutaneously 5 mg daily for 5 days.

Statistical analysis was performed by means of Pearsons correlation coefficients. *P* values smaller than 0.05 were considered statistically significant.

## RESULTS

Hyperintensive lesions were shown on PD- and T2-weighted images in 270 of 277 patients (97.5%). The most frequently they were shown in periventricular white matter (in 100% of cases), in subcortical localization (52.2%) and in the corpus callosum (44.4%). The less frequently - in brain cortex (only in one case - 0.4%) (Table I).

Plaques could be clearly seen on T1-weighted images as the hypointense foci in only 38.1% of all cases. They were imperceptible or easy to overlook on T1-weighted images in 61.9% which shows the poor usefulness of the unenhanced T1-weighted images in MS lesions detection. T1-weighted images are usually abnormal in acute phase and in long standing cases.

TABLE I

Localization of plaques

| Localization | Number of patients | % |
|---|---|---|
| periventricular | 270 | 100.0 |
| subcortical | 141 | 52.2 |
| corpus callosum | 120 | 44.4 |
| brain stem | 98 | 36.3 |
| internal capsule | 83 | 30.7 |
| cerebellum | 55 | 20.4 |
| basal ganglia | 13 | 4.8 |
| brain cortex | 1 | 0.4 |

TABLE II

Cortical atrophy of the CNS

| Atrophy of the cortex of | Number of patients | | % of the group of patients with atrophy | % of all the patients | |
|---|---|---|---|---|---|
| frontal lobes | 70 | | 70 | 25.9 | |
| parietal lobes | 57 | | 57 | 21.1 | |
| temporal lobes | 42 | 100 | 42 | 15.5 | 37 |
| cerebellum | 21 | | 21 | 7.8 | |
| occipital lobes | 2 | | 2 | 0.7 | |
| no atrophy | | 170 | | | 63 |
| | | 270 | | | 100 |

In 12 patients MR examination was performed after the intravenous administration of contrast medium - Gd-DTPA. The enhancement of the acute plaques was observed on T1-weighted images in all of them. In 48 cases oedema around the plaques was shown on PD- and T2-weighted images. The signs of the acute phase of MS were visualised in 17.8% of all patients. These signs are the result of the increased blood-brain barrier permeability. In 82.2% of patients the plaques were chronic.

In majority of cases white matter hyperintensities were focal (69.6%). Only in 1.9% of all cases they were confluent. In 28.5% both focal and confluent lesions were observed. Confluent changes were found around the anterior and posterior parts of the lateral ventricles.

The shrinkage of chronic lesions accounts for the ventricular dilatation found in long standing cases of MS. In our material subcortical brain atrophy was visualised in 16.7%. Cortical brain atrophy was observed more frequently: in 37% (Table II).

The brain MR imaging sign most specific for MS probably is an abnormal corpus callosum. Callosal atrophy can be encountered relatively early in the disease, in the absence if clinical disability. It was found in 64.9% of our patients.

Only in 98 cases the results of CT examinations were available, 68 of them were normal. Only in 15 cases hypodense foci were found on CT. In 22 -

TABLE III

The results of CT examinations

| Result of CT | | Number of patients | | % | |
|---|---|---|---|---|---|
| normal | | | 68 | | 69.4 |
| abnormal | atrophy | 15 | | 15.3 | |
| | hypodense foci | 8 | 30 | 8.2 | 30.6 |
| | atrophy and hypodense foci | 7 | | 7.1 | |
| | | 98 | | | 100.0 |

TABLE IV

MR *versus* CT

| Results of the examinations | | CT - number of patients | MR - number of patients |
|---|---|---|---|
| normal | | 68 | 0 |
| abnormal | cortical and/or subcortical atrophy | 15 | 15 |
| | callosal atrophy | 0 | 47 |
| | focal changes | 15 | 98 |

brain atrophy was shown. Callosal lesions and atrophy cannot be demonstrated by means of CT (Tables III and IV).

Perhaps the most important outcome of the last 10 years research is that MRI has emerged as a highly sensitive and independent marker of disease activity that can be used in the context of trials of experimental treatments. In our case the study group consisted of 83 patients with relapsing-remitting MS, randomised to receive placebo or a new immunosupressive drug 2-chlorodeoxyadenosine (cladribine, 2-CDA). The patients were followed-up both clinically and with MRI. The patients receiving placebo turned out to be more compliant to any changes (increase/decrease of the number/size) of the plaques. It was statistically significant ($P$=0.01096). The most encouraging finding was that the number of new plaques was twice as big in the placebo group (8) as in the cladribine group (4) - not significant because of small numbers.

Dicrease of plaques size was found mainly in women . No correlation between age of the patients and plaques changes was established.

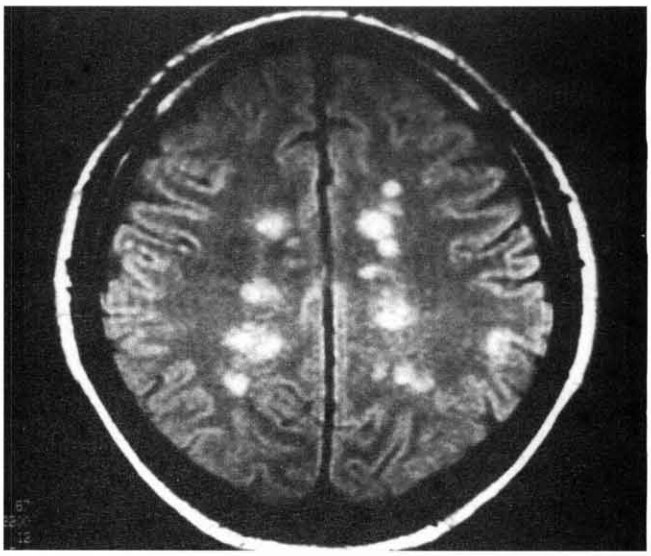

Fig. 1. Typical periventricular localization of plaques. PD-weighted image, axial plane.

## DISCUSSION

Magnetic resonance imaging has had an enormous impact on medicine. It has revolutionized the investigation of neurological disorders in general and multiple sclerosis in particular. It is now basic diagnostic method in MS beside anamnesis and physical examination, evoked potentials and cerebro-spinal fluid electrophoresis (oligoclonal bands). None of these methods alone is sufficient to reach the absolutely sure diagnosis. That is why it is very important to use all of them (David et al. 1990, Paolino et al. 1990). The preponderance of MR is underlined in cases of clinically probable MS (Paolino et al. 1990) and as far as the evaluation of disease activity and progression is concerned (Baum et al. 1990, Weinshenker and Nelson 1990). Some authors consider MR (sensitivity 97%) as much more sensitive than evoked potentials (46-89%) but less than CSF electrophoresis (Baumhefner et al. 1990). Patients with certain other neurologic diseases may at times resemble patients with MS to the extent that they satisfy the clinical criteria for definite MS. MR plays an important role in diagnosing these diseases and differentiating them from MS

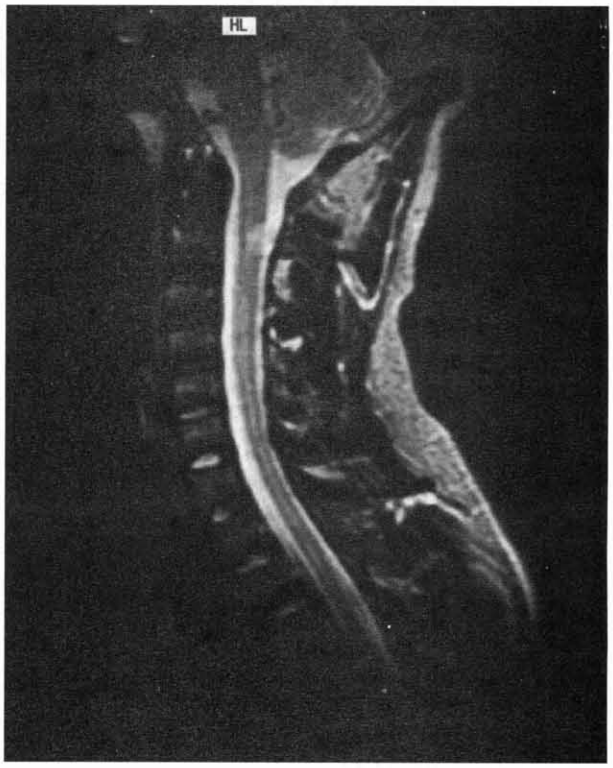


Fig. 2. Plaques in cervical part of spinal cord (C2). T2-weighted image, sagittal plane.

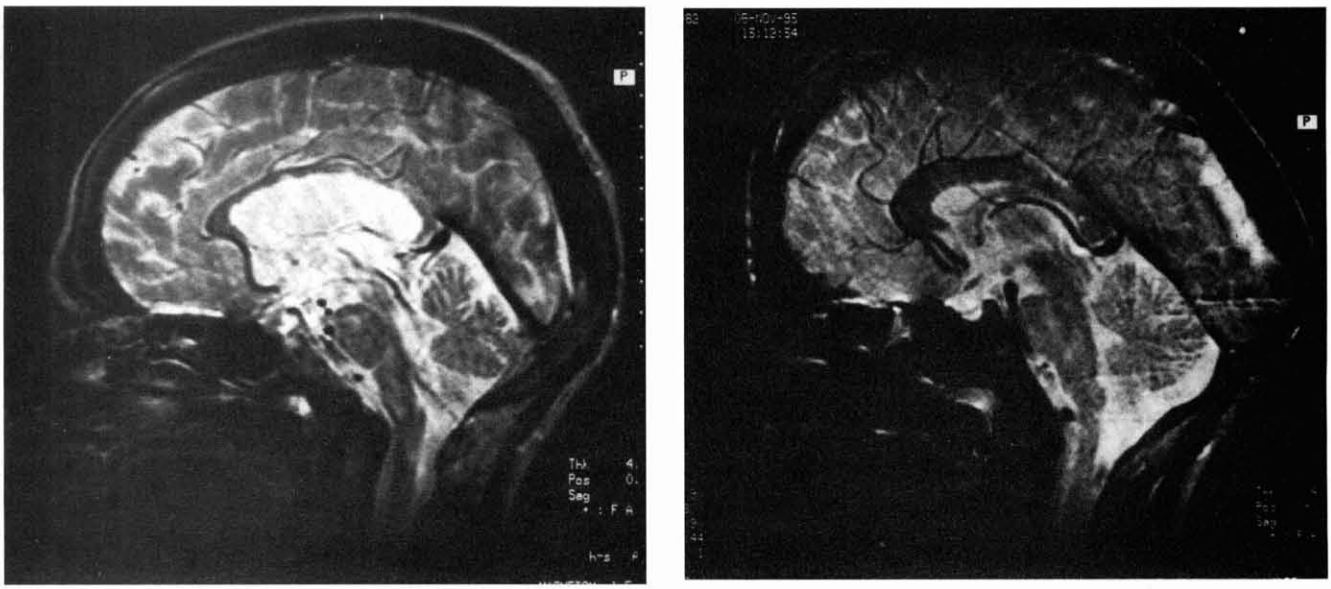

Fig. 3. T2-weighted images, sagittal plane. A, atrophy of the corpus callosum. B, normal corpus callosum.

(Rudick et al. 1986). Hyperintense (PD- and T2-W) lesions in brain (Fig.1) and/or in spinal cord (Fig.2) and the clinical data lead to the suspicion of MS. One has to take into account that lesions of the type seen in MS may occur also in other diseases, e.g. hypertension, migraine, Alzheimer's disease, encephalitis, vasculitis and in normal ageing (Yetkin et al. 1991, Barkhof 1992). Nevertheless there are certain specific features on brain MR images which can make a diagnosis of MS more probable. There must be at least 3 hyperintense foci. The finding of lesions greater than 5 mm, abutting the bodies of lateral ventricles and in the infratentorial region is specific for MS (Offenbacher et al. 1993). Lack of hyperintensities in brain does not exclude MS (Mushlin et al. 1993) - the lesions may be present only in spinal cord or in optic nerves.

Analysing our material we found that the periventricular region is the most common localization of plaques and that callosal atrophy (Fig. 3) is more specific for MS than cortical and subcortical brain atrophy. This confirms the previous literature reports (Gean-Martin et al. 1991, Barkhof 1992, Cendrowski 1993, Thorpe, Miller 1994). We also found very small frequency of cortical lesions which is consistent with other reports (Ormerod et al. 1987, Cendrowski 1993) although it has also been suggested that cortical plaques are much more frequent (Barkhof 1992).

The poor usefulness of T1-weighted images (except when the contrast medium is administered) has been reported by the other authors (Runge et al. 1984, Koopmans et al. 1989) as well as the presence of focal and confluent lesions (Koopmans et al. 1989).

The only imaging possibility available before the era of magnetic resonance - computerized tomography - did not (in majority of cases) reveal any abnormalities in patients with multiple sclerosis. Hypodense foci found in some cases are not specific for this disease. CT can only show brain atrophy but is unable to visualise callosal atrophy. The sensitivity and specificity of MR is much higher. It shows plaques not only in brain but also in spinal cord and even in optic nerves (Sosnowski et al. 1993) thanks to its great resolution.

The role of MR in treatment monitoring in MS has already been reported (Barkhof 1992, Thorpe, Miller 1994). Autoimmune processes seem to have a major role in etiopathogenesis of MS. Cladribine is an imunosupressive drug, a highly specific anti-lymphocyte agent. It has been used with success in treatment of lymphoid leukaemias, notably hairy cell leukaemia and non-Hodgkin lymphomas. It has also been used in treatment of chronic progressive

MS by Sipe et al. who concluded that it influences favourably the course of chronic progressive MS (Sipe et al. 1994).

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