

## Multiple sclerosis: diagnostic value of computerized tomography with delayed scanning after a double-dose of contrast medium in comparison with other diagnostic tests

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### Abstract

In 63 cases of clinical definite or suspected MS we compared the results of CSF analysis, VEP, BAEP, CT scanning without and after double dose contrast, in 17 cases also those of MRT. We found that CSF analysis had the highest rate of abnormal findings, followed by MRT. VEP and CT with double dose contrast showed similar sensitivity, while BAEP and CT without contrast had disappointing results. We think that CT with delayed scanning after double dose contrast can be a very useful investigation in early and doubtful cases of MS, until MRT will become a more widespread and less expensive investigation.

**Keywords:** Multiple sclerosis, CT scanning with double dose contrast, CSF analysis, evoked potentials, MRT.

### 1 Introduction

Multiple sclerosis is the most common neurological disease in Northern Europe and North America. The diagnosis is still primarily based on clinical findings. During the last 10 years several new laboratory and clinical procedures have been developed for diagnosis. None of them can produce results which are specific for MS alone, but all of them can help to confirm the diagnosis by demonstrating neurological dysfunctions and lesions.

Our intention was to compare the results of various diagnostic tests to find out how each test can help confirm the diagnosis of MS. Our special interest was to test delayed CT scanning with double-dose contrast against other methods.

### 2 Patients and methods

We examined 53 patients (39 female, 14 male, two thirds of them aged between 20 and 40), some of whom were examined two or three times during various exacerbations of MS, so that we had a total of 63 cases.

According to the diagnostic criteria of McALPINE and LUMSDEN [19], 32 cases had definite, 12 probable and 19 possible MS. 13 patients had the first exacerbation of MS. We compared the results of CSF analysis, brain stem auditory evoked and visual evoked potentials, CT scanning without and with delayed scanning with high dose contrast; in 17 cases we also had the results of nuclear resonance imaging.

CSF was examined for pleocytosis, a CSF increase of IgG, and, because of technical reasons, for oligoclonal bands in only 15 cases.

For recording brain stem auditory evoked potentials, we applied monaural clicks of 500  $\mu$ s duration and with a frequency of 10 clicks per second. The auditory evoked responses were obtained from electrodes on the mastoid and vertex and averaged after amplification with a band pass of 150–3000 Hz. At least two averages were obtained from each ear. Most important was the measurement of the latency of P3, P4, and P5. Aberrations of more than 1,5 of the standard deviation were considered to be abnormal.

Visually evoked potentials were recorded with silver disc electrodes placed 5 cm above the nasion andinion and on the vertex at the middle of the nasion-inion-distance. The stimulus was given foveally and parafoveally by an alternating black and white TV-cherckerboard system at a frequency of once per second. Responses were amplified by a bandpass of 5–100 Hz and 100 responses per eye were averaged. We regarded aberrations of P2-latency and amplitude and latency differences of more than twice of the standard deviation between the two sides as abnormal.

The CT examination was performed on a Siemens Somatom and Somatom D3 in axial maximal 8 mm continuous "cuts". After the precontrast scan, 200 ml of a solution of iodine contrast media with a

content of 74g iodine (Urografin 76% or Solustrast 370) were applied in a rapid drip infusion and a second scan was taken after two hours. We considered multifocal or single hypodense or contrast enhancing lesions in the white matter, especially in a periventricular position as suggesting MS.

The NMR examinations were performed at the Radiologic Institute of the Charlottenburg Clinic of the Free University of Berlin with a 0,35 tesla Magnetom (Fa. Siemens) with a head-scanning coil of 25 cm diameter. The cerebrum was examined with a multiple slice technique in axial planes with 10 mm thick slices in 2 spinecho sequences with a repetition time TR of 1600 ms and TE of 35 and 70 ms (SE 1600/35 and SE 1600/70 ms). T1 dependent images were also made in the plane of the cella media. Details of these procedure are described by BAUM, SCHÖRNER et al. [2], who also performed the NMR examinations reported in our study.

### 3 Results

The results of our study are listed in table I. Although some of the results in the various groups are not of statistical significance because the number of patients examined was too small, we converted the number of abnormal findings into percentages to make the comparison easier.

With 93%, the CSF analysis showed the highest rate of abnormal findings among all examinations. CSF was positive for CSF-IgG or/and oligoclonal bands in all patients with definite MS. The BAEP and VEP were altered in 36% and 60%, respectively. In 74% of those patients in which both methods were performed at the same time, at least one of the two tests could detect lesions.

The results of the CT examinations without enhancement showed only 26% abnormal findings in all cases and by far the lowest rate of abnormal findings of all tests studied. In contrast to this, in 58% of all patients and in at least 50% of patients in each group the CT scans two hours after infusion of double-dose contrast medium showed single or multiple lesions indicating MS.

The MR imaging was much more sensitive in detecting lesions than the CT: In 14 of 17 cases which were examined, MRT was able to show parenchymal lesions so that after CSF analysis, MRT had the second highest rate of detecting irregularities in cases of definite or suspicious MS. In 16 cases we could compare the results of MR imaging with CT with delayed double-dose contrast. In nearly all of these cases

NMR showed parenchymal lesions which could not be seen on the double-dose delayed CT scan. In five of these 16 cases, NMR showed multiple lesions, while CT was normal. The only case of definite MS which had a normal MRT scan was under immunosuppressive drug therapy at the time of the examination; in this case all other tests, except for CSF analysis, which could not be performed, were also negative.

### 4 Case reports

We have taken three cases, to illustrate the uses of CT and NMR imaging in diagnosing MS in early stages and in difficult cases. New differential diagnostic difficulties which can arise through these methods are also described.

**Case 1.** A 27-year-old nurse consulted us because of abducens paresis on the right side, which had appeared 5 days before admission. Her medical history included only the usual childhood diseases. During the examination the abdominal reflexes on the left side seemed to exhaust more quickly than those on the right; otherwise the neurological status was normal. CSF analysis revealed a slight pleocytosis, an increase of CSF IgG, and oligoclonal bands. CT without contrast was normal, but the delayed scan with double contrast showed an enhancing lesion in the white matter near to the left ventricle and two further lesions above the plane of the ventricles (Figure 1). On the third day after admission the patient could be discharged with the diagnosis of MS and corresponding information and medical advice.

**Case 2.** A 47-year-old female had complaints pointing to MS for as long as 20 years. First of all she suffered recurrent short-termed visual impairment. Later the patient complained of trouble in both legs and in the right arm and therefore consulted several hospitals. First, circulatory defects were assumed, then a C7 syndrome. The myelography showed no abnormal findings. Later myositis was suspected. We saw the patient in the Internal Department of our hospital, where she was examined for suspected osteoporosis. At this time the patient had complained of gait disorders and micturition problems for two years. The neurological examination showed signs of slight bilateral leg spasticity, the triceps reflex seemed to be stronger on the right side. In addition to this the patient complained of hypesthesia of the third finger of the right hand. CSF analysis revealed a pleocytosis of 20/3 and increase of CSF IgG. Brain stem auditory evoked responses were abnormal on the right side, various VEP could hardly be differentiated. CT showed a hypodense lesion in the left cerebellum, the delayed scan after double-dose contrast added an enhancing lesion adjacent to the right ventricle. MR imaging detected multiple lesions (Figure 2).

The patient herself had feared to have MS, as did her sister, for a long time. Possibly this fixation lead to a misjudgement at the beginning of the disease when her defects could

not substantiated. The case shows the importance of certain proof of lesions by a method which can not be influenced by the patient for the final diagnosis.

**Case 3.** A 41-year-old patient with an unremarkable medical history came to us with the suspicion of polyradiculitis. The clinical findings (reduction of all sensitive qualities up to C3, right-sided hemiataxia, hypesthesia of right trigeminus with otherwise normal status) as well as the results of CSF analysis (moderate pleocytosis, normal protein, an increase of CSF IgG, and oligoclonal banding) lead us to the assumption of MS. CT showed two hypodense lesions in right and left parietal lobes. This result was compatible with MS plaques or postinfectious defects. MR imaging detected multiple lesions (Figure 3), which the radiologists interpreted as signs of metastases which were also compatible with the clinical findings. Further laboratory tests showed no indication of an infection. The spontaneous remission of symptoms without any therapy largely excluded metastases. The CT control scan three weeks after the first also showed a remission of the foci.

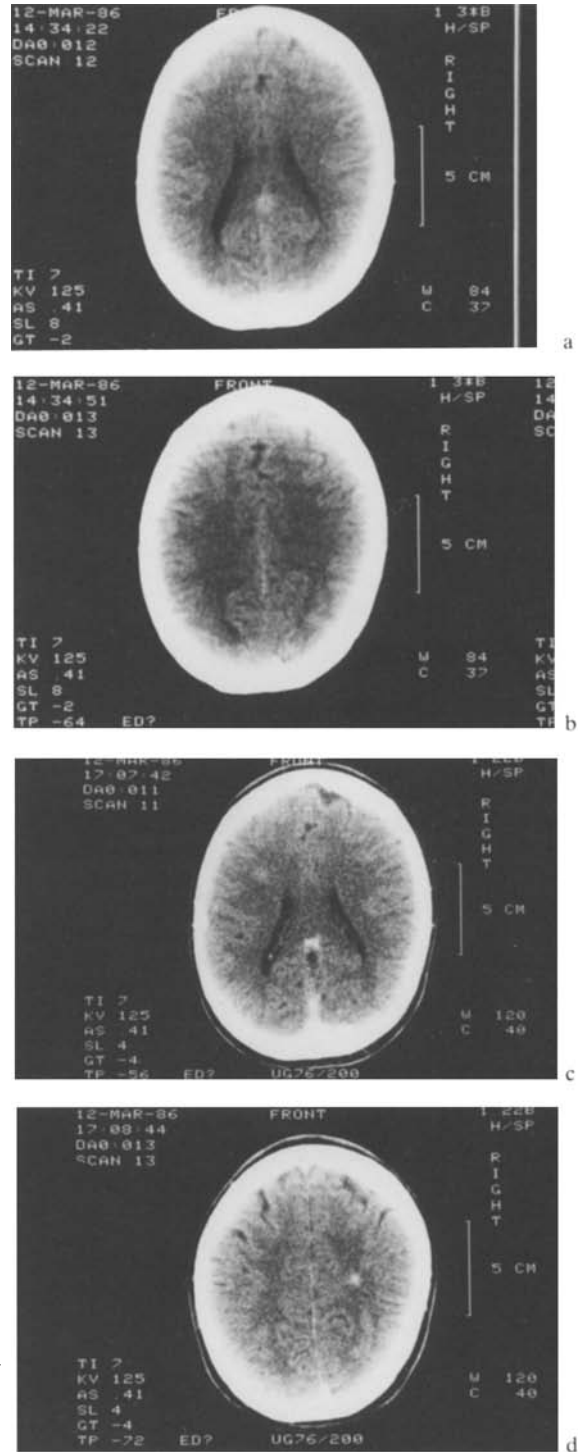
## 5 Discussion

We are aware of the fact that these results are not of high statistical significance because of the rather low number of cases in the various groups. It was our concern, however, to obtain a survey of the validity of these methods in the diagnosis of MS by comparing the results of the various tests in the same cases.

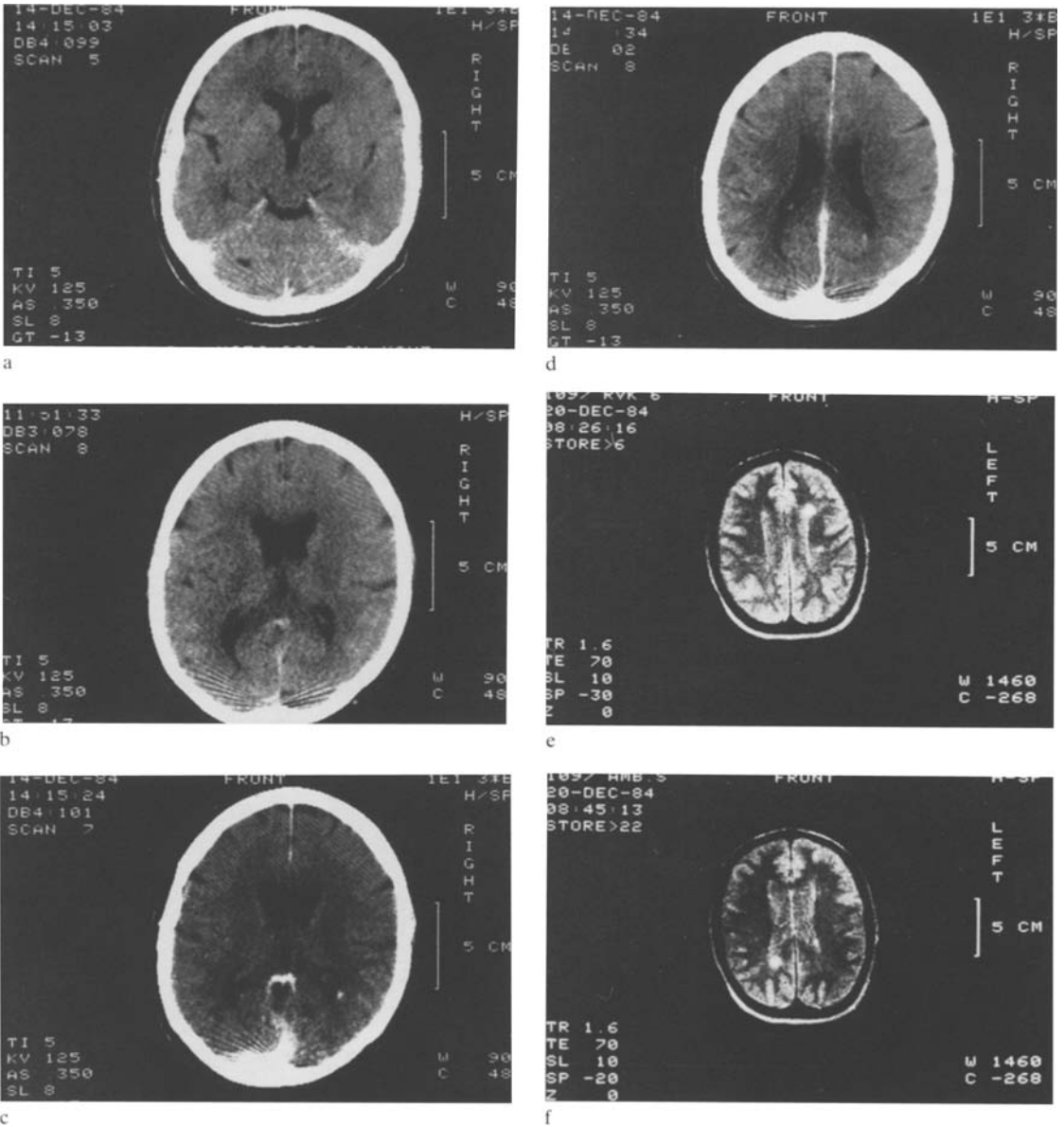
It was shown that CSF analysis which detects an increase of CSF IgG and oligoclonal bands is still the most important test with regard to sensitivity and costs. We were disappointed in the results with BAEP and VEP, which in our cases had lower detection rates than those reported in the literature [1, 4, 7, 8, 12-14, 16, 19-23, 27, 29]. Further studies will show whether this might be due to too strict evaluation criteria.

Of much importance for us were the results of CT and MRT. Next to CSF analysis, MRT imaging was the most sensitive method for detection of abnormal findings. It detected lesions in 14 of 17 patients (82%), a result in the range provided by the literature [2, 6, 9, 10, 11, 18].

Although the results of CT imaging are clearly not as good as those of MRT, the detection rate of 58% for the delayed scan after double-dose contrast appears to be remarkable, particularly because the detection rate was over 50% in all groups with questionable MS. In contrast to this, other authors recorded abnormal CT findings in 21% to 63% [3, 5, 9, 15, 19, 21, 26, 28] depending on the number and clinical state of patients as well as the imaging method (without, with normal and with double-dose contrast).



**Figure 1.** Case 1. Normal CT scan without contrast (a, b). After infusion of double-dose contrast, demarcation of two enhanced lesions in peri- and supraventricular white matter, right and left (c, d).

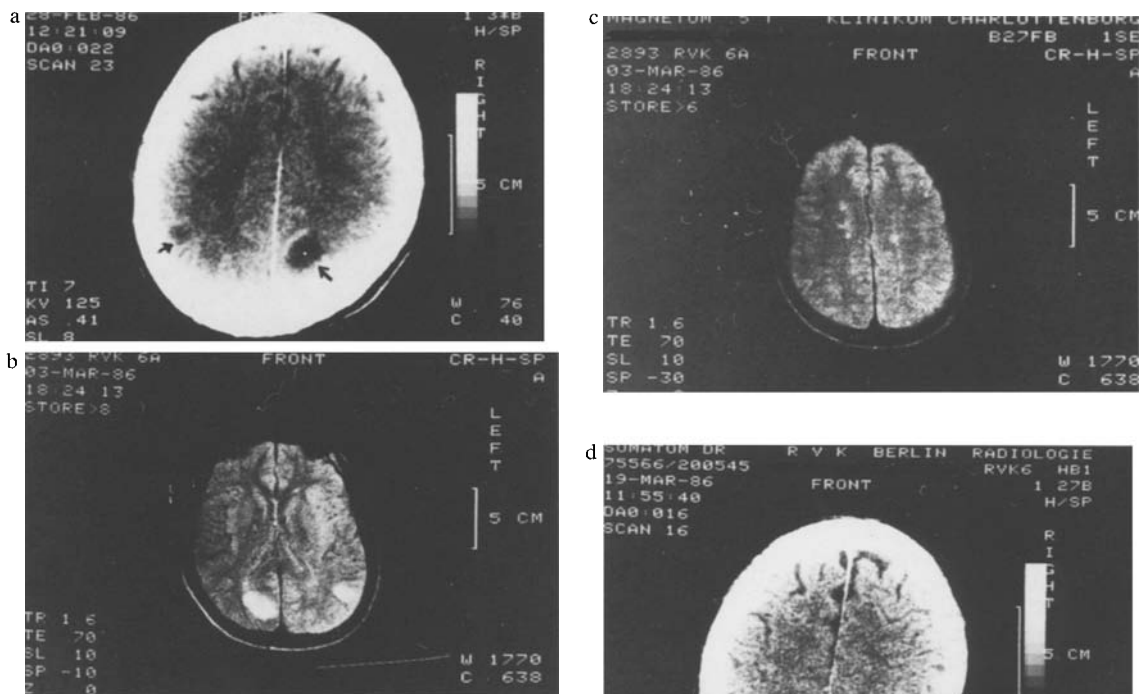


**Figure 2.** Case 2. In native scan only left cerebellar hemispheric hypodensity (a, b). Delayed double dose contrast

scan showing two periventricular enhancements on the right side (c, d). NMR showing further lesions (e, f).

The very disappointing detection rate of only 26% by the nonenhanced scan, confirmed the observations of SEARS et al., SPIEGEL et al., VINUELA et al., and EBERS et al. [5, 24, 26, 28] that CT imaging with delayed scanning after double-dose contrast produces a substantially higher yield of information, and that the application of a double-dose of contrast medium plays the most important role. Although both MRT and CT are very expensive methods, they are exceedingly helpful in the diagno-

sis of early and doubtful cases in which the certain objective substantiation of multiple lesions is of great importance and which cannot be replaced by clinical findings, not even with evoked potentials. This was demonstrated in cases 1 and 2. Nevertheless, as case 3 demonstrates, MRT and CT can also lead to new difficulties in differential diagnosis and thus should only be interpreted in connection with medical history, clinical findings, and the results of CSF analyses.



**Figure 3.** Case 3. First CT showing two hypodensities one in the right and one in the left parietal lobe (a, lesions marked by arrows). MRT showing multiple lesions (b, c). Control CT three weeks later (d) shows complete remission of left and partial remission of right focus corresponding to remission of symptoms.

**Table I.** Incidence of abnormal findings using various methods in cases of definite, probable, possible and first exacerbation of MS.

Patients with MS	CSF	AEP	VEP	AEP + VEP	CT without contrast	CT with double-dose-contrast-medium	MRT
Total	63 50 of 54 (93%)	20 of 55 (36%)	38 of 63 (60%)	41 of 55 (74%)	16 of 61 (26%)	35 of 60 (58%)	14 of 17 (82%)
Definite	32 23 of 23 (100%)	11 of 29 (38%)	19 of 32 (59%)	21 of 29 (72%)	10 of 31 (32%)	18 of 31 (58%)	7 of 8 (88%)
Probable	12 11 of 12 (92%)	3 of 11 (27%)	9 of 12 (75%)	10 of 11 (90%)	2 of 12 (16%)	7 of 11 (63%)	3 of 4 (75%)
Possible	19 16 of 19 (84%)	6 of 15 (40%)	10 of 19 (53%)	10 of 15 (66%)	4 of 18 (22%)	10 of 18 (55%)	4 of 5 (80%)
First exacerbation	11 of 13 (85%)	5 of 12 (42%)	7 of 13 (54%)	8 of 12 (66%)	2 of 12 (17%)	7 of 12 (58%)	3 of 5 (60%)

**6 Summary**

Medical history and clinical findings as well as CSF analyses still are the most important methods for the diagnosis of MS. However, doubtful cases or during the first exacerbation of MS, evidence of multiple and asymptomatic lesions can be of great impor-

tance. Because of its great sensitivity, MRT is the best method to gain this evidence. However, until this method becomes widespread and less expensive, we consider CT with double-dose contrast and delayed scanning to be a very useful tool for the diagnosis of MS.

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