

Regular Article

Multiple sclerosis with extensive lesions, left hemiplegia, mental dysfunction and retrobulbar neuritis

KANA OGAWA, MD, MASAHIKO KISHI, MD, TERUYUKI KURIHARA, MD,
KEN IKEDA, MD, AND MASAO KINOSHITA, MD
Fourth Department of Medicine, Toho University School of Medicine, Meguro, Tokyo, Japan

Abstract

Multiple sclerosis (MS) is usually diagnosed on the basis of the typical clinical course, with remission and exacerbation in multiple parts of the central nervous system (CNS). Recently, magnetic resonance imaging (MRI) has made a large contribution to the diagnosis of patients with MS. But it is difficult to make a definite diagnosis due to clinical variability of the disease and variable MRI findings. We report the case of a 26-year-old woman who developed progressive left hemiplegia, mental dysfunction, and had extensive bilateral cerebral white matter lesions diagnosed by brain MRI. Complete recovery from the left hemiplegia followed the use of corticosteroid, and her brain MRI findings also improved after medication. Early in the clinical course it was difficult to differentiate between multiple sclerosis and granulomatous angiitis of the CNS. After recovery from the first episode of left hemiplegia and mental dysfunction, she developed acute visual disturbance five months after her first admission. Readmission followed and her retrobulbar neuritis was successfully treated by methylpredonisolone pulse therapy. In summary, she experienced two episodes of neurological deficit, had left hemiplegia and mental dysfunction associated with multiple lesions in bilateral cerebral white matter in brain MRI, and the left retrobulbar neuritis with delay of P100 by visual evoked potential study. Due to these two episodes we concluded that she had multiple sclerosis. Though the initial diagnosis was difficult, prompt treatment and close follow-up was important, since multiple sclerosis and granulomatous angiitis of the CNS can both recur.

Key words

isolated angiitis of the central nervous system, large demyelinating lesions, magnetic resonance imaging, multiple sclerosis.

INTRODUCTION

We report the case of a 26-year-old Japanese female who developed acute left hemiplegia and mental confusion and had very extensive white matter lesions shown by magnetic resonance imaging (MRI) studies. Five months later she developed left retrobulbar neuritis. It was difficult to make a definite diagnosis before the second episode.

Since granulomatous angiitis of the central nervous system (CNS) and multiple sclerosis (MS) can both

recur and can respond to corticosteroid therapy, it is difficult to make a definite diagnosis by the first episode of neurological illness, but close follow-up and prompt therapy at each episode may eventually provide a correct diagnosis.

The patient showed symptoms in late 1997 when she suddenly ceased her long-standing use of the Internet because she kept forgetting her password and made continual typing errors. The following day her speech reduced and very soon she was saying nothing at all to her family. She became silent and did not use her left hand. One week after her speech reduction she visited the bathroom and had a bowel movement fully dressed. The following day her mother noted a limp in her left leg. One day later she experienced urinary incontinence and would not eat. The next day she attended a nearby hospital and

Correspondence address: Kana Ogawa, Fourth Department of Medicine, Toho University School of Medicine, 2-17-6 Ohashi, Meguro, Tokyo 153-0044, Japan

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underwent neuroradiological examinations including brain computed tomography (CT) and MRI and was noted as having an unusually diffuse brain disorder, though a definite diagnosis was not made. Subsequently, she became unable to walk and her general condition deteriorated.

Admitted to our neurosurgery department, she had brain MRI studies which revealed diffuse brain white matter disorder. Past history revealed fibrile convulsions at the age of one year and otitis media at the age of 10 years. There was no history of allergies or of surgery. She did not use alcohol or tobacco and had no history of oral contraceptive use or any regular medication. The family history was unremarkable.

The patient was physically mature but obese. On general physical examination her blood pressure (BP) was 136/92 mmHg and her pulse rate was 78 b.p.m. and steady. Her temperature was 36.5°C and respiration was 18/min. She had no skin eruptions or evidence of lymphadenopathy.

Neurological examinations

At neurological examination the patient was awake and lying quietly. She did not initiate any conversation. Her left leg was abducted due to the left hemiplegia, and there was no spontaneous movement of her left arm and hand and no involuntary movement otherwise. When questioned she answered with one or two words. She was able to perform simple addition and could follow simple instructions appropriately. Her orientation to time and place was preserved, though she had retrograde amnesia covering the previous two weeks. Judgement was poor, but she displayed insight. She did not experience hallucinations or delusions. She had normal vision and the optic fundi were normal. The pupils were round, equal in size, and reacted to light and accommodation. The extraocular movements were full. She had central facial palsy on the left side, and her neck was supple. The deep tendon reflexes were increased to 2+ bilaterally and the extensor toe signs were positive bilaterally. She had left hemiplegia. Pain and temperature sense was decreased to 5/10 on the left upper and lower extremities. Coordination was normal on the right side. She was unable to perform a finger-to-nose test on the left side, nor heel-to-shin test, due to left hemiparesis. No tremors or seizures were noted.

The impression upon admission was that of extensive and acute demyelinating disorder involving cerebral white matter bilaterally but more extensively on the right brain. She had left hemiparesis and increased deep tendon reflexes, with positive extensor toe signs bilaterally. The differential diag-

nosis included acute multiple sclerosis, progressive multifocal leukoencephalopathy, acute disseminated encephalomyelopathy, primary lymphoma of the brain, neoplastic angioendotheliosis, mitochondrial myopathy, encephalopathy, lacticacidosis, and stroke-like episodes (MELAS), and cerebral granulomatous angiitis.

Laboratory examinations

Complete blood cell count, serum electrolytes, renal and liver function tests, and urinalysis were normal; the erythrocyte sedimentation rate was 12 mm/h. Cholesterol was 163 mg/100 mL and glucose was 98 mg/100 mL. The lactic dehydrogenase (LDH) was 380 U and the creatine kinase (CK) 79 U. The following laboratory tests were negative or normal: HIV, HTLV-1, cortisol at 06.00 h, angiotensin-converting enzyme and very long-chain fatty acids. Serum immuno-electrophoresis and agarose-gel electrophoresis gave normal patterns; tests for rheumatoid factor, antinuclear antibodies. The CH50 was 45.5 U/mL (normal range is 30–40).

Concerning cerebrospinal fluid (CSF), the lumbar puncture yielded clear, colourless CSF that contained 2 cells/mm³, of which 82% were mononuclear cells and 18% polymorphonuclear cells. The CSF glucose was 86 mg/100 mL, and the protein 36 mg/100 mL. Oligoclonal IgG band was absent, total IgG was 2 mg/100 mL, and myelin basic protein was 1.7 ng/mL. Culture of CSF was negative for fungi, mycobacteria and other micro-organisms. Cytologic examination of CSF was negative for tumour cells. Virus antibody screening, hepatitis B and C antibodies, antigen tests, Waaler–Rose and Epstein–Barr (EB) viral antibodies were normal or of non-diagnostic finding. Chest radiograph and ECG were normal. An electroencephalogram was abnormal because of right-sided delta and theta slowing.

Concerning neuroradiological studies, a resonance MRI scan of the brain, performed on the first day of hospitalization, revealed predominantly white matter abnormality, characterized by diffuse, hypointense T1-weighted and hyperintense T2-weighted signal abnormality of the deep white matter of the bilateral cerebral hemispheres. The lesions were mainly in the white matter, but the right white matter lesion was so extensive that the high intensity area partially spread to the right parietal cortical grey matter, which could indicate brain oedema (Figs 1,2). On the T1-weighted images, the white matter lesions were well-enhanced with gadolinium (Fig. 1).²⁰¹ TlCl scintigraphy of the brain showed no remarkable enhancement, rCBF SPECT with ¹²³I-IMP showed low perfusion in the right parietal, frontal and posterior temporal region.

Figure 1. T1-weighted (TR 500/TE 15) brain magnetic resonance imaging (MRI) after gadolinium administration demonstrates diffuse irregular enhancement in the lesions of bilateral white matter.

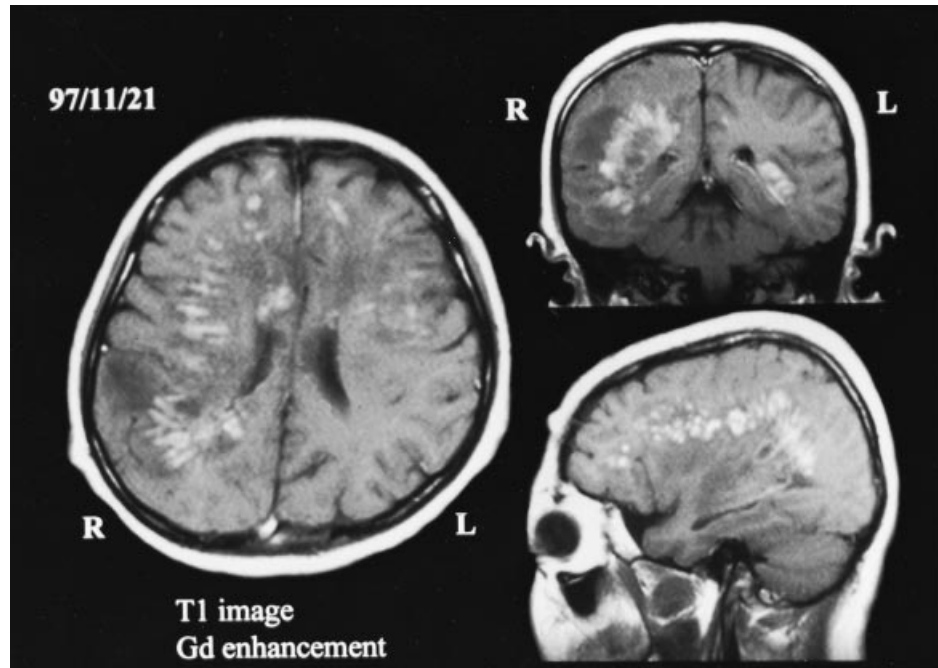
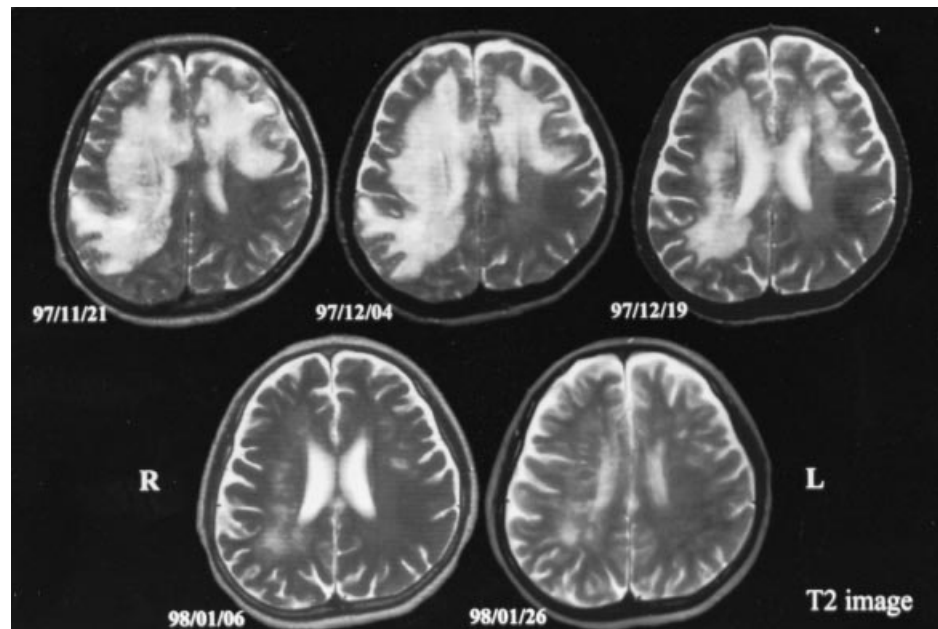


Figure 2. T2-weighted (TR 4000/TE 15) brain magnetic resonance imaging (MRI) on 21 November shows high signal areas in the frontal and parietal white matter bilaterally. The right white matter lesion was so extensive that the high intensity area partially spread to the right parietal cortical grey matter, which could indicate brain oedema. Follow-up studies two and four weeks later show marked improvement in the white matter lesions. Brain MRI two and five weeks after this show further improvement.



rCBF SPECT with ^{99m}Tc -ECD revealed that bilateral brain blood flow was not low, but low perfusion was seen in the right parietal, temporal and frontal base. Cerebral angiogram was normal.

Clinical course

The patient was transferred to the neurology department and treated with a 2-day course of intra-

venous (i.v.) methylprednisolone of 500 mg/day followed by 5-day course of i.v. prednisolone (as much as 60 mg/day). Following this, her clinical status improved. On the third day she was able to move her fingers, and on the seventh day she could walk by herself. On the fourteenth day her left hemiparesis completely improved. Mental dysfunction gradually improved and she became able to communicate with people using complete sentences. She began to talk to

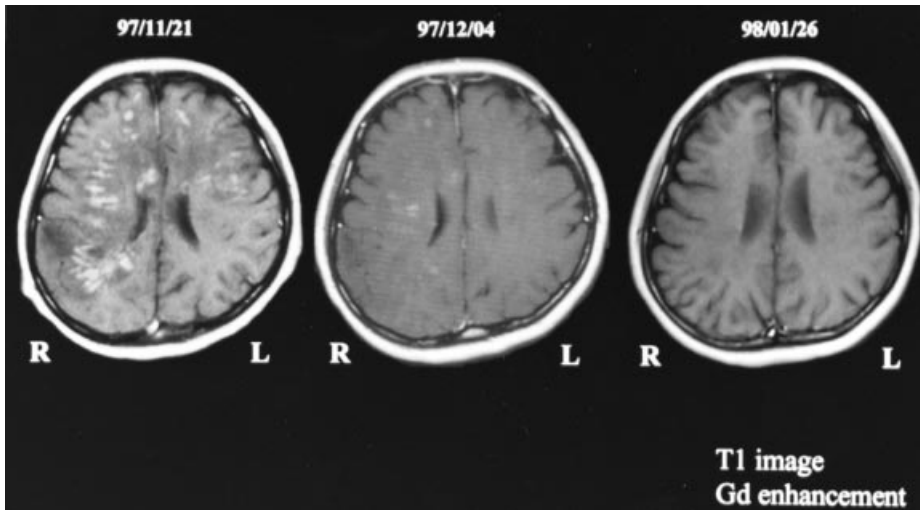


Figure 3. Serial studies of T1-weighted (TR 500/TE 15) brain magnetic resonance imaging with gadolinium enhancement also showed improvement in the course of the illness.

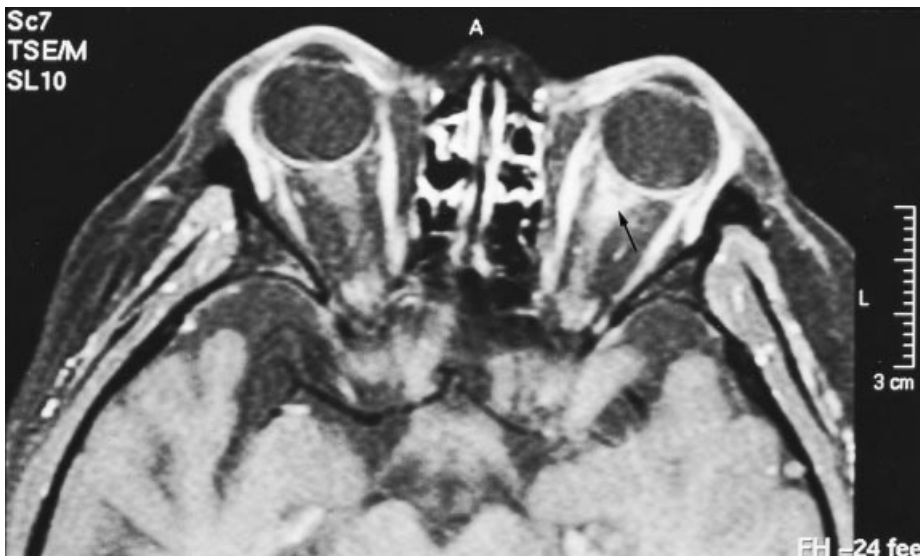


Figure 4. T1-weighted (TR 500/TE 15) brain magnetic brain imaging after gadolinium administration demonstrates enhancement in the left optic nerve (arrow) directly behind the left eye, indicating retrobulbar neuritis.

her mother more spontaneously and her mathematical ability improved to two-digit simple addition and subtraction. Her short-term memory improved to a level that was almost normal and she became able to carry out the activities of daily living. The large white matter lesions observed by the initial brain MRI had decreased in size by the twenty-fourth day and her condition was almost normal condition in two months (Figs 2,3). As she clinically improved, prednisolone was reduced to 20 mg/day. She was discharged after fifty days. By then she could walk by herself, carry out daily activities independently, and communicate without assistance. Her Wechsler Adult Intelligence Scale, Revised (WAIS-R) score at the time of discharge was 70 points. This result is

borderline, and indicated some persisting cognitive dysfunction.

Upon the second admission 5 months later the patient was monitored at the outpatient clinic and did well until mid-April 1998, when she developed acute left visual disturbance. She was readmitted and visual evoked potential (VEP) revealed delayed P100 on left side. She was treated with intravenous methylprednisolone for 3 days and thereafter oral prednisolone (100 mg/day), after which her vision rapidly improved. Oral prednisolone was reduced and she was discharged in late May 1998. Magnetic resonance imaging of the brain demonstrated lesion in the left optic nerve (Fig. 4). The VEP (P100) was 119 msec on the right side but was prolonged to 148 msec on the left side.

DISCUSSION

The case began with progressive mental dysfunction and left hemiplegia, showing marked improvement with steroid pulse therapy followed by oral steroids. Brain MRI indicated extensive white matter lesions in the bilateral cerebral hemispheres. The clinical, neuroimaging features, and the clinical response to steroids suggested several differential diagnoses, including myelinoclastic diffuse sclerosis (a variant type of multiple sclerosis), adrenoleukodystrophy, various leukoencephalopathies, and atypical primary CNS lymphoma, all excluded by cerebrospinal fluid findings, cerebral angiography and thallium scintigraphy. Acute disseminated encephalomyelopathy was another possible differential diagnosis. Another possibility was idiopathic granulomatous angiitis of the CNS (IGANS), which predominantly involves the small and medium-sized arteries and veins of the leptomeninges and brain parenchyma. In the previous reports they demonstrated granulomatous, lymphocytic, or necrotizing inflammation with granulomas present in less than half the cases.¹ However, pre-mortem diagnosis is difficult and in most cases correct diagnosis occurs by autopsy. Moreover, even brain biopsy results are not always satisfactory, and correct diagnosis can not be made in 8–18% of cases.^{2–5} For these reasons, open brain biopsy is recommended, though this cannot be done easily when we consider the invasiveness of open biopsy and the unsatisfactory diagnostic rate. It is also necessary to start therapy as soon as possible without spending too much time on investigations, since the neurological manifestations, including disturbance of consciousness, and the progressive nature of the disorder, require that the patient be treated quickly. In our case the patient and the family refused to allow brain biopsy and a pathologically definite diagnosis could not be obtained. Although MRI features resembling demyelinating disease have been reported with IGANS, bilateral, diffuse, relatively symmetric white matter changes mimicking leukoencephalopathies and leukodystrophies are limited to several case reports.^{1,6,7} Recently, Pasquale *et al.* reported a case of IGANS with widespread cerebral white matters, as reported here.⁸ In our case the widespread white matter lesions were unique and strongly enhanced by gadolinium, and improved with steroid therapy. Although IGANS is a rare disorder, it is important to think of the disease as described by Launess when we see a patient with undiagnosed fluctuating neurological symptoms, with progressive disturbance of consciousness, cognitive dysfunctions, and focal neurological signs.⁹ Although we could not

get the typical findings of CFS, the possibility of MS had remained from the first admission because of the multiple clinical features. Some patients with MS may have cognitive and emotional defects that correspond to degenerative brain changes. In some instances, neuropsychological impairment may be the initial or predominant symptom of MS.¹⁰ The characteristic brain MRI findings of MS are multiple white matter lesions seen as high signal areas on T2-weighted sequences, and these are predominantly located around the lateral ventricles in irregular and asymmetrical patterns.¹¹

While monitoring this case in the out-patient clinic, the patient suddenly developed left visual disturbance. She was readmitted and VEP studies and MRI of the optic nerve revealed retrobulbar neuritis, a very common lesion in multiple sclerosis. At this point the most probable diagnosis is multiple sclerosis rather than IGANS. With these two episodes of exacerbation, the patient fulfilled the diagnostic criteria of multiple sclerosis. Although the diagnosis was not conclusive at the first admission, close follow-up and prompt treatment with steroid pulse and oral corticosteroid during exacerbations quickly resolved the neurological symptoms, and lead to the diagnosis of acute MS with bilateral extensive cerebral white matter lesions in MRI, followed by the left optic nerve involvement five months later. Additionally, multifocal MRI white matter lesions are seen in many disorders other than multiple sclerosis, but Fazekas *et al.* have applied the rule that two of the following three findings are required: a lesion abutting the body of the lateral ventricles; an infratentorial lesion, and a lesion >5 mm in diameter. An evaluation of 1500 consecutive patients using these criteria yielded a sensitivity of 81% and specificity of 96% for the diagnosis of MS.^{11,12} However, MRI findings should never be used in isolation to establish a diagnosis of MS. The clinical findings and age of the patient must be carefully considered.

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