

Bilateral Demyelinating Tumefactive Lesions in Three Children With Hemiparesis

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ABSTRACT

We present the results from the evaluations of three children ages of 2, 7, and 11 years with hemiparesis and multiple white-matter lesions on magnetic resonance images (MRIs). The initial symptoms were mainly acute/subacute hemiparesis in all and headache/vomiting in one of them. Before admission, one of them had a history of upper respiratory tract infection, whereas another had undergone urinary tract surgery, and the other reported no history of any infection or stress-related factor. In all of the children, MRI showed multiple superficial and deep white-matter hyperintensity in T_2 -weighted and proton density images with perifocal edema in the acute phase. During the symptomatic period, all of the patients underwent corticosteroid treatment. Whereas two of the patients demonstrated signs of recovery during the first week of treatment, the other patient demonstrated almost a full recovery with minimal neurologic sequela. Follow-up MRI demonstrated not only a remarkable decrease in the size and number of the lesions, with complete resolution for many of them, it also demonstrated a loss of contrast enhancement. None of these three patients, who had been followed up clinically and through MRI for 5 years, have shown either a clinical relapse or new lesions. The clinical pictures and MRI of the children were different in some aspects from acute multiple sclerosis and acute disseminated encephalomyelitis. Regarding both the clinical follow-up and treatment strategy, it is essential and interesting to state the fact that tumefactive lesions involving both hemispheres are likely to appear during the monitoring of the monophasic courses among inflammatory demyelinating diseases of childhood such as acute disseminated encephalomyelitis. (*J Child Neurol* 2002;17:655–660).

Inflammatory demyelinating diseases include a large spectrum and various clinical presentations in childhood. Acute disseminated encephalomyelitis, childhood cerebellitis, postimmunization inflammatory demyelinating diseases (optic neuritis, transverse myelitis, etc), multiple sclerosis, and some metabolic and toxic diseases constitute the majority of inflammatory demyelinating diseases in childhood.¹ A relapsing and remitting course can be associated with many of these diseases (multiple sclerosis, homocystinuria, Leigh's disease, etc), but clinical features and laboratory findings usually indicate the correct diagnosis.² We

report three children who presented with hemiparesis as the main clinical feature, monophasic encephalopathy, and multifocal/tumefactive white-matter lesions detected in magnetic resonance imaging (MRI). The clinical pictures and MRI findings of these patients are discussed in an attempt to characterize the lesions and to assign the cases to one of the inflammatory demyelinating diseases, especially acute disseminated encephalomyelitis and multiple sclerosis.

CASE REPORTS

Patient 1

A 2-year-old girl was admitted with a history of left-sided weakness and headache that had developed within the previous 3 days. One week after the onset of symptoms, MRI showed two large bilateral demyelinating lesions of T_1 -weighted hypointensity and T_2 -weighted hyperintensity, exerting minimal mass effect in the centrum semiovale (Figures 1 and 2). No contrast enhancement was observed (see Figure 2). Corticosteroid therapy was initiated by a neurosurgeon, who referred her to our clinic on the tenth day of the symptoms. Dexamethasone 0.5 mg/kg was initiated, gradually reduced,

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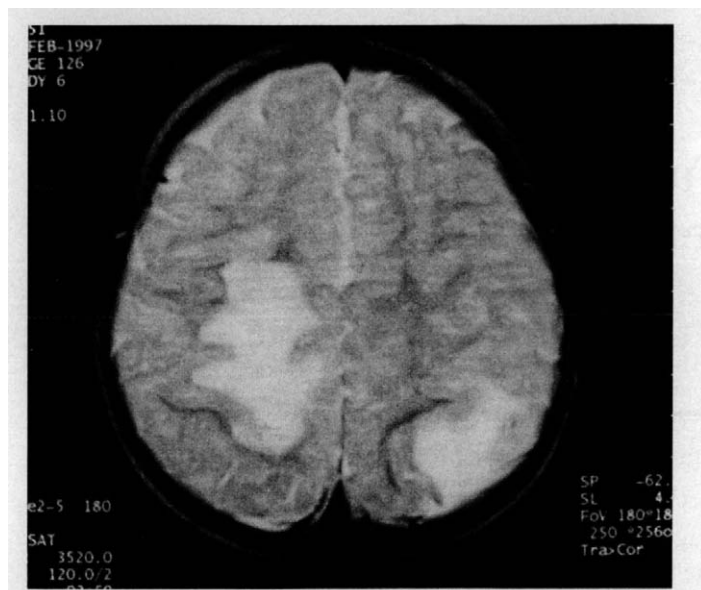


Figure 1. Patient 1: T₂-weighted axial, fourth day of symptoms. Two large lesions in the white matter.

and eventually ceased over a period of 1½ months. Partial resolution of hemiparesis was noted 3 days after the administration of corticosteroids. Medical history did not suggest any prenatal problems, neurodevelopmental milestones, or systemic diseases. There was no history of vaccination or infection antedating the illness. The findings of systemic examination were normal. Neurologic examination showed a mild left upper motoneuron paresis (4/5) with hyperreflexia and extensor plantar reflexes. She had a hemiparetic gait. Complete blood count, sedimentation rate, blood urea nitrogen, serum electrolytes, and liver function tests were all normal. Screening for sickle cell disease was negative. Urinalysis excluded homocystinuria. Cerebrospinal fluid findings were normal, cul-

tures and viral serology were negative, immunoglobulin G index was 0.55, and no oligoclonal band was detected in cerebrospinal fluid. Electroencephalography (EEG) showed generalized slowing (3.5–4.5 Hz). Mental status was also normal. There was no abnormality on ophthalmologic examination. The findings of chest radiography, electrocardiography, and echocardiography were normal. Magnetic resonance angiography revealed normal neck and cerebral vessels. The patient partially recovered 3 weeks after the onset of symptoms. She could partially control her left hand. The corticosteroids were tapered and discontinued at the end of 6 weeks. Except for left hyperreflexia, follow-up examinations (at the end of 2 months and 57 months, respectively) were normal.

Patient 2

A 7-year-old boy presented with left-sided weakness that had developed over the previous 2 days, followed by headache a day after the onset of weakness. On the third day of symptoms, he had nausea and vomiting and could not walk. Magnetic resonance imaging performed 5 days after the onset of symptoms showed white-matter lesions with perifocal edema and mass effect in the right parietal, left parietal, and left frontal areas (Figures 3 and 4). There were nodular and diffuse contrast enhancements (see Figure 4). The lesions were thought to be of neoplastic nature by a neurosurgeon at another institution, and corticosteroid therapy was started 6 days after the onset. Pre-, peri-, and postnatal history was unremarkable. No history of migraine or migraine equivalents was present. Physical examination was within normal limits. On neurologic examination 13 days after the onset, he displayed mild left upper motor paresis (4/5) with hyperreflexia and Babinski reflex on the left side. Complete blood count, sedimentation rate, blood urea nitrogen, serum electrolytes, and liver function tests were within the normal range. Screening for sickle cell disease and vasculitis was negative. Urinalysis for homocystinuria was nonrevealing. No atypical cells were found in cerebrospinal fluid. The other findings are shown in Table 1. Pattern visual evoked potentials, chest radiography, electrocardiography, and echocardiogram were within the normal range. The IQ score was 110 (Alexander Test). Electromyographic and EEG activities were also within normal limits. There was a dramatic clinical improvement 12 days after the administration of corticosteroids. On the 20th day of the illness, a considerable decrease in the lesions was observed on MRI. Dexamethasone was gradually reduced and eventually ceased in a month. Seven months after the onset, MRI showed minimal focal gliosis in the precentral gyrus (Figure 5). No abnormalities were found during a follow-up period of 5 years.

Patient 3

An 11-year-old boy presented with focal motor status epilepticus in the right extremities that developed 2 days after a urinary tract operation. The seizures were kept under control by administration of intravenous clonazepam. Hemiparesis was detected on the right side. Inquiry into prenatal, natal, delivery, and mental-motor neurodevelopmental features did not reveal any abnormal findings. A history of recurrent urinary infections complicated by renal failure was obtained. There was a first-degree consanguineous marriage. No family member suffered from any neurologic disorder. On physical examination, his weight and height were below the 3rd per-



Figure 2. Patient 1: T₁-weighted axial, with contrast. No contrast enhancement.

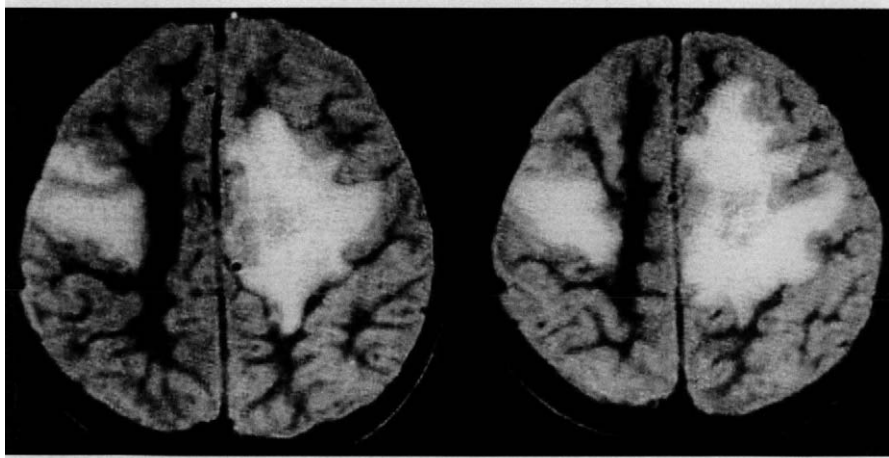


Figure 3. Patient 2: T₂-weighted axial, fifth day of symptoms. Bilateral, multiple, irregular, tumor-like, large white-matter lesions.

centile. Neurologic examination showed right upper motor hemiparesis (0/5 in the upper limb, 3/5 in the lower limb) and hyperreflexia with Babinski reflex on the right side. Magnetic resonance imaging showed bilateral, multiple, irregular lesions (Figure 6) and heterogeneous contrast enhancement (Figure 7). Complete blood count and biochemical investigations were normal, except levels indicating mild to moderate renal failure. His IQ was 72 (Alexander Test). All cerebrospinal fluid findings were normal. EEG showed generalized, bilateral slow waves. Bilateral multiple, irregular, white-matter hyperintensities were detected on MRI (see Figure 6). Corticosteroid treatment (2 mg/kg of methylprednisolone

orally) was initiated, after which the patient completely recovered within 5 days. Total period of intake of methylprednisolone was 13 weeks. At the end of 5-year follow-up, he exhibited normal findings on neurologic examination. Follow-up MRI (at the end of 3 weeks and 1 year, respectively) revealed normal findings (Figure 8) (see Table 1).

DISCUSSION

Acute disseminated encephalomyelitis often presents as widespread central nervous system disturbances with coma

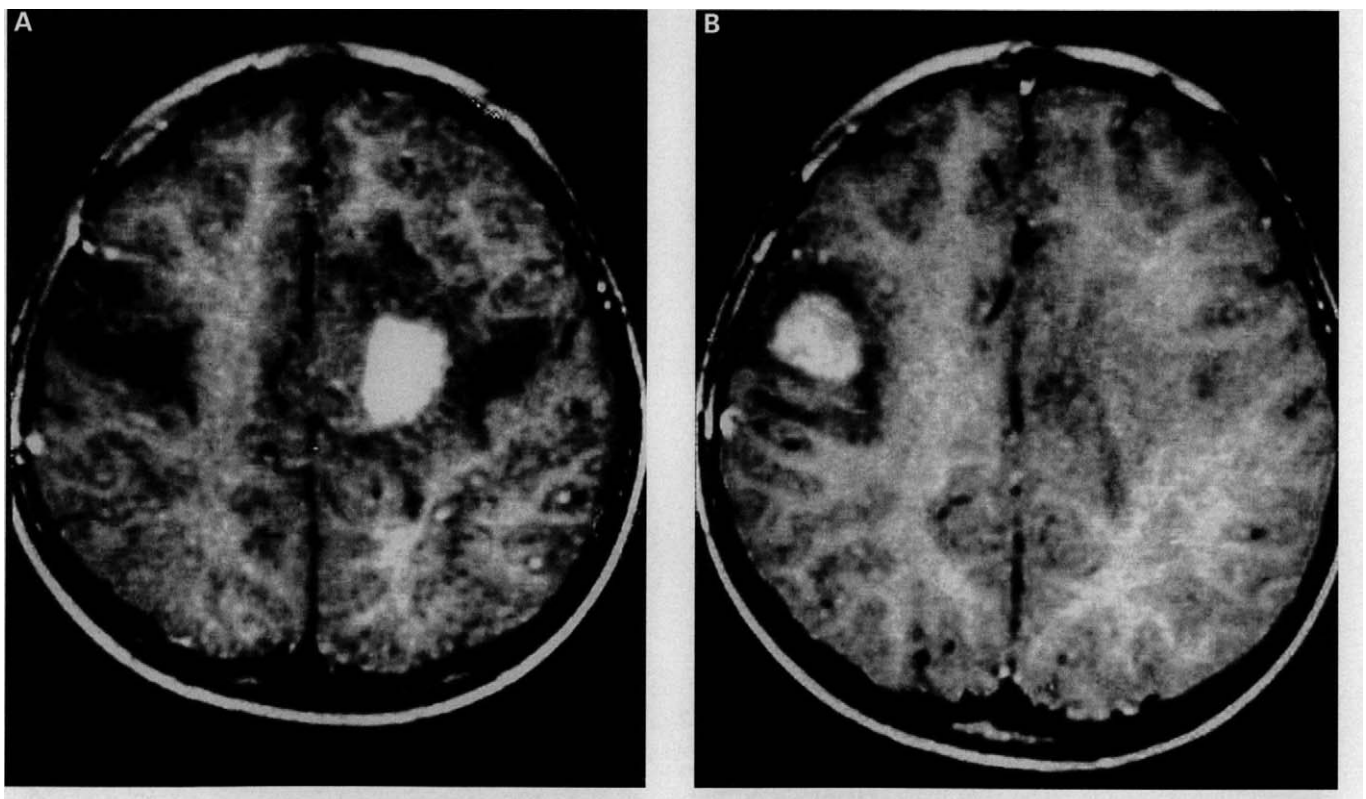


Figure 4. Patient 2: T₁-weighted axial, with contrast. Nodular and diffuse contrast enhancement in both A and B.

Table 1. Clinical Features and Laboratory Findings of Patients

Sex	Age (yr)	Preceding Findings	Cerebrospinal Fluid	Initial MRI	Clinical Data	Neurologic Examination	Control MRI	Follow-up (mo)
1 F	2	—	Protein 29 mg/dL Glucose 50 mg/dL IgG index: 0.55 OB (negative)	Bilateral, two large demyelinating lesions in superficial and deep white-matter with mild gray-matter involvement No CE (4th day of symptoms)	Acute/subacute left hemiparesis including face	1. Almost complete recovery (brisk reflexes on the left) (3rd wk, 2nd mo) 2. Almost normal (brisk reflexes on the left) (57th month)	Marked but incomplete resolution No NL, no CE (7th wk)	57 No NE
2 M	7	Nonspecific upper respiratory tract infection	Cells ↑ 15/μL (lymph) Protein 31 mg/dL Glucose 67 mg/dL IgG index: 0.78 OB (negative) No atypical cell	Bilateral, multiple, irregular, tumor-like white-matter lesions with mass effect Diffuse and nodular CE (5th day of symptoms)	Acute/subacute left motor hemiparesis including face, headache, vomiting	1. Complete recovery (18th d) 2. Normal (66th mo)	1. Partial resolution No NL (20th d) 2. Marked but incomplete resolution No NL, no CE (2nd mo) 3. Minimal focal gliosis in the same region, no NL (7th mo)	66 No NE
3 M	11	Urinary tract infection	Protein 25 mg/dL Glucose 67 mg/dL OB (negative)	Bilateral, multiple, irregular, white-matter lesions Heterogeneous CE (1st day of symptoms)	Right focal motor seizure, right motor hemiparesis including face	1. Complete recovery (6th d) 2. Normal (3rd wk) 3. Normal (negative 12th mo) 4. Normal (59th mo)	1. Marked but incomplete resolution No NL, no CE (3rd wk) 2. No NL (12th mo)	59 No NE

MRI = magnetic resonance imaging; OB = oligoclonal band; CE = contrast enhancement; NL = new lesion; NE = new episode.

or drowsiness, headache, seizures, fever, and multifocal neurologic signs.¹ It can occur with measles, varicella, and nonspecific upper respiratory tract infections or even without a recognizable preceding event. Whereas there was no history of antecedent infection or vaccination in our first patient, the third and second patients had urinary tract surgery and upper respiratory tract infection, respectively. Sometimes it can be difficult to differentiate acute disseminated encephalomyelitis from the acute forms of multiple sclerosis. In contrast, multiple sclerosis usually presents as a monosymptomatic syndrome, such as optic neuritis or subacute myelopathy.³ It can also become manifest by antecedent events like acute disseminated encephalomyelitis. Acute disseminated encephalomyelitis is usually a monophasic illness, although a few recurrent cases have been reported.³⁻⁷ Nevertheless, no clinical feature is exclusive to one or the other disorder. More diffuse encephalopathic disturbances can rarely be seen with multiple sclerosis.³

Hemiparesis involving the face is an uncommon presentation of primary demyelinating disorders of the central nervous system and can cause diagnostic confusion, especially if the disease is monophasic. It is rare in definite multiple sclerosis.^{5,8} Khan et al described two adult patients with multiphase disseminated encephalomyelitis presenting as alternating hemiplegia.⁵ The diagnosis was made on the typical appearance on MRI and findings of the brain biopsy.

There were bilateral, multiple, scattered, contrast-enhancing nodular lesions in a female patient and two large lesions in the left subcortical white matter in a male patient. Dagher et al described a male patient who developed hemiparesis following flulike symptoms.⁹ Magnetic resonance imaging

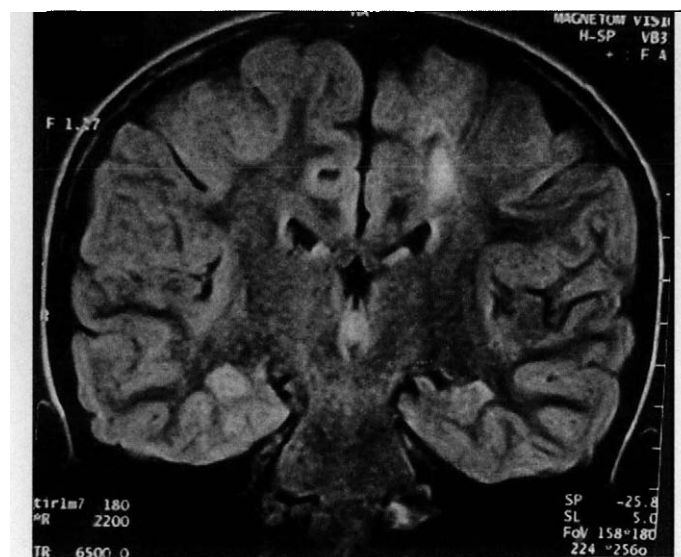


Figure 5. Patient 2: flair coronal, seventh month of the disease. Minimal focal gliosis in the left centrum semiovale.



Figure 6. Patient 3: T₂-weighted axial, first day of the disease. Bilateral multiple, irregular white-matter lesions in both A and B.

showed a peritrigonal lesion with moderate mass effect and homogeneous contrast enhancement. The diagnosis of these authors for this patient was also acute disseminated encephalomyelitis, and corticosteroid therapy resulted in a favorable outcome. Our diagnosis was acute disseminated encephalomyelitis in patient 3, who developed hemiparesis after focal status epilepticus and showed characteristic findings on MRI.

Cerebrospinal fluid in acute disseminated encephalomyelitis can be normal or can show mild leukocytosis with elevated protein levels or oligoclonal bands, as in multiple sclerosis.³ Although mild cerebrospinal fluid pleocytosis



Figure 7. Patient 3: T₁-weighted axial with contrast. Heterogeneous contrast enhancement.

was detected in patient 2 (15 white blood cells/ μ L), cultures remained negative, and no atypical cells were found. The presence of oligoclonal bands is a characteristic feature of multiple sclerosis; however, they can also be found in acute disseminated encephalomyelitis.³ They were observed neither in the blood nor in the cerebrospinal fluid of our patients.

Lesions of acute disseminated encephalomyelitis are seen in the supra- and infratentorial white matter as asymmetric foci of high signal intensity on long TR images as in

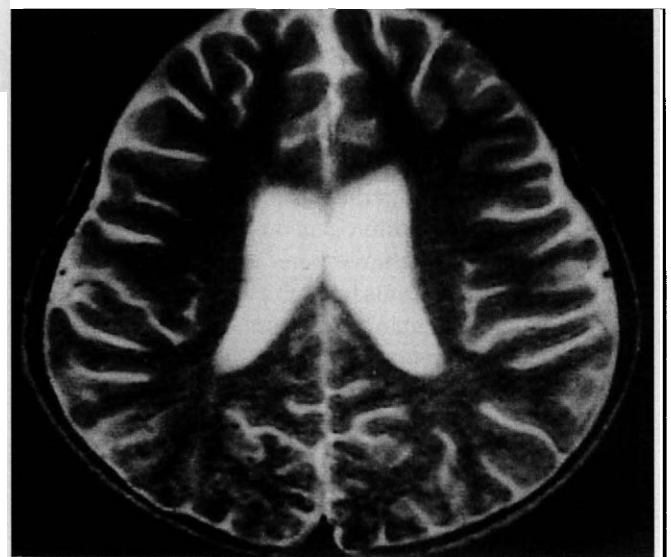


Figure 8. Patient 3: T₂-weighted axial, third week of the disease. Complete recovery and no new lesions.

patient 3 (see Figure 6). They vary greatly in size and number. Gray-matter involvement is less common. In our patients, the disease course, clinical presentations, findings of cerebrospinal fluid, and MRI suggested acute disseminated encephalomyelitis, especially in patient 3. Plaques are sharply demarcated and are frequently found adjacent to the ventricles. The presence of multifocal asymmetric white-matter lesions on MRI is not sufficient evidence to distinguish between multiple sclerosis and acute disseminated encephalomyelitis in patients with a single episode of neurologic disturbance.³ Lesions of multiple sclerosis occur at varying times. However, occurrence of new lesions is not expected in acute disseminated encephalomyelitis, provided that the follow-up period is sufficiently long. The interval that indicates that the patient has acute disseminated encephalomyelitis and not multiple sclerosis is at present uncertain. In our patients, no newly formed abnormalities were detected during a 5-year follow-up.

That bilateral multiple white-matter lesions were seen in all of our patients raised questions concerning a diagnosis of Schilder's disease.⁹⁻¹² In patient 1, two large bilateral lesions were localized superficially and deeply in the white matter (see Figure 1). However, the clinical features were very different from Schilder's disease in this patient. Demyelination with mass effect has been reported both in acute disseminated encephalomyelitis and multiple sclerosis.^{5,9,13} Whereas mass effect was more prominent in patient 2 than in patient 1, there was no mass effect in patient 3. Signs of tumefactive demyelination in inflammatory demyelinating conditions are important in avoiding the need for biopsy and risky treatment. Extensive and relatively symmetric abnormalities were found in the cerebral white matter in patients 1 and 2 (see Figures 1 to 5). Kepes described a possible immunologically mediated entity presenting with tumefactive demyelinating lesions with atypical features and histories not consistent with multiple sclerosis has been described.¹ Such extensive lesions are often mistaken for neoplasms or abscesses, as in patient 2.

Contrast enhancement noticed in demyelinating processes is caused by focal breakdown of the blood-brain barrier and may be suppressed by corticosteroids. Since acute disseminated encephalomyelitis is usually a monophasic disease, it has been postulated that all lesions would show contrast enhancement as they would all be active.³ Diffuse, nodular, ring-like, and heterogeneous gadolinium-enhanced demyelinating lesions have been reported.¹³⁻¹⁵ Contrast enhancement was not observed in patient 1 (see Figure 2), whereas heterogeneous (see Figure 7) and nodular (see Figure 4) enhancements were observed in patients 3 and 2, respectively. No contrast enhancement was observed on follow-up MRI of our patients.

Similarly, follow-up MRI demonstrated a marked decrease in the size and number of lesions, with complete resolution of some demyelination areas, as occurs in the

course of clinical improvement in acute disseminated encephalomyelitis.^{3,15} Control MRI showed complete resolution in our patients (see Table 1).

During the 5-year period of the follow-up of our three patients, it was noteworthy that they had only one clinical episode. The picture here is very much like that of acute disseminated encephalomyelitis, as the clinical findings and monophasic pacing suggest. The cranial MRI of patient 3 in particular confirms this diagnosis. On the other hand, those very large lesions on both hemispheres, as detected in two of our patients, are rare in acute disseminated encephalomyelitis or multiple sclerosis. It is striking that in the first two cases tumor biopsy was considered. Awareness of such cases is clinically important in that they can be promptly treated simply by using oral medication instead of resorting to invasive attempts, which are highly likely to cause complications.

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