

Subtle Encephalomyelitis in Children: A Variant of Acute Disseminated Encephalomyelitis

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Abstract

Four children with chronic, mild, nonspecific symptoms are described in whom magnetic resonance imaging (MRI) showed the presence of multifocal white-matter lesions suggestive of acute disseminated encephalomyelitis. The children ranged in age from 14 months to 15 years. The clinical picture was vague and inconclusive and consisted of several months of headaches, irritability, clumsiness, and personality change. Physical examinations were noncontributory. Laboratory investigation revealed no other cause of the demyelination. All of the patients have done well without any treatment, with a disappearance of symptomatology. The white-matter lesions on MRI scan in these children may indicate subtle exposure to a myelinolytic antigen. It has been suggested that such an exposure may create a state of complete or partial resistance to the encephalitogenic potential of the next infection or immunization. With complete resistance, the patient remains healthy and with partial resistance progressive demyelination results. Verification of these findings by others would suggest a possible benefit of a multicenter study of such patients, with virological, HLA testing, and long-term follow-up, in understanding the etiopathogenesis of multiple sclerosis. (*J Child Neurol* 1989;4:213-216).

In four children with variable clinical presentations, white-matter lesions visualized by magnetic resonance imaging (MRI) of the head suggested acute disseminated encephalomyelitis. None of the clinical presentations suggested acute disseminated encephalomyelitis, but the MRI clearly defined alterations in cerebral white matter. The children may have had a one-time exposure to a myelinolytic antigen; their clinical course supports this contention.

Case Reports

Case 1

A 13-month-old boy was evaluated for shakiness and apparent head pain. The parents had noted the child would episodically grab his head, cry, and lie down several times during the day. Similar episodes awoke him at night. He

appeared excessively tired. The problem had been present for two months and had begun after a respiratory infection. Examination was unremarkable except for an extensor plantar response on the left. Electroencephalogram (EEG) revealed 1 to 2 Hz occipital slowing. A computed tomographic (CT) scan of the head was normal; however, MRI of the brain revealed multifocal areas of increased signal intensity in the white matter of the occipital and right frontal lobes on T₂-weighted images (Figure 1). Cerebrospinal fluid (CSF) revealed two immunoglobulin bands, while serum was homogeneous. CSF immunoglobulin G synthesis was slightly elevated (9.2 mg/day). Myelin basic protein was borderline increased (4 ng/mL). Values for leukocyte enzymes (including galactocerebrosidase, arylsulfatase, β -hexosaminidase A, β -mannosidase, and β -galactosidase) and very long chain fatty acids were normal. Within months, the patient's symptoms were in complete remission. A follow-up MRI six months later revealed no further changes. Two years after the initial presentation, the patient is well.

Case 2

A 15-year-old girl experienced several weeks of sore throat, low-grade fever, and fatigue, which were followed by emotional lability, inappropriate crying, shaking, and hallucinations. An EEG and a CT scan were normal. One psychiatrist made a diagnosis of "schizophreniform psychosis" and another of "atypical psychosis." Several months after presentation, a third psychiatrist referred the patient for neurological consultation. An interval history showed that the

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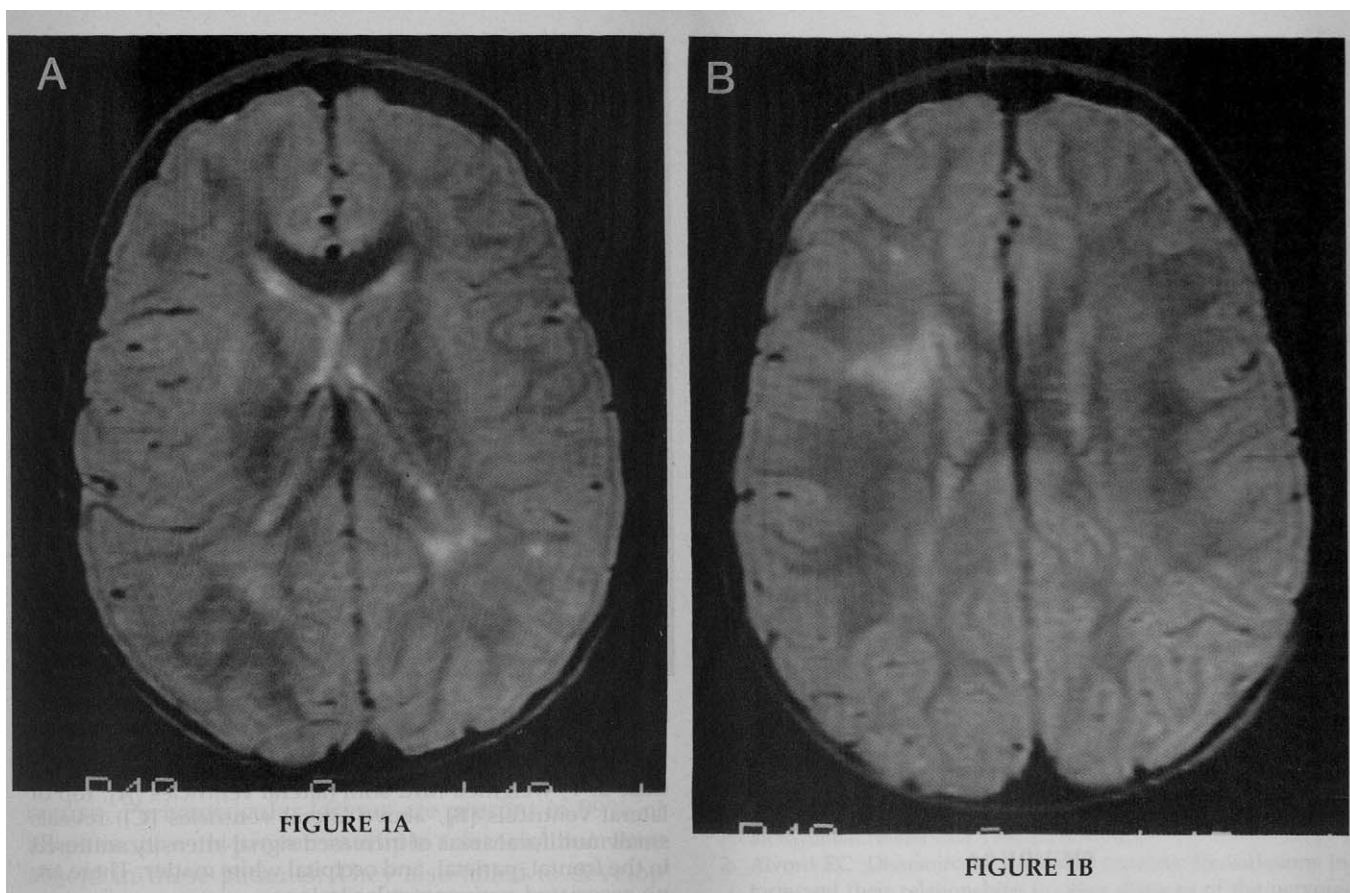


FIGURE 1

Case 1. T₂-weighted MRI scan through the level of the frontal horns (A) and bodies (B) of the lateral ventricles demonstrates patchy areas of increased signal intensity in deep white matter adjacent to the atria of the lateral ventricles and in the posterior right frontal lobe.

patient had improved. Examination revealed dyskinetic movements of the head and neck thought to be related to medication. MRI revealed multifocal small areas of increased signal intensity on T₂-weighted images in the frontal, parietal, and occipital white matter bilaterally (Figure 2). CSF revealed 14 lymphocytes/ μ L and normal sugar and protein levels. Values for immunoglobulin, brain stem auditory and somatosensory evoked potentials, lysosomal enzymes (see above), and very long chain fatty acids were all normal. The patient is no longer on medication and has returned to her previous state of psychological and intellectual functioning. She is a B student in high school now, 1 $\frac{3}{4}$ years from the onset of her illness.

Case 3

A 5-year-old boy with a 2 $\frac{1}{2}$ -month history of headaches was referred for neurological consultation. He complained of a constant headache but would intermittently cry and grab his head. Periods of altered behavior with staring and decreased responsiveness were also noted. He exhibited trouble with memory, weakness, periods of falling down, and shortness of attention span. Before the onset of this illness, the patient was considered normal. The physical examination was notable for the presence of excessive anxiety and emotional

lability. The neurological examination was entirely unremarkable. CT scan, chemistry profile, and sedimentation rate were normal. EEG demonstrated right temporal sharp activity. MRI revealed multifocal areas of increased signal intensity on T₂-weighted images in the posterior cerebral white matter. The patient gradually improved and returned to normal within eight months of the onset of the illness. A second MRI scan eight months after the first showed no further changes.

Case 4

A 2-year-old girl was examined for dizziness and unsteadiness experienced after riding a swing. The pediatrician had noted an extensor plantar response immediately after the episode, which lasted less than one hour. Family history was only remarkable for the presence of unexplained cerebral hemorrhages in two relatives. Additional history revealed that the patient had become severely irritable and febrile after her first and only diphtheria/pertussis/tetanus (DPT) immunization. The neurological examination was entirely normal. MRI demonstrated extensive multifocal areas of increased signal intensity on T₂-weighted images in the cerebral white matter bilaterally more prominent on the left than the right. Complete blood count, sedimentation

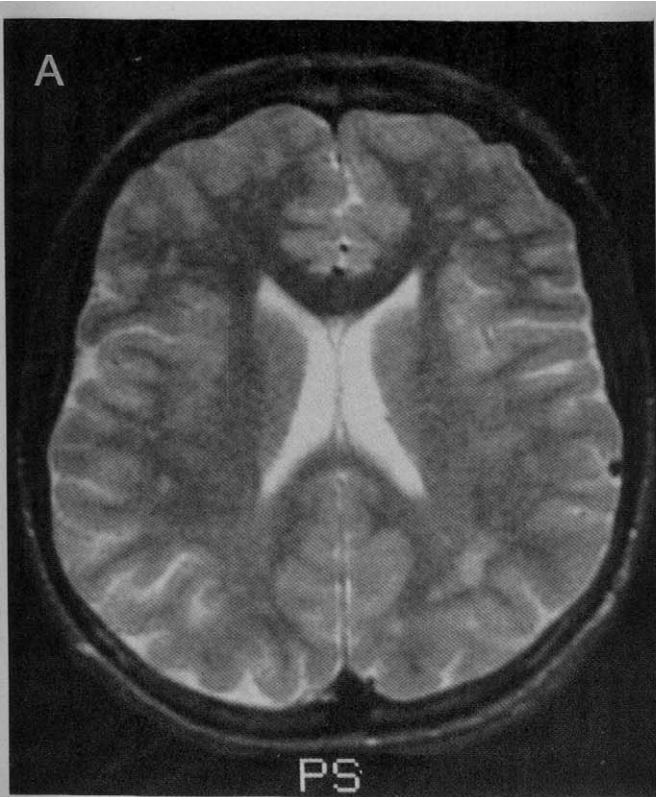


FIGURE 2A

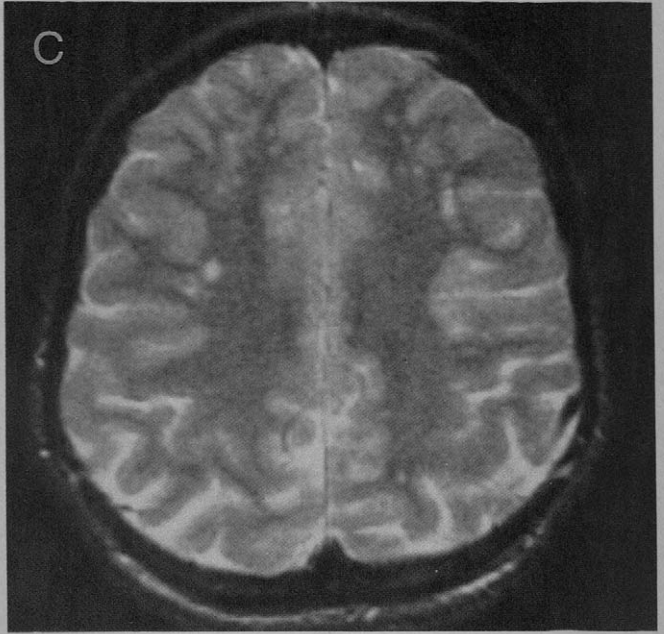


FIGURE 2C

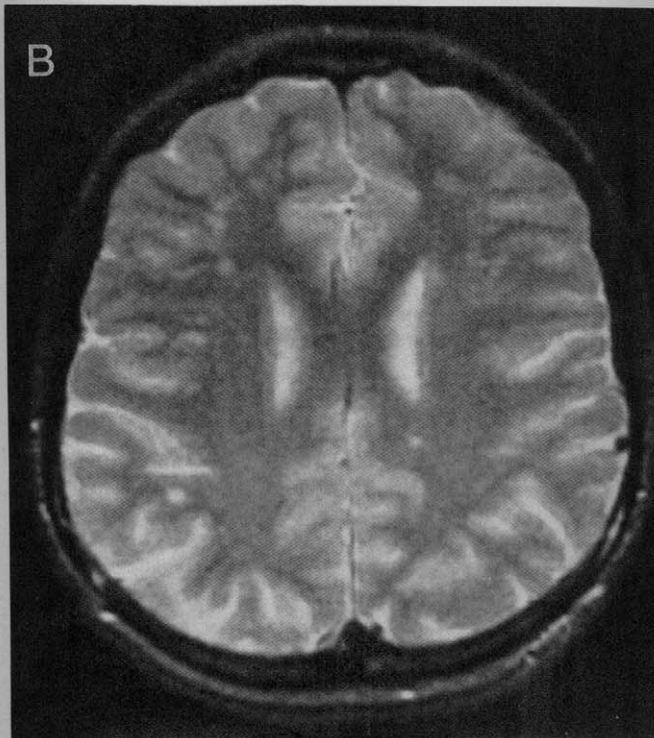


FIGURE 2B

FIGURE 2

Case 2. T₂-weighted MRI scan (lateral ventricles [A], top of lateral ventricles [B], above lateral ventricles [C]) reveals small multifocal areas of increased signal intensity scattered in the frontal, parietal, and occipital white matter. There are no associated periventricular lesions.

rate, and chemistry profile were normal. CSF examination including immunoglobulins and myelin basic protein was normal. Values for lysosomal enzymes (see above) and very long chain fatty acids were normal. The patient has been without problems for six months. Follow-up MRI at six months revealed no change.

Discussion

Acute disseminated encephalomyelitis is a well-known and highly variable clinical disorder that occurs spontaneously or after vaccinations or infections. The disorder has generally been considered acute, with significant neurological decompensation commonly marked by coma, seizures, ataxia, or paralysis.¹ Less severe varieties have also been discussed.² The condition has usually been diagnosed after specific clinical circumstances such as ataxia following varicella or by excluding other etiologies.

In the present report, three children had histories of headache and emotional lability over a period of months; the oldest patient exhibited a more serious psychiatric disturbance. One child had a severe reaction to a DPT immunization. All four children enjoyed subsequent resolution of their symptoms without any

therapy. CSF immunoglobulins were abnormal in one child, and a low-grade pleocytosis was present in another.

Several authors have described the appearance of acute disseminated encephalomyelitis on MRI, thus establishing the diagnostic value of the technique.^{3,4} The clinical and MRI findings were recently reviewed by Marks et al.⁵ Multifocal lesions are present on T₂-weighted images in the cerebral white matter, cerebellum, basal ganglia, and brain stem. With or without resolution of the lesions, there may be clinical improvement. In the present report, the white matter was abnormal in all four children. Because the lesions associated with acute disseminated encephalomyelitis are multifocal, vasculitis is an alternate diagnosis but is more likely if gray matter is involved. White-matter degenerative disease is also a consideration, particularly when lesions are coalesced; however, the clinical appearance, the laboratory data, and the multifocal distribution of the lesions argue against the degenerative disease in these four patients.

Multiple sclerosis has been reported in very young children⁶ but could not be established in the present four patients on the basis of either MRI or clinical course. Periventricular lesions are present in 99% of all patients with proven multiple sclerosis⁷ but were absent in these patients. They also failed to develop additional lesions in the six months between their first and second scan, as would be expected with multiple sclerosis.⁸

Alvord et al have suggested a hypothesis to account for the etiology of multiple sclerosis.⁹ Common infectious agents may have encephalitogenic or demyelinating epitopes that sensitize cells or induce antibodies. In sufficient numbers, the sensitized cells evoke acute disseminated encephalomyelitis and/or antibodies; insufficient numbers induce complete or partial resistance to the encephalitogenic potential of subsequent infections or immunizations. Complete resistance then bestows health, but partial resistance may predispose the patient to acute disseminated encephalomyelitis or multiple sclerosis.

The MRI scans of these four children illustrate a possible demyelinating episode and consequently indicate a potential marker for identifying a subtle antigenic myelinolytic effect. Whether such an effect might indicate sensitization or resistance to the subsequent development of a chronic demyelinating disease cannot be determined at this time. Clearly,

however, the long-term study of these and similar children could help to delineate the etiopathogenesis of multiple sclerosis and to test Alvord's hypothesis. The recent report of an HLA-antigen pattern similar to multiple sclerosis in patients with acute disseminated encephalomyelitis is a potentially important avenue of investigation that was not carried out on these patients.¹⁰

These four cases underscore the advisability of investigating by MRI persistent subtle illnesses in children, such as poorly explained irritability, headaches, or atypical psychiatric illness. The possibility that such patients could be resistant or susceptible to multiple sclerosis should be considered and evaluated. The presence of multifocal lesions in the white matter on MRI scans in children could be an important marker of exposure to a demyelinating antigen. If these findings are confirmed by others, a comprehensive, multicenter registry could be considered to promote long-term investigation of these potential neuropathological markers of multiple sclerosis.

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