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Case report

Diffuse white matter lesions associated with herpes simplex encephalitis as observed on magnetic resonance imaging

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A 2-year-old boy with herpes simplex encephalitis developed diffuse brain lesions involving the white matter of both cerebral hemispheres. These lesions in the white matter were clearly observed on magnetic resonance imaging (MRI) with the T2-weighted sequence, and were found to have spontaneously disappeared on subsequent MRI performed 7 weeks later. Brain lesions associated with herpes simplex encephalitis in the literature are reviewed and the pathogenesis in the present case is discussed.

Keywords: Herpes simplex encephalitis; Brain lesions; White matter; Magnetic resonance imaging

1. INTRODUCTION

Herpes simplex encephalitis (HSE) is caused by the herpes simplex virus (HSV), which selectively affects the cortex of the brain, often with temporal lobe focality. Pathologically, HSE is a necrotizing hemorrhagic process [1], in which there may be contiguity with the sub-arachnoid space, and which rarely involves deeply the white matter of the brain in a diffuse manner. Magnetic resonance imaging (MRI) is a relatively new diagnostic modality, which may be superior to computed tomography (CT) for delineating the lesions in HSE. We report a child who developed diffuse lesions in the white matter of both cerebral hemispheres, which were clearly demonstrated on MRI.

2. CASE REPORT

A 2-year-old Japanese boy was admitted to a local hospital on 28 January 1989, after he suddenly developed a high fever of up to 39.5°C and right-sided convulsive seizures. As the convulsions became progressive and occurred in rapid succession, the patient gradually became drowsy and confused. He was transferred to our center 6 days later for further evaluation and treatment.

On admission, the patient was lethargic and did not properly respond to vocal commands. There were no obvious motor or

sensory abnormalities, and his reflexes were equal bilaterally in both the upper and lower limbs. Physical examination was unremarkable. A lumbar puncture yielded cerebrospinal fluid (CSF) showing mononuclear pleocytosis, but no elevation of the protein level. A hemogram, urinalysis, and other chemical studies exhibited normal results.

A plain CT scan revealed a wedge-shaped area of high density involving the cerebral cortex of the left frontal region. This lesion was delineated as a high-intensity area in T1-weighted images (spin-echo, TR = 650 ms, TE = 40 ms), and as a widespread high-intensity area in T2-weighted images (spin-echo, TR = 2000 ms, TE = 80 ms) (Fig. 1a), compared with on plain CT. Serial cerebral angiography failed to reveal definite abnormalities. An electroencephalogram (EEG) showed abnormal, paroxysmal activity characterized by periodic lateralized epileptiform discharges (PLEDs) in the left frontocentral region.

Gradually, the patient regained consciousness and the convulsive seizures were completely controlled by means of anticonvulsant therapy. However, intravenous administration of acyclovir, an antiherpetic agent, at a daily dosage of 30 mg/kg, was then initiated and continued for a period of 6 days, because 7 days after admission the titers of HSV neutralizing antibodies were found to be significantly elevated in both serum and CSF. These increasing HSV antibody titers finally led to the diagnosis of acute herpes simplex encephalitis. Subsequently, the patient was again evaluated by enhanced CT and T2-weighted MRI (Fig. 1b), on which a new focus of encephalitis was indicated in the cortex of the right frontal region, as judged from the characteristic gyral

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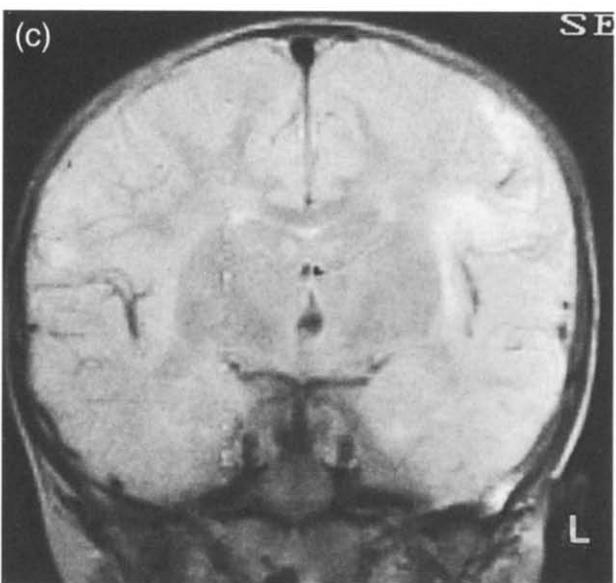
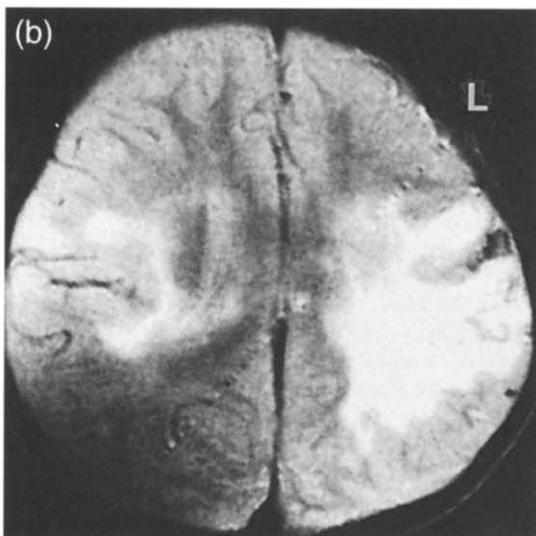
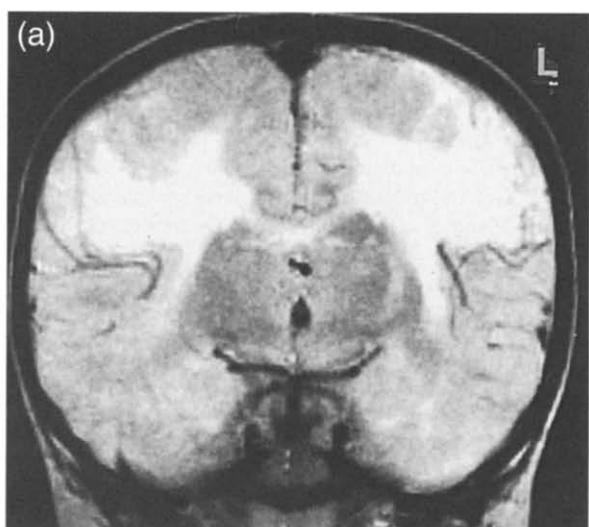
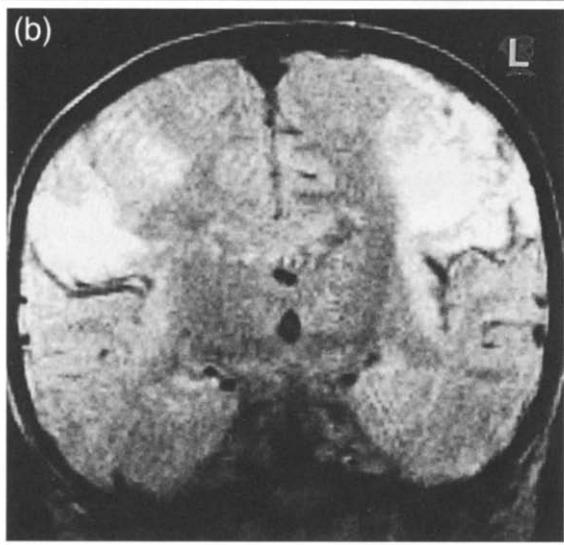
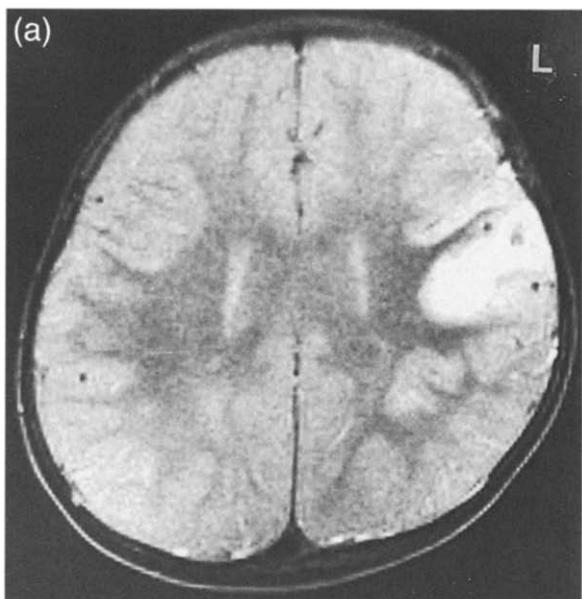


Fig. 1. a: T2-weighted MR imaging, an axial view (spin-echo, TR = 2000 ms, TE = 80 ms) performed on admission, showing a widespread area of high signal intensity involving the cerebral cortex of the left frontal region, in comparison with that on plain CT. b: T2-weighted MR imaging, a coronal view (spin-echo, TR = 2000 ms, TE = 80 ms) obtained 2 weeks after admission, showing a new focus of encephalitis in the cortex of the right frontal region.

Fig. 2. a: T2-weighted MR imaging, a coronal view (spin-echo, TR = 2000 ms, TE = 80 ms) performed 55 days after admission, demonstrating areas of high signal intensity involving the white matter of both cerebral hemispheres. b: T2-weighted MR imaging, an axial view (spin-echo, TR = 2000 ms, TE = 80 ms) performed 55 days after admission, illustrating the dominance of the white matter lesions in the left cerebral hemisphere. c: T2-weighted MR imaging, a coronal view (spin-echo, TR = 2000 ms, TE = 80 ms) obtained 7 weeks after the white matter lesions had been observed, showing marked regression of the white matter lesions.

configuration of the contrast enhancement on CT and the high intensity on MRI.

MRI performed 55 days after admission demonstrated extensive areas of high signal intensity involving the corpus callosum and the white matter of both cerebral hemispheres in T2-weighted images (Fig. 2a,b). Plain CT showed diffuse low-density areas extending to the semioval centers of both hemispheres. CSF obtained at that time showed both an increased protein content (97 mg/ml) and increased myelin basic protein (MBP; 12 ng/ml). Despite the presence of the diffuse lesions demonstrated by MRI, the patient remained neurologically rather stable, exhibiting right-sided hemiparesis and moderate speech disturbance. Seven weeks later, MRI revealed marked regression of the white matter lesions (Fig. 2c). The CSF protein and MBP levels were also within normal limits.

The patient gradually recovered over a period of 3 months and was discharged, still exhibiting slight weakness of the right upper limb and very mild speech disturbance.

3. DISCUSSION

The prognosis of HSE is generally considered ominous, whereas there are some patients who show only mild manifestations of HSE [2], and recover to the point where they can resume an independent life. In the present case, spontaneous regression of the neurological signs and symptoms was observed even prior to acyclovir therapy. The mechanism underlying such spontaneous recovery has to date not been fully elucidated.

There have been some reports concerning the MRI appearance of HSE [3,4], which described an increased water content caused by inflammation in the affected brain cortex. In the present case, T2-weighted MRI characteristically demonstrated widespread increased signal intensity in the left frontal lobe, which was confirmed on contrast CT as a gyral blush pattern. MRI was found to play a significant role in delineating the extent of the inflammatory process of HSE.

Of particular interest in the present case, however, were the T2-weighted MR images obtained following acyclovir therapy, in which diffuse increased signal intensity was observed in the

white matter of both cerebral hemispheres and the corpus callosum. In addition, the CSF protein and MBP levels were found to be significantly elevated at the time when the MRI was performed, but they gradually decreased to within the normal range without any specific treatment. Though the mechanisms underlying these findings on both MRI and CSF remain to be elucidated, they suggest the presence of a reversible change of the white matter such as edema of a considerable degree associated with an immune-mediated complication of a viral infection [1,5]. On the other hand, the direct invasion of HSV into the white matter is unlikely to have been the cause of the reversible process of edema or myelin damage, because pathological changes due to HSV infection are characterized by the irreversible process of hemorrhagic necrosis [1].

While there have been some reports describing transitory neurotoxicity associated with acyclovir [6,7], in the present case no data were obtained which indicate the cause-effect relation between the lesions of the white matter observed on MRI and acyclovir.

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