

# Serial Changes on Diffusion-Weighted Magnetic Resonance Imaging in Encephalitis or Encephalopathy

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It is recognized that diffusion-weighted magnetic resonance imaging is a sensitive method of detecting cerebral lesions in various neurologic disorders. This report presents two patients with acute encephalitis or encephalopathy who manifested similar serial changes on diffusion-weighted magnetic resonance imaging. Clinically, Patient 1, a 2-year-old male, was diagnosed as having hemiconvulsion-hemiplegia-epilepsy syndrome and Patient 2, a 9-month-old male, acute encephalitis associated with exanthema subitum. Despite the different etiology and the distribution of lesions, diffusion-weighted magnetic resonance imaging of these two patients revealed high-intensity lesions in the subcortical white matter in the acute phase, and then in the cortex, or basal ganglia, or both. In the convalescent phase, high-intensity lesions disappeared and brain atrophy developed. These serial changes were not recognized using other conventional methods. Although the exact mechanism for these serial changes remains unknown, these changes might reflect some pathogenic mechanism in acute encephalopathy or encephalitis. © 2006 by Elsevier Inc. All rights reserved.

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## Introduction

Diffusion-weighted magnetic resonance imaging reveals signal changes related to decreased water diffusion, and high-intensity areas on diffusion-weighted magnetic resonance imaging indicate cytotoxic edema. Evidently diffusion-weighted magnetic resonance imaging can demonstrate cerebral lesions in various neurologic disorders [1-3], which are not apparent using other conventional methods such as T<sub>2</sub>-weighted magnetic resonance imaging and the fluid-attenuation inversion recovery method. In acute encephalitis or encephalopathy in children, diffusion-weighted magnetic resonance imaging is reported to be an effective method for detecting early abnormalities in the brain as high-intensity lesions [4-8]. However, serial changes on diffusion-weighted magnetic resonance imaging have not been fully investigated in acute encephalitis or encephalopathy. This report discusses cases in two children presenting similar serial changes on diffusion-weighted magnetic resonance imaging during the course of acute encephalitis or encephalopathy.

## Case Report

### Patient 1

This 2-year-old male was born without any complications. His development was mildly delayed. He had not developed meaningful speech at the onset of this episode. Fever developed, and the next day he had a right hemiconvulsion lasting approximately 2 minutes. After that, right flaccid hemiplegia and mild disturbance of consciousness continued, so he was referred to our hospital on the next day. On admission, pyrexia was not present. Although he was awake, he could not recognize surrounding situations well. Routine laboratory examinations revealed no remarkable abnormalities. Cerebrospinal fluid examination indicated a total cell count of 1/mm<sup>3</sup>, total protein of 11.2 mg/dL, and glucose of 63 mg/dL. Paired sera titers of immunoglobulin G and immunoglobulin M antibody for influenza virus, human herpesvirus type 6, herpes simplex virus, Epstein-Barr virus, or parvo-virus B19 were not elevated. Electroencephalography revealed slow waves in the left hemisphere. Brain computed tomography revealed a diffuse low-density lesion in the left whole hemisphere. Magnetic resonance imaging disclosed a diffuse high-intensity lesion in the left hemisphere, predominantly in the cortex in T<sub>2</sub>-weighted images, and a high-intensity lesion in the subcortical white matter of the left hemisphere in diffusion-weighted magnetic resonance imaging (Fig 1A). Clinically he was diagnosed as having hemiconvulsion-hemiplegia-epilepsy syndrome.

After admission, right hemiconvulsion developed several times and treatment including dexamethasone, mannitol, and midazolam was administered. Six days later, his seizures ceased. Magnetic resonance

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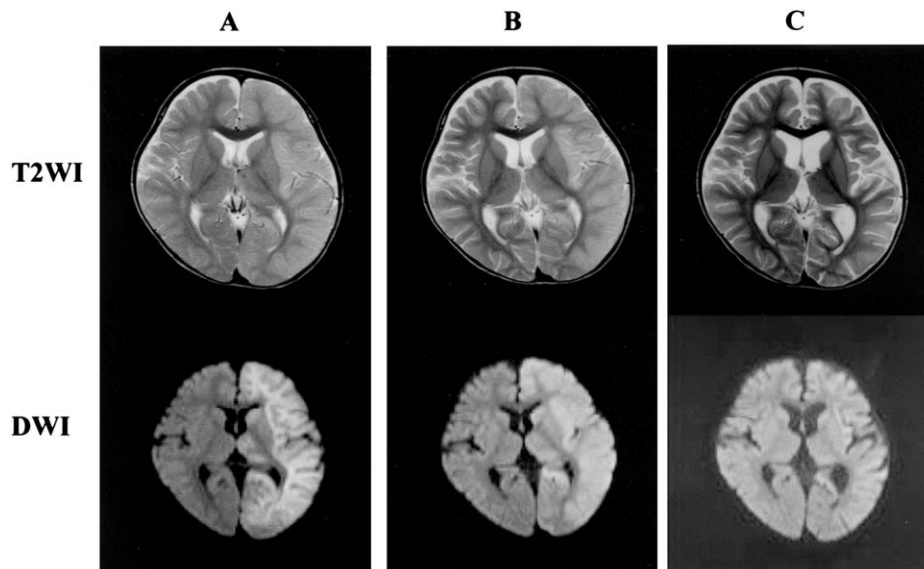


Figure 1. Diffusion-weighted magnetic resonance imaging (TR5000.0 msec, TE 86.0 msec) and  $T_2$ -weighted magnetic resonance imaging (TR3650.0 msec, TE 95.0 msec) of Patient 1 in the acute phase (A), 6 days later (B), and 18 days later (convalescent phase) (C). (A) A high signal abnormality on diffusion-weighted imaging throughout the left hemisphere predominantly involving the white matter. (B) A predominantly cortical abnormality in diffusion-weighted imaging. (C) Brain atrophy in the affected lesion. The high-intensity lesion on diffusion-weighted imaging disappeared.

imaging revealed a high-intensity lesion in the whole left cortex on diffusion-weighted magnetic resonance imaging (Fig 1B). Eighteen days later magnetic resonance imaging documented brain atrophy, and the high intensity in  $T_2$ -weighted images and diffusion-weighted magnetic resonance imaging disappeared (Fig 1C). Although he manifested mild right hemiplegia and mental retardation, at present he can walk without support and babble.

### Patient 2

This 9-month-old male was born without any complications. The family and prenatal histories were not contributory. He developed normally until this episode. Generalized convulsion associated with high-grade fever developed. Two days later, pyrexia disappeared and

generalized evanescent eruption developed. Thus he was diagnosed as having exanthema subitum from his clinical symptoms. On the next day, frequent afebrile generalized seizures developed and he was referred to our hospital. On admission, he was comatose and totally inactive. Physical examination revealed no abnormal findings, and neurologic examination disclosed no lateralizing finding. Routine laboratory examinations detected no abnormal findings except for mildly increased values of aspartate transaminase (100 IU/L) and alanine transaminase (59 IU/L). Cerebrospinal fluid examination disclosed a total cell count of  $12/\text{mm}^3$ , total protein of 28 mg/dL, and glucose of 62 mg/dL. Polymerase chain reaction for human herpesvirus type 6 or 7 was negative, and paired sera titers of immunoglobulin G and immunoglobulin M antibody for human herpesvirus type 6 or 7 were not elevated. Electroencephalogram disclosed diffuse delta

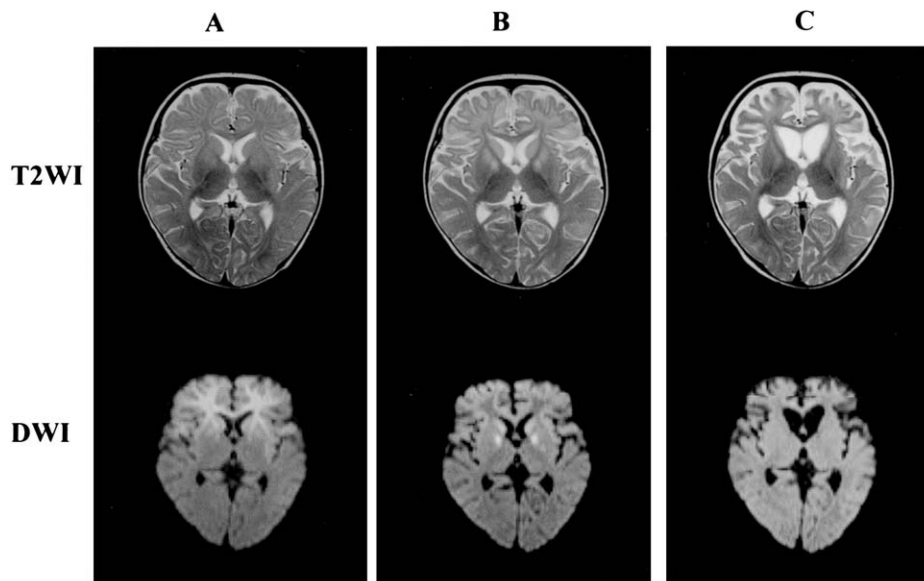


Figure 2. Diffusion-weighted MRI and  $T_2$ -weighted MRI of patient 2 in the acute phase (A), 9 days later (B), and one month later (convalescent phase) (C). (A) A high signal abnormality on DWI in the frontal lobe predominantly involving white matter. (B) A predominantly cortical and basal ganglia abnormality on DWI. (C) Brain atrophy in the affected lesion. The high intensity lesions on DWI disappeared.

activity. Brain computed tomography revealed low-density lesions in bilateral frontal lobes. Brain magnetic resonance imaging documented high-intensity lesions in bilateral frontal lobes on T<sub>2</sub>-weighted magnetic resonance imaging, and high-intensity lesions in the subcortical white matter in his frontal lobes in diffusion-weighted magnetic resonance imaging (Fig. 2A).

Intensive treatment including dexamethasone and glycerol was administered, and the patient recovered gradually. Nine days later, magnetic resonance imaging revealed high-intensity lesions in the frontal lobe in T<sub>2</sub>-weighted images and high-intensity lesions in the cortex of the frontal lobes, caudate nucleus, and globus pallidus in diffusion-weighted magnetic resonance imaging. High-intensity lesions in the subcortical white matter on diffusion-weighted magnetic resonance imaging disappeared (Fig. 2B). One month later, high-intensity lesions in both T<sub>2</sub>-weighted magnetic resonance imaging and diffusion-weighted magnetic resonance imaging disappeared and brain atrophy was observed in the affected areas (Fig. 2C). The patient recovered well without residual rash; however, he had some neurologic sequelae including mild spastic diplegia.

## Discussion

These two patients were diagnosed as having acute encephalitis or encephalopathy of unknown origin. Clinically, Patient 1 was diagnosed with hemiconvulsion-hemiplegia-epilepsy syndrome and Patient 2 with acute encephalitis associated with exanthema subitum. Despite the different etiology and the distribution of lesions, they manifested similar serial changes in their diffusion-weighted magnetic resonance imaging. Diffusion-weighted magnetic resonance imaging of these two patients revealed high-intensity lesions mainly in the subcortical white matter in the acute phase. Several days later these high-intensity lesions disappeared from the subcortical white matter and high-intensity lesions developed in the cortex or basal ganglia. In the convalescent phase, high-intensity lesions in both white matter and cortex disappeared and brain atrophy developed. These serial changes in diffusion-weighted magnetic resonance imaging were not apparent in T<sub>2</sub>-weighted magnetic resonance images and have not been fully investigated previously in acute encephalitis or encephalopathy.

A high signal in the diffusion-weighted magnetic resonance imaging is interpreted as a decrease in the diffusivity of water within the neural tissue. This decrease indicates cytotoxic edema. Diffusion-weighted magnetic resonance imaging can reveal high-intensity lesions in the cerebral infarction [1], hypoxic encephalopathy [2], metabolic encephalopathy and status epilepticus [3]. Evidently, diffusion-weighted magnetic resonance imaging is more sensitive than conventional magnetic resonance imaging in the early stages of the disease process and the usefulness of diffusion-weighted magnetic resonance imaging in the early diagnosis of acute encephalopathy or encephalitis has been reported [4-8].

Tokunaga et al. [4] and Tsuchiya et al. [5] reported that diffusion-weighted magnetic resonance imaging can detect early abnormalities as high-intensity lesions and was a more sensitive method than T<sub>2</sub>-weighted

magnetic resonance imaging and the fluid-attenuation inversion recovery method in diagnosing encephalitis or encephalopathy caused by influenza. It has been reported that high-intensity lesions in the white matter appeared during the acute phase of human herpesvirus type 6 encephalitis [7,8], which suggests cytotoxic edema of glial cells and myelin. Hemiconvulsion-hemiplegia-epilepsy syndrome [9] is characterized by prolonged seizures with unilateral predominance followed by the development of hemiplegia during the febrile illness in children as in our Case 2. Freeman et al. [10] reported three patients similar to our second patient, with hemiconvulsion-hemiplegia-epilepsy syndrome who were demonstrated to have striking neuroimaging findings suggestive of diffuse cytotoxic edema confined to one hemisphere, including extensive diffusion-weighted magnetic resonance imaging abnormalities. Hisano et al. [11] reported a case of acute infantile hemiplegia in a 3-year-old male after convulsive status epilepticus, whose clinical course and magnetic resonance imaging findings were similar to those of the cases presented here. Diffusion-weighted magnetic resonance imaging demonstrated high-intensity lesions in the white matter 6 days after the seizure episode and subsequently in the gray matter after a further 7 days. The authors supposed that the insult associated with status epilepticus was not sufficient to cause acute necrosis, but instead caused an acute decrease in oxygenation and a disruption in the energy supply to the neural tissue. However, the exact mechanism for such a progression in the abnormal signal distribution in diffusion-weighted magnetic resonance imaging remains unclear. There are also some case reports of diffusion-weighted magnetic resonance imaging abnormalities observed in patients with focal status epilepticus. The mechanism underlying the restricted diffusion of water in epileptogenic tissue still remains a matter of great interest. Serial changes in diffusion-weighted magnetic resonance imaging have not reported in acute encephalitis or encephalopathy until now.

These serial changes on diffusion-weighted magnetic resonance imaging might reflect some pathogenic mechanism in patients in general. However, it is unclear whether these changes may reflect inflammation or epileptogenic abnormalities. Further investigation will be necessary to elucidate whether these serial changes are common in acute encephalitis or encephalopathy, or epilepsy.

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