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Case Report

Longitudinal magnetic resonance imaging changes in Japanese encephalitis

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Abstract

Background: Japanese encephalitis is a flavivirus that can cause pandemic encephalitis, and is prevalent in Southeast Asia and Australia. Brain images of patients with Japanese encephalitis are characterized by thalamic lesions, distinct from those seen in viral encephalopathies caused by the herpes simplex virus and West Nile virus.

Aim: Herein, we describe for the first time a time-dependent magnetic resonance imaging pattern in Japanese encephalitis in a 10-month-old Japanese boy.

Case: The patient was a previously healthy 10-month-old Japanese boy, who exhibited acute-onset flaccid tetraplegia and loss of tendon reflexes.

Results: Brain MRI showed characteristic thalamic changes on diffusion weighted images from spotty to uniform and from the left to the right side, associated with low apparent diffusion coefficient maps. These images suggest that the Japanese encephalitis virus may first affect the unilateral thalamus, possibly expanding to the other side, with characteristic patterns changing from spotty to uniform in a manner consistent with the presentation of cytotoxic edema.

Conclusion: This report first showed longitudinal magnetic resonance changes in Japanese encephalitis, which may help in accurate diagnosis and in discrimination from other etiologies.

Keywords: Japanese encephalitis; Magnetic resonance imaging; Thalamic lesion

1. Introduction

The Japanese encephalitis virus is a flavivirus, mainly prevalent in Asia and Australia [1]. The annual incidence of Japanese encephalitis is 50,000 to 175,000 worldwide, and the mortality rate is as high as 30% [2]. Thus, prompt diagnosis is essential for prevention of viral expansion.

Brain images in Japanese encephalitis are usually characterized by bilateral thalamic lesions on magnetic resonance imaging (MRI) [3–8], which is distinct from the findings observed in viral encephalopathies caused by herpes simplex virus and West Nile virus [9–11]. However, to the best of our knowledge, there has been no MRI report regarding time-dependent changes in thalamic lesions in Japanese encephalitis. Here, we demonstrate for the first time a characteristic

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longitudinal MRI pattern from the acute to chronic phase in a Japanese boy with Japanese encephalitis.

2. Case report

A previously healthy 10-month-old Japanese boy was admitted to our hospital due to high fever, lethargy, and eye-deviation to the left side. On admission (day 1), he showed consciousness disturbance with eye-deviation to the left side. He also exhibited flaccid paralysis of extremities, associated with accelerated deep tendon reflexes and bilateral Babinski signs. There was no nuchal rigidity, but numerous marks caused by mosquito bites were observed on his extremities.

Blood examination revealed a leukocyte level of 15,000/μL and the C-reactive protein level was 0.02 mg/dL. Cerebrospinal fluid examination revealed mild pleocytosis at 34 cells/μL, a protein level of 33 mg/dL, and a glucose level of 70 mg/dL. All bacterial cultures including of the cerebrospinal fluid, blood, pharynx, stool, and urine were negative. Polymerase chain reaction detected Japanese encephalitis RNA in the cerebrospinal fluid, whose titers were increased at ×10 (day 2), ×80 (day 10), and ×160 (day 79). Thus, we finally diagnosed Japanese encephalitis. Immunization for *Haemophilus influenzae*, *Streptococcus pneumoniae*, pertussis, diphtheria, and tetanus had been completed, but not for Japanese encephalitis.

Brain computed tomography (CT) on day 1 revealed mild swelling of the brain without abnormal densities (Fig. 1A). Electroencephalogram on day 2 showed diffuse slow waves throughout the brain (Fig. 1B), followed by low activity in the chronic phase without any paroxysmal discharge (data not shown). Brain MRI on day 4 revealed spotty high intensities mainly on the left thalamus on diffusion weighted images (DWI), which were associated with low apparent diffusion coefficient maps, suggesting cytotoxic edema (arrows, Fig. 2a, d, g). Subsequent MRI studies on day 7 revealed a new right thalamus lesion in addition to the original, left one (Fig. 2b, e, h), which changed from a spotty to a diffuse uniform pattern (Fig. 2c, f, i). DWI were sufficiently sensitive to detect these lesions, and fluid-attenuated inversion recovery (FLAIR) images also detected these DWI lesions, suggesting that the Japanese encephalitis virus may initially affect the unilateral thalamus causing cytotoxic edema, associated with gliosis on both thalami, at least in this patient. Thereafter, the bilateral thalami became atrophic with small cavitation on day 66 (Fig. 3a–i), and the patient developed permanent severe spastic tetraplegia.

3. Discussion

We herein demonstrated, for the first time, characteristic imaging patterns in Japanese encephalitis, from spotty to uniform and from the left to the right side, with high intensities on DW and FLAIR images. These lesions were associated with low apparent diffusion coefficient maps, suggesting that these thalamic lesions were consistent with the presentation of cytotoxic edema. Although numerous studies have included brain images of Japanese encephalitis, there has been no previous report on the changes in thalamic lesions. Thus, our findings may provide insight on the mechanism involved in thalamic invasion by the Japanese encephalitis virus.

Flaviviruses, include the West Nile virus, Japanese encephalitis virus, and Murray Valley encephalitis virus [1]. All types of flavivirus are known to cause encephalopathy/encephalitis. Although MRI images of West Nile encephalitis usually show non-specific brain lesions in the deep white matter, brainstem, and spinal cord [8–11], some studies have also reported the involvement of the bilateral basal ganglia and thalamus. [12,13].

Murray Valley encephalitis is known to show thalamic hyperintensity on T2-weighted images, with

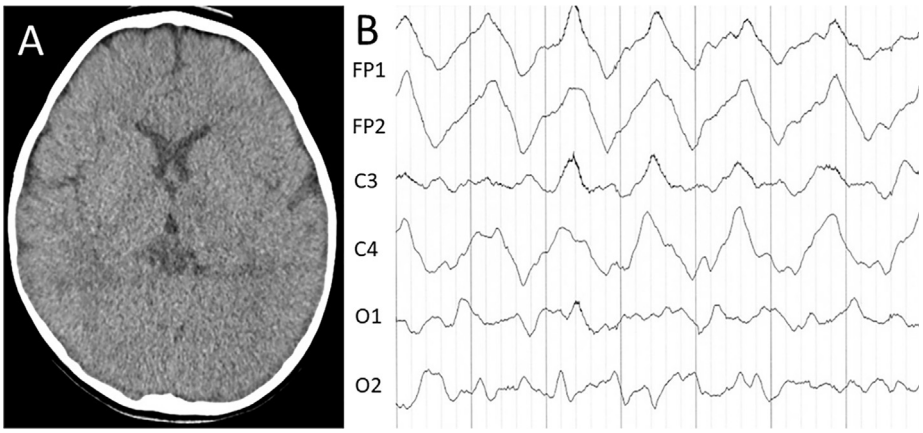

Fig. 1. Brain computed tomography (CT) and electroencephalogram. Brain CT on day 1 revealed mild swelling of the brain (A). Electroencephalogram on day 2 showed diffuse slow waves predominantly at the bilateral frontal lobes (B).

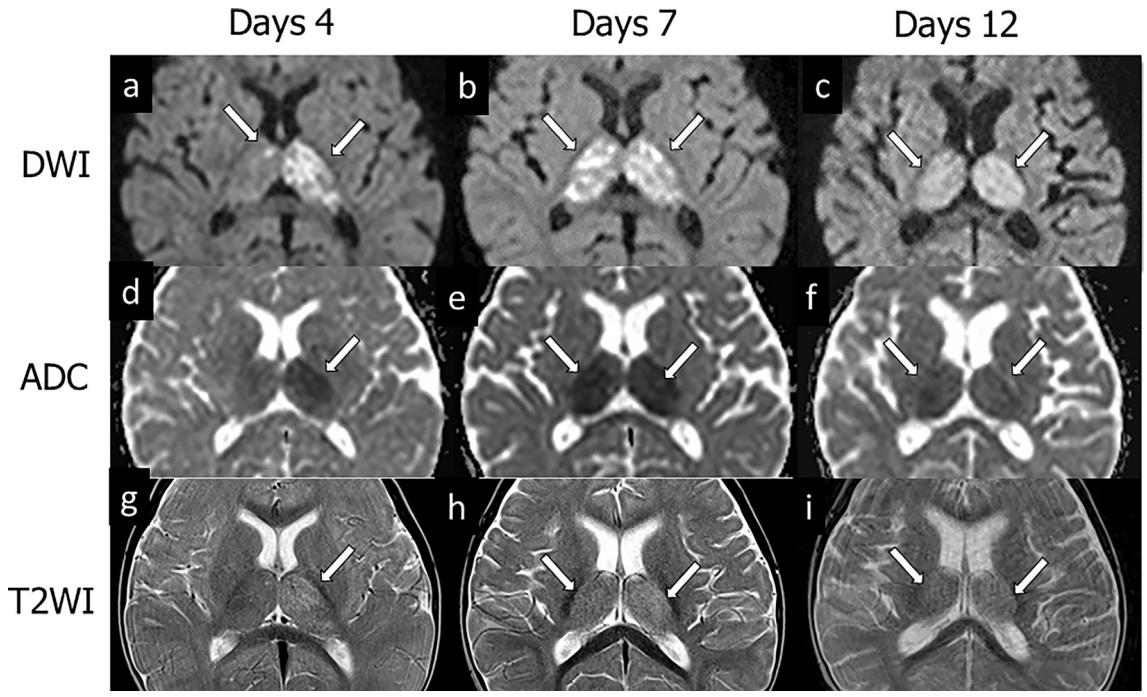

Fig. 2. Brain magnetic resonance imaging (MRI) in the acute phase. Brain MRI revealed signal changes in the thalamus, from spotty to uniform, on DWI on days 4 (a), 7 (b), and 12 (c), on ADC on days 4 (d), 7 (e), and 12 (f), and on T2-weighted images on days 4 (g), 7 (h), and 12 (i). Thalamic lesions are indicated by arrows. Abbreviations: MRI: magnetic resonance imaging, DWI: diffusion weighted imaging, ADC: apparent diffusion coefficient.

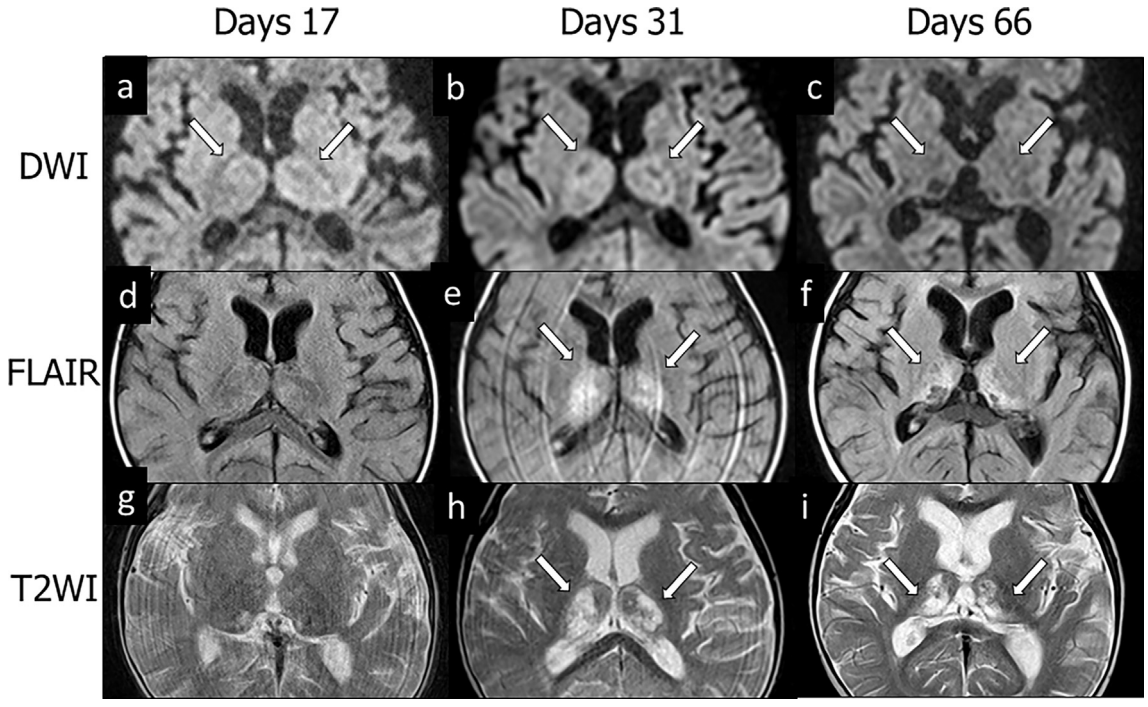

Fig. 3. Brain MRI in the chronic phase. Brain MRI revealed changes in the thalamus, from swelling to atrophy with cavitation on DWI on days 17 (a), 31 (b), and 66 (c), on FLAIR on days 17 (d), 31 (e), and 66 (f), and on T2-weighted images on days 17 (g), 31 (h), and 66 (i). Thalamic lesions are indicated by arrows. Abbreviations: MRI: magnetic resonance imaging, DWI: diffusion weighted imaging, FLAIR: fluid-attenuated inversion recovery.

involvement of the red nucleus, substantia nigra, and cervical cord [14]. Thus, bi-thalamic involvements are characteristic of Japanese encephalitis, West Nile encephalitis, and Murray Valley encephalitis, suggesting that flaviviruses may mainly affect the thalamus.

The most significant findings of this study are the following. First, there were characteristic changes in the thalamic lesions on MRI. These lesions had high intensities on DWI, associated with low apparent diffusion coefficient values, suggesting that the thalamic lesions were consistent with cytotoxic edema. Although one report reported lower frequency of cytotoxic edema in Japanese encephalitis than in herpes simplex encephalitis [4], the spotty to uniform patterns in this patient may reflect the pattern of viral replication in the thalamus. On this patient's MRI, DWI was most sensitive to detect acute cytotoxic thalamic lesions in the acute phase and T2-weighted and FLAIR images reflected subsequent vasogenic edema and gliosis after tissue necrosis in the chronic phase. Although Japanese encephalitis can also cause basal ganglia and midbrain lesions, these characteristic imaging findings may help in the accurate diagnosis of Japanese encephalitis.

Second, there was a spreading pattern from the left to the right side on MRI. This spreading pattern in the thalamus in Japanese encephalitis has not been well reported. These characteristic patterns from the left to the right side in this patient may be explained via independent blood flow or via axonal guidance using inter-thalamic adhesion. Since medial lesions on the left thalamus of this patient seemed to be first affected on MRI, we should consider that the Japanese encephalitis virus may be transmitted from the left to the right through inter-thalamic adhesion. To verify this hypothesis, we need to accumulate more MRI images of Japanese encephalitis cases.

How the thalamus is specifically impaired by the Japanese encephalitis virus remains to be elucidated. However, recent studies on the involvement of the thalamus have been developed both clinically and experimentally. Thalamic lesions were reported by a study conducted in India [2] in 82% of patients with Japanese encephalitis; 7% of which were unilateral and 75% bilateral Interestingly, these thalamic lesions are known to change on CT over time, from hypodense in the acute phase to normal dense in the chronic phase, which is known as the 'fogging effect,' followed by bilateral thalamic atrophy [3].

In animal experiments using pigs, the RNA of the Japanese encephalitis virus mostly accumulates in the thalamus and basal ganglia, suggesting that the virus specifically replicates in these regions [1]. Thus, the characteristic MRI features in this patient may reflect this viral replication process. The Japanese encephalitis virus also replicates in the cortical area and basal ganglia, which is clinically consistent with the finding that the patient developed brain atrophy during the chronic phase.

In conclusion, our findings of longitudinal MRI changes, from spotty to uniform and from the left to the right side, may indicate the specific pattern of how the Japanese encephalitis virus affects the thalamus in humans.

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