
CASE REPORT

Magnetic Resonance Imaging Findings of Japanese Encephalitis

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ABSTRACT

The initial clinical presentation of Japanese encephalitis is usually non-specific and can be similar to other causes of encephalitis or encephalopathy. Early and accurate diagnosis requires a high index of suspicion by both physician and radiologist. This report describes the magnetic resonance imaging findings of 2 patients with Japanese encephalitis in both the acute and convalescent stages, together with a brief review of the literature.

Key Words: Flavivirus, Japanese encephalitis, Magnetic resonance imaging, Thalamus

INTRODUCTION

Japanese encephalitis (JE) is an acute encephalomyelitis that is a primary viral encephalitis with the vector being a mosquito. This disease occurs throughout Asia, including Japan, Korea, Thailand, and India. In Hong Kong, the incidence of JE is very low. This report presents the clinical and magnetic resonance imaging (MRI) findings of 2 patients with JE who were recently diagnosed at Tuen Mun Hospital. The first patient came from Shenzhen while the second patient is the first reported local patient in the past 7 years.

CASE REPORT 1

A 6-year-old boy presented in May 2002 with a 3-day history of fever, cough, running nose, and sore throat after returning from Shenzhen. He had good past health, normal development, and vaccination was up to date. At clinical examination, he was lethargic with a Glasgow Coma Scale (GCS) score of 12/15. The provisional diagnosis was central nervous system infection. Lumbar puncture was performed. Cerebrospinal fluid (CSF) showed an elevated white cell count with lymphocytes predominant and elevated protein content. Culture was negative for bacteria and tuberculosis. Urgent computed tomography (CT) of the brain showed subtle

hypodensity over the right thalamic region. An initial diagnosis of encephalitis was made and intravenous ampicillin, claforan, and aciclovir were started. However, his clinical condition rapidly deteriorated with a decrease in GCS score to 10/15 and he developed left hemiplegia.

MRI of the brain was performed on the second day of admission, which demonstrated an ill-defined T1 hypointense T2 hyperintense lesion in the right thalamus (Figure 1). On diffusion-weighted images, the scan displayed mild hyperintensity (Figure 2). The left thalamus, brainstem, and cerebellum were unremarkable. Magnetic resonance angiogram of the circle of Willis and cerebral vasculature were normal. The 2 major diagnostic considerations were encephalitis and acute infarction. With the clinical presentation and involvement of the thalamus, JE was considered as one of the most likely diagnoses. This diagnosis was later confirmed by serology.

Clinically, the patient's consciousness gradually improved with supportive treatment. He was discharged in early June with mild left hemiplegia. Follow-up MRI of the brain was performed in mid-June 2002 for emotional instability and mutism. There was partial resolution of the right thalamic T2 hyperintensity.

Unfortunately, the patient developed further clinical deterioration in terms of progressive dullness, left-sided hypertonia, and brisk lower limb reflex. He was also frequently prone to unprovoked shouting and crying. A

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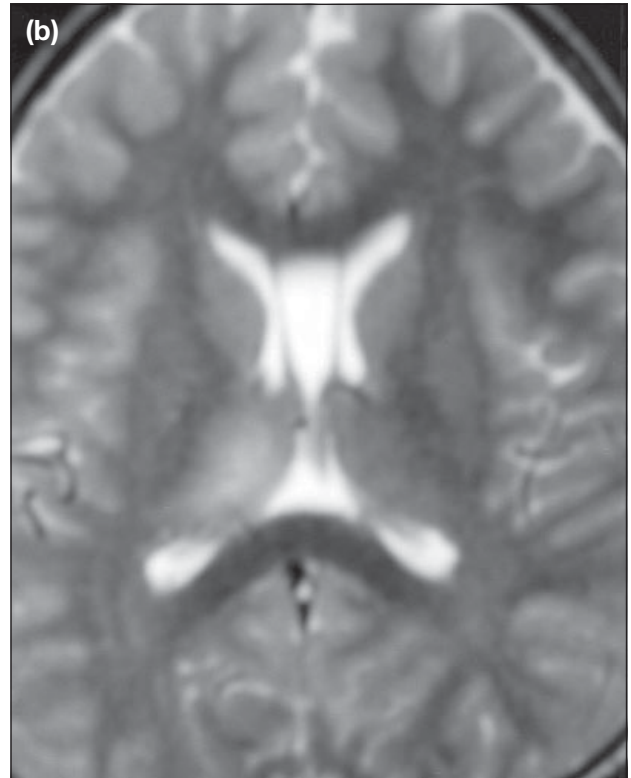
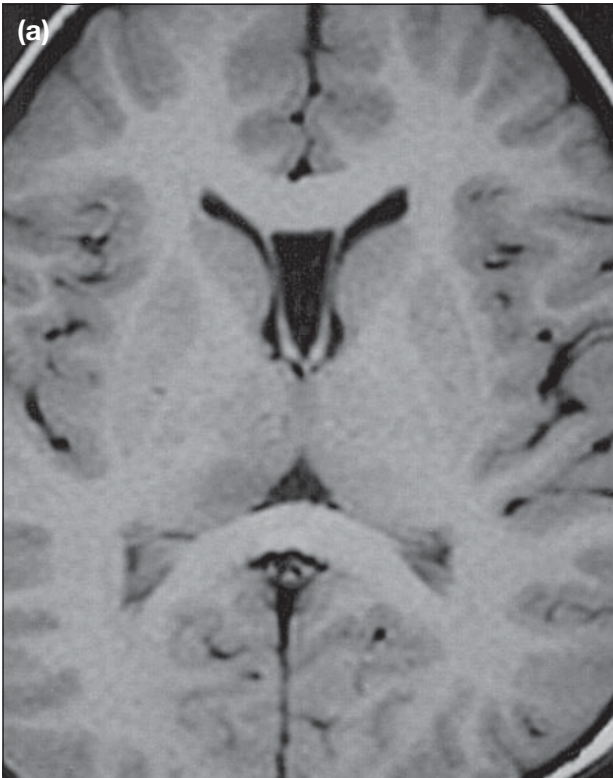


Figure 1. Axial magnetic resonance imaging of the brain. (a) Axial T1 image showing subtle hypointensity at the right thalamus; and (b) axial T2 image showing abnormal hyperintense signal at the right thalamus.

third MRI revealed newly developed T1 hypointense and T2 hyperintense signal in the right occipital lobe, bilateral hemispheres, inferior vermis, and tonsils of cerebellum. The findings were suggestive of early relapse resulting in a biphasic illness pattern.

These abnormal T2 hyperintensities were resolved on the subsequent MRI. However, there was atrophy of brain parenchyma, particularly in the bilateral cerebellar hemispheres. He had severe residual neurological sequelae of cerebral palsy and repeated attacks of generalised tonic-clonic convulsions.

CASE REPORT 2

A 39-year-old woman residing in Yuen Long presented with a 3-day history of fever and confusion. She had no recent travel history. At examination, the GCS score was 9/15. There was no neck stiffness or any long tract sign. The first CT scan on the day of admission was normal. Lumbar puncture was performed and CSF examination showed no features of encephalitis. Empirical intravenous treatment of penicillin G, claforan, and aciclovir was commenced.

MRI, performed 5 days after the onset of her illness, revealed ill-defined T1 hypointense and T2 hyperintense

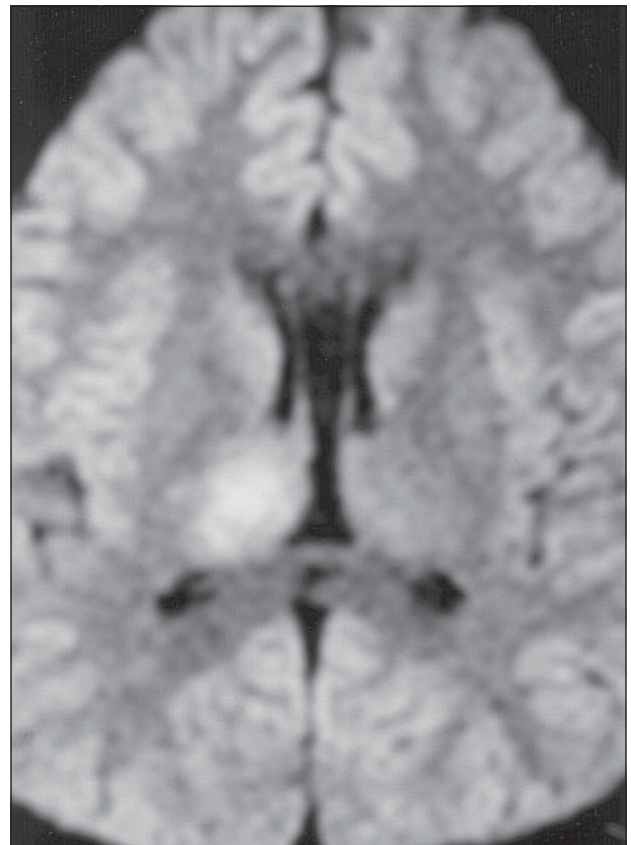


Figure 2. Diffusion-weighted image demonstrating mild hyperintense signal at the right thalamus, indicating fluid restriction.

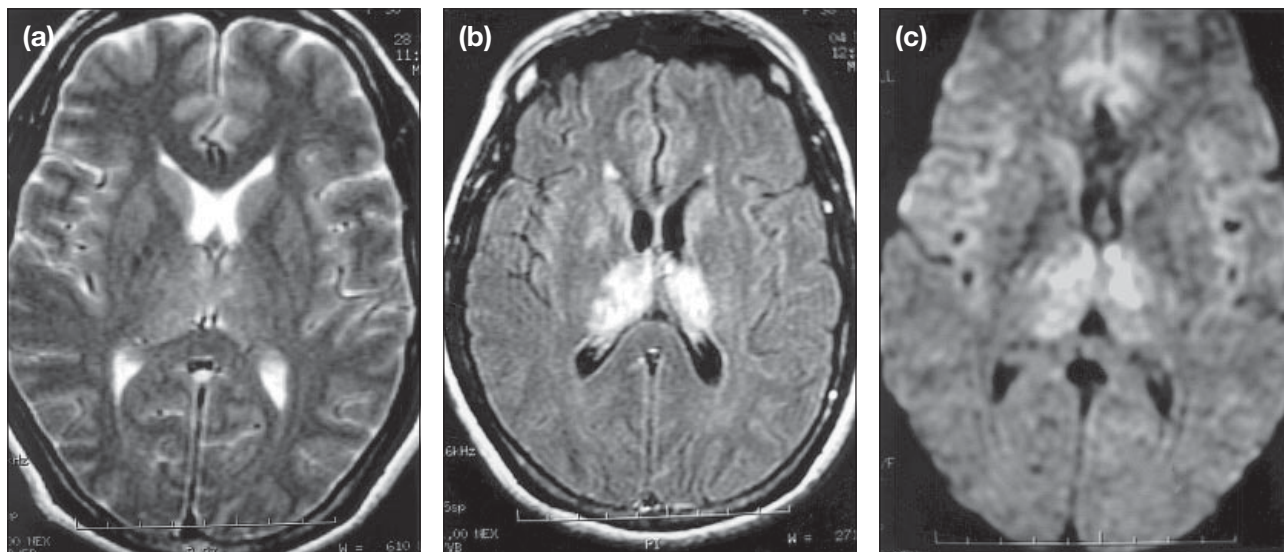


Figure 3. Axial magnetic resonance imaging of the brain. (a) T2 image showing a subtle high-signal intensity lesion in the thalamus; (b) fluid-attenuated inversion recovery sequence; and (c) diffusion-weighted images. The thalamic lesions appear hyperintense and more conspicuous on these sequences.

areas in the bilateral thalamic nuclei (Figure 3) and in the inferomedial part of the left temporal lobe. These areas showed restricted diffusion in diffusion-weighted images.

A small area of restricted diffusion was also found at the dorsal part of the right mid-brain (Figure 4). There was no significant contrast enhancement. The rest of the brain was normal and the ventricles were not dilated.

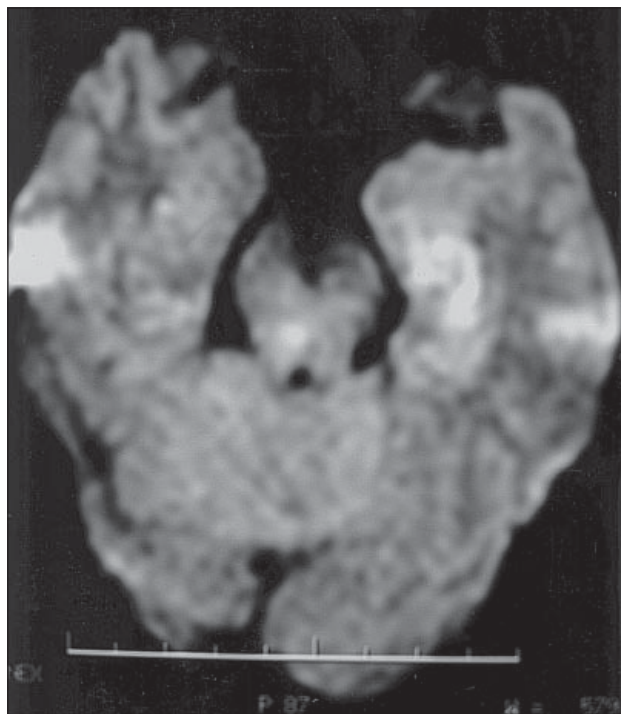


Figure 4. Diffusion-weighted image showing a small area of restricted diffusion at the dorsal part of the right mid-brain.

Radiological diagnosis of JE was made. This diagnosis was later confirmed by serology.

The patient's condition further deteriorated and she became tetraplegic. She required mechanical ventilation support shortly after the MRI study. She was transferred to the intensive care unit for further treatment and supportive care. A follow-up MRI 1 month later demonstrated deterioration in the extent of involvement in the bilateral thalami and inferomedial aspect of the left temporal lobe. In addition, new lesions were found in the substantia nigra (Figure 5).

Two months later, she was successfully weaned off mechanical ventilation and was transferred to a convalescent hospital for rehabilitation. Unfortunately, her neurological status only marginally improved and she remained tetraplegic.

DISCUSSION

JE is caused by infection with the JE virus, which belongs to the mosquito-borne flavivirus group. This disease is endemic in Southeast Asia and usually occurs in the summer and early autumn. *Culex tritaeniorhynchus* is the most important vector. Pigs and birds such as herons and sparrows are the natural hosts. Humans are accidental hosts. The majority of infected humans have subclinical disease. Overt clinical disease represents less than 2% of all infections. When clinically apparent, JE can present as acute fulminant neurological disease with fever, rigor, headache, rapid development of focal neurological signs, and unconsciousness. The disease

often results in death, with an overall fatality rate of 25%. Most of the survivors will develop permanent neurologic and psychiatric sequelae.¹ The definitive serologic diagnosis of JE is based on antibody detection in serum and CSF by immunoglobulin M (IgM) capture enzyme-linked immunosorbent assay test.

As illustrated in the second patient described here, the most characteristic MRI finding of JE is bilateral T2 thalamic hyperintensity.² Unilateral involvement has also been reported but is less common. Other common sites of involvement include basal ganglia, substantia nigra, red nucleus, pons, hippocampus, cerebral cortex, and cerebellum. Subcortical white matter involvement is also reported in some patients, but this has always been in combination with the more characteristic gray matter lesions.³⁻⁵ Some lesions, especially those in the thalamus, may be haemorrhagic.² Enhancement is not usually observed, indicating only minor blood-brain barrier deficit. Similar MRI findings can be seen in viral encephalitis caused by other members of the flavivirus genus such as West Nile virus and Murray Valley encephalitis virus.^{6,7}

The underlying reason for the symmetrical involvement of the deep gray matter structures by these flaviviruses is unknown. Inherent metabolic activity levels and vascular supplies of these structures may play a role.⁶ Abe et al discovered autoantibodies to myelin basic protein and neurofilaments in some patients with JE and raised the possibility of a superimposed immunologic component to this disease that may selectively involve certain portions of the central nervous system.⁴

Apart from viral encephalitis, a number of conditions can also result in bilateral thalamic oedema.⁸ Among potential vascular aetiologies are deep venous thrombosis and arterial infarction due to thrombosis, embolisation, or spasm of the basilar artery or its perforating branches. Acute disseminated encephalomyelitis and systemic lupus erythematosus can sometimes present with bilateral thalamic or deep nuclei lesions. The diagnosis of Wernicke's encephalopathy, Wilson's disease, and osmotic myelinolysis may be aided by relevant clinical history and laboratory investigation. Bithalamic glioma usually presents less acutely than vascular or inflammatory pathology.

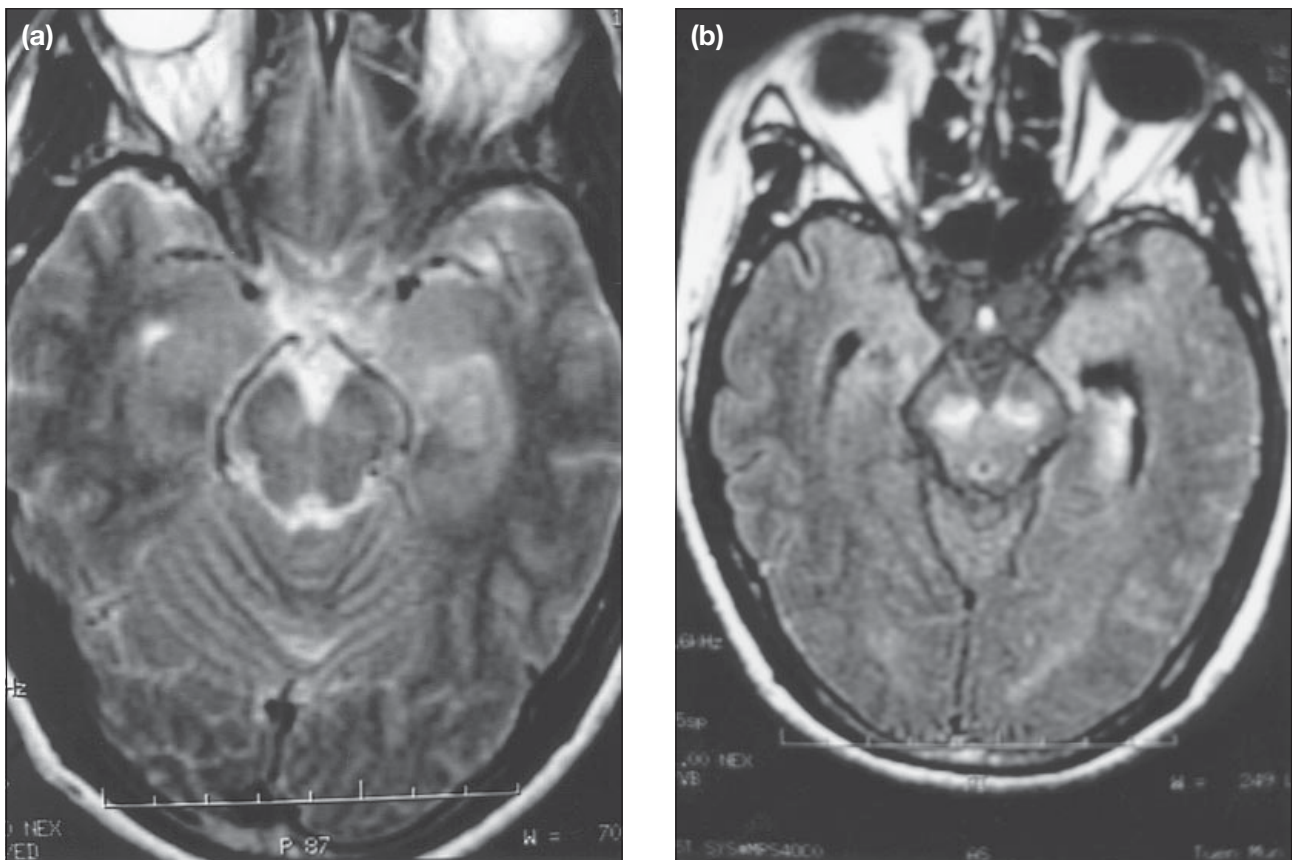


Figure 5. Follow-up magnetic resonance imaging of the brain of patient 2. (a) T2-weighted image; and (b) fluid-attenuated inversion recovery sequence image demonstrating new lesions in the bilateral substantia nigra. There is also abnormal high-signal intensity at the inferomedial aspect of the left temporal lobe.

Our first patient demonstrated the classical clinical features of the biphasic illness pattern of JE, which has only been reported once before by Pradhan et al.⁹ In this study, 6 patients who had an early relapse of JE resulting in a biphasic clinical course were reviewed and it was found that the clinical manifestations are quite different during the first and second phase of illness. Fever, rigors, headache, body aches, altered consciousness, rigidity, and tremors predominated the first phase. During the second phase, behavioural changes, dystonia, pen-oral dyskinesia, drooling, mutism, and muscle wasting were the important features. He also discovered that there was no increase in antibody titres against JE virus during the second phase of the illness compared with the first phase. Radiologically, fresh lesions appeared during the second phase at the sites known for their involvement in JE, suggesting viral recrudescence. These authors suggested that the genetic variant of the virus or host factor may be responsible for this biphasic illness pattern, which does not necessarily mean a bad prognosis.

At present there is no specific antiviral therapy for JE. This probably partially accounts for the associated high fatality rate. However, in an endemic area, it is important to differentiate JE from herpes simplex encephalitis, which is treatable with aciclovir.

CONCLUSIONS

JE is a rare disease in Hong Kong. Recognition of the MRI findings will aid in early diagnosis, particularly before serologic confirmation is available. In the appropriate setting, bilateral T2 thalamic hyperintensity, in particular haemorrhage, should raise the suspicion of JE, especially in endemic areas.

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