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CASE REPORT

Japanese viral encephalitis mimicking stroke with an initial manifestation of hemiplegia

Huan-Wen Chen [a], Liang-Wen Ding [b], Chih-Cheng Lai [c], Tse-Kai Tseng [d], Wei-Lun Liu [c,*]

[a] Department of Internal Medicine, Lotung Poh-Ai Hospital, Yi-Lan, Taiwan
[b] Department of Intensive Care Medicine, Lotung Poh-Ai Hospital, Yi-Lan, Taiwan
[c] Department of Intensive Care Medicine, Chi Mei Medical Center, Liouying, Tainan, Taiwan
[d] Department of Radiology, Lotung Poh-Ai Hospital, Yi-Lan, Taiwan

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Japanese encephalitis (JE) is an endemic disease in Taiwan. After the program to vaccinate children against JE was implemented in 1968, the incidence of JE gradually started to decrease, but it is still an important infectious disease here. Neurological manifestations in JE vary highly during the initial stage of the disease. Focal neurological symptoms, such as hemiplegia, are rarely reported. A 46-year-old male with the initial presentation of abrupt hemiplegia and fever developed mental confusion after 1 day. No bacterial pathogen was isolated from the blood or cerebrospinal fluid (CSF). A diagnosis of JE was confirmed based on the presence of JE virus-specific immunoglobulin M in the CSF and serum samples. It is necessary to consider JE when a patient presents with abrupt hemiplegia with fever followed with mental confusion and seizure, especially if the patient comes from a JE-endemic area.

Introduction

Japanese encephalitis (JE) is one of the leading causes of acute encephalopathy affecting children and adolescents in the tropics. After the program to vaccinate children against JE was first implemented in 1968, the annual incidence of JE in Taiwan began to decrease,[1] but it is still an important endemic disease in this country. The disease typically progresses through prodromal, encephalitic and convalescent stages. Its initial manifestation varies widely and it is often difficult to diagnose early. This is because some of the disease-elicited deficits of JE may be confused with noninfectious ischemic attacks. The present case report is an example of a rather rare initial manifestation of JE associated with hemiplegia and fever.

* Corresponding author. Department of Intensive Care Medicine, Chi Mei Medical Center, Liouying, 201, Taikang Village, Liouying Township, Tainan County 73657, Taiwan.
E-mail address: medrpeterliu@gmail.com (W.-L. Liu).

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Case report

A 46-year-old male patient had some pre-existing underlying diseases, including diabetes mellitus and hypertension, presented at the hospital. He had no history of travel in the past 3 months. The patient and his wife could not remember his vaccination history. He was sent to our emergency department with acute-onset right hemiplegia and low-grade fever (of around 38°C). One day later, the patient developed mental confusion and could not understand simple questions or instructions, so he could not be assessed by the mini mental state examination or judgment, orientation, memory, attention, abstract thinking calculation.

At this time, the patient was admitted to the intensive-care unit (ICU) for further evaluation. The patient's body temperature was 40.3°C when he was transferred. No evidence of nausea, vomiting, proptosis, orbital pain, carotid bruits, nuchal rigidity or seizure was noted.

Neurological examinations of this man revealed a Glasgow coma scale of $E_2V_2M_4$; his pupils were isocoric, and his light reflex and all his stretch reflexes were considered brisk. The muscle power grade of his right limbs was 2, and the muscle power grade of his left limbs was 4. Laboratory data at this time revealed the following values: leukocytes 7,400/μl (64.1% neutrophils; 8.3% monocytes; and 27.3% lymphocytes); hemoglobin 16.2°g/dl; rheumatoid factor <20 IU/ml; C3, 126 mg/dl (normal range: 83–161); C4 30.4 mg/dl (normal range: 17.0–48.5); C-reactive protein 0.18 mg/dl (normal range <0.8); and antinuclear antibody profile, negative. The chest plain film and brain computed tomography scan were both normal on the day of admission to the ICU. The patient then underwent brain magnetic resonance imaging (MRI), which revealed the presence of small hyperintense signals involving the left basal ganglion and thalamus on diffusion-weighted sequences (DWIs) (Fig. 1) with low apparent diffusion coefficient (ADC) values (Fig. 2). Lumbar puncture was performed because infection of the central nervous system could not be excluded. Examinations of the cerebrospinal fluid (CSF) revealed an initial pressure of 120 mmH2O and a cloudy appearance. The CSF cell count was 80 (81% lymphocytes and 19% neutrophils) with a protein level of 48 mg/dl and a glucose level of 133 mg/dl (blood glucose level of 256 mg/dl). Microbiological stains for Gram-positive and Gram-negative bacteria, fungi, Indian ink and acid-fast bacilli all proved negative. Other tests, including the venereal disease research laboratory slide test and various bacterial cultures, also proved negative.

Based on the CSF findings, an empiric antimicrobial agent with acyclovir was prescribed for our patient. Due to poor consciousness, he was intubated on day 2 after admission to the ICU to protect his airway. He suffered from seizure on day 4. His Glasgow coma scale decreased to $E_1V_EM_2$. Repeated lumbar puncture revealed only improving pleocytosis subsequent to antimicrobial therapy (Table 1).

Six days later, an immunoglobulin M antibody-capture enzyme-linked immunosorbent assay for JE virus was conducted and revealed positive results for serum and CSF, which confirmed the diagnosis. Two weeks later, the patient's poor level of consciousness persisted and tracheostomy was performed for maintenance of the patient's airway patency. Subsequent to a further 4 weeks of primarily supportive intensive care, the patient was discharged to a general ward, although his neurological recovery was quite slow. Two months later, this patient still had a low Glasgow coma scale score of $E_{1-2}V_EM_{2-4}$.

Discussion

JE is an arthropod-borne viral infection that is a leading cause of encephalitis in southern and eastern Asia. Infection with JE is often asymptomatic; the ratio of

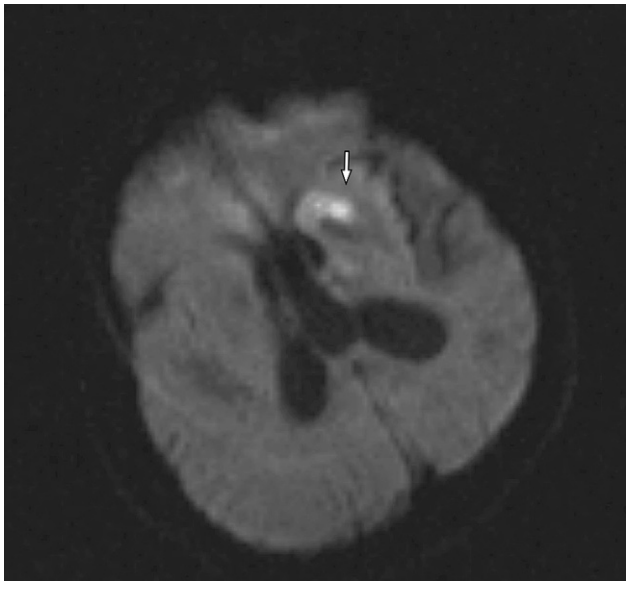

Figure 1. MRI of the patient's brain revealed the presence of small hyperintense signals involving the left basal ganglion and thalamus on diffusion-weighted sequences.

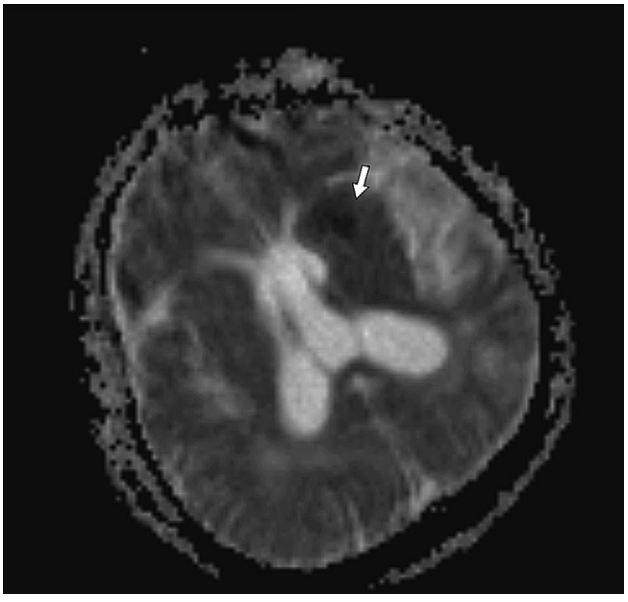

Figure 2. MRI of the patient's brain revealed low apparent diffusion coefficient values involving the left basal ganglion and thalamus.

Table 1 Cerebrospinal fluid (CSF) findings

	Appearance	White blood cell count (neutrophils %/lymphocyte %)	Protein (mg/dl)	Sugar CSF/ blood (mg/dl)	Initial pressure (mmH_2O)
1st CSF study	Cloudy	80 (19/41)	48	133/256	130
2nd CSF study	Clear	48 (17/83)	104	135/260	165

asymptomatic to symptomatic infections varies from 25:1 to 1,000:1.[2,3] The onset of this illness can be abrupt, acute, subacute or gradual.

The course of the disease can be conveniently divided into three separate stages: (1) a prodromal stage preceding CNS symptoms; (2) an encephalitis stage marked by CNS symptomatology; and (3) a late stage revealed by recovery or the persistence of signs of CNS injury.[4] The prodromal stage of JE is characterized by high-grade fever with or without rigors, headache, general malaise, nausea and vomiting.[4] This process is then followed by an encephalitic stage, which typically manifests with alter sensorium, convulsion, neck stiffness, muscular rigidity, mask-like face and abnormal body movements.[4] Apart from the classical presentation of JE, other atypical presentations, such as affected individuals revealing a flaccid paralysis-like illness, have been reported as the initial presenting feature.[5] Behavioral abnormality, alteration in sensorium, seizure and neurological deficit are common clinical presentations in the encephalitis stage.[6,7] The neurological deficit includes hemiplegia, quadriplegia or cerebellar signs, and is not a rare presentation in the encephalitis stage.[6,7] The latest review points out that the upper limbs are more commonly affected than the lower limbs.[6]

To the best of our knowledge, only three cases of JE have been reported in which the patient has suffered from hemiplegia as an initial clinical presentation.[8–10] Hemiplegia is therefore a rare presentation during the prodromal phase of JE. Our patient came from a JE-endemic area of Taiwan, and presented with right hemiplegia at the onset of his illness. It progressed to the encephalitic stage within 24 hours of onset. Although we could not exclude the coexistence of stroke and JE, such progression of his condition would appear to suggest that hemiplegia could be one of the various presentations of JE. Clearly, then, clinicians should keep this differential diagnosis in mind, especially when patients manifest with fever upon presentation and if they reside in a JE-endemic area.

MRI of the brain for our patient revealed a unilateral basal-ganglion and thalamus lesion that featured a hyperintense signal over a DWI image (Figure 1) and a rather low ADC value (Figure 2). These features could explain our patient's symptom of right hemiplegia. The MRI appearance that we observed may be related to certain pathological changes having occurred, including congestion, perivascular cuffing and thrombus formation, changes that often occur following viral invasion.[11] It is also possible that these changes are responsible for the presence of cytotoxic edema that leads to restricted diffusion and a low ADC value.[12] In a previous study, the thalamus was reported to be the most commonly involved region during MRI examination of JE patients.[13] Such an observation would appear to be consistent with the findings for our patient. Prakash et al reported that MRI featuring a DWI image would be helpful in making an early and accurate diagnosis of JE.[14]

For our patient, the initial absence of headache, neck stiffness, and his disturbed consciousness further complicated the diagnosis. The present case serves as a good example of the broad diversity and the relative rarity of the initial manifestations of JE. It is therefore necessary to take JE into consideration when a patient presents with abrupt hemiplegia with fever followed with mental confusion and seizure, especially if the patient comes from a JE-endemic area. For such patients, MRI with DWI would appear to be helpful in arriving at a correct and timely diagnosis.

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