Periodic Lateralized Epileptiform Discharges in Influenza B-Associated Encephalopathy

Akira Kurita*,**, Hiroyuki Furushima**, Haruo Yamada** and Kiyoharu Inoue*

Abstract

An 18-year-old woman presented with coma, hemi-comvulsions, and transient periodic lateralized epileptiform discharges (PLEDs). Serological tests were positive for influenza B, and cerebrospinal fluid PCR for herpes simplex virus DNA was negative. Magnetic resonance imaging later showed abnormal signal intensity in the temporal lobe ipsilateral to the PLEDs. Influenza-associated encephalopathy may cause hemiconvulsions and PLEDs, and can mimic herpes simplex encephalitis.

Key words: PLEDs, hemiconvulsions, electroencephalography, MRI, temporal lobe

Introduction

Acute encephalopathy and postviral encephalomyelitis are occasional central nervous system complications of influenzal infection (1, 2). Electroencephalography is of value in patients with such complications, especially in patients with seizures. Although periodic lateralized epileptiform discharges (PLEDs) are sometimes observed in patients with herpes simplex encephalitis (3, 4), to our knowledge no report to date has documented PLEDs in influenza-associated encephalopathy or encephalitis. In this communication, we present a patient with influenza B-associated encephalopathy characterized by hemiconvulsions and PLEDs in the initial stage of the disease, and abnormal signal changes on magnetic resonance imaging (MRI) were demonstrated later in the temporal lobe ipsilateral to the PLEDs.

Case Report

An 18-year-old female high school student suddenly lost consciousness at school following a 3-day history of high-grade fever and coughing on January 22, 1999. She was immediately transferred to a local emergency clinic. In ambulance, she was comatose with a respiration rate of 12 and cardiac rate of 132 a minute. Her blood pressure was 160/62 mmHg. At the emergency clinic, a right hemiconvulsion developed, followed by a secondary generalized convulsion and respiratory arrest, for which she was immediately intubated and artificially ventilated. Right hemiconvulsion recurred en route to our hospital. She had a history of bronchial asthma, which had been well controlled over the previous 10 years. There was no history of syncope or convulsive seizure.

On examination, she was comatose and febrile, and on forced ventilation. There were no signs of meningeal irritation or focal neurological deficits except for brisk tendon reflexes and bilateral extensor plantar responses. The results of general physical examinations were unremarkable. The white cell count was 11,400/μl with 84.9% neutrophils, 7.4% lymphocytes, 6.3% monocytes, and 1.4% eosinophils; the hemoglobin concentration was 7.9 g/dl, and the platelet count was 25.7×10⁴/μl. Serum levels of urea and electrolytes, hepatic enzymes, C-reactive protein and immunoglobulins (IgG, A, M), and results of coagulation tests were all normal. The serum iron concentration was low (290 μg/l). Results of urinalysis were normal. A lumbar puncture revealed clear cerebrospinal fluid (CSF) under a normal pressure of 16 cmH₂O, with 1 lymphocyte/μl, 0.85 g/l glucose (blood glucose 1.45 g/l), and 0.25 g/l protein. An electroencephalogram (EEG) on admission showed diffuse PLEDs in the left hemisphere, composed of sharp waves mixed with slow waves, occurring at intervals of approximately 1.0 to 1.5 seconds (Fig. 1). Chest radiographs showed no abnormalities. Brain computed tomography (CT) on admission was unremarkable.

Based on a provisional diagnosis of herpes simplex encephalitis, treatment was started with acyclovir (1,000 mg/day), dexamethasone (12 mg/day), and anticonvulsants. On the 5th hospital day, the patient regained consciousness and was extubated. The right hemiconvulsions again developed with an axillary temperature of 40°C. Brain MRI on the 8th hospital day was unremarkable, and the CSF was normal again. During the following 5 days, she was febrile and occasionally confused without convulsions. An EEG on the 12th hospital day showed slow
Figure 1. EEG on admission revealed PLEDs, which were seen diffusely over the left hemisphere. These were composed of sharp waves mixed with slow waves, and occurred at intervals of approximately 1.0 to 1.5 seconds.

alpha waves mixed with occasional slow waves in the theta range without any periodic activities. From the 14th hospital day, the patient’s condition improved, and the acyclovir was discontinued 3 days later. By the 27th hospital day, the patient had become afebrile and was free of any neurologic or psychiatric symptoms. Brain MRI on the 32nd hospital day demonstrated an area of abnormally high signal intensity on T2-weighted and fluid attenuated inversion recovery (FLAIR) images and area of low signal intensity on T1-weighted images in the left hippocampal region without contrast enhancement (Fig. 2).

Serum complement fixation (CF) titer for influenza B virus on admission was 1:128, and the hemagglutination inhibiting (HI) antibody titer for influenza B-1 virus on the 13th hospital day was 1:2,048. The CF titer was decreased to 1:16, whereas the HI titer remained high (1:2,048) 16 weeks later. The CSF was negative for antibodies to influenza B virus. Serum and CSF enzyme immunoassay antibody (EIA) titers and CSF PCR assay for herpes simplex virus were all negative. Serological tests failed to demonstrate any other virus antibody responses, including those for varicella-zoster (EIA), cytomegalovirus (EIA), mumps (EIA), measles (EIA), Japanese encephalitis (HI), parainfluenza 1 and 2 (HI), and influenza A (CF). Viral cultures from the throat, serum, and CSF were negative.

The patient was discharged on the 35th day, with a full neurologic and intellectual recovery. The follow-up MRI 1 month after the previous examination revealed regression of the left hippocampal high intensity on T2-weighted and FLAIR images.

Discussion

In January 1999, influenzal infection was an epidemic in Japan (5). In this 18-year-old patient, a diagnosis of influenza B-associated encephalopathy was made on the basis of the prodromal illness, clinical course, and the positive serological tests for influenza B virus, with consideration of the epidemiological data. Since results of numerous CSF studies were unremarkable, and the neurologic symptoms suddenly appeared at the height of the influenza infection, we believe this patient’s condition to be acute encephalopathy, rather than postviral encephalitis (1, 2).

PLEDs sometimes occur in acute cerebral infarctions, neoplasia and inflammatory conditions (3, 4, 6), especially in herpes simplex encephalitis (4). Greenberg et al (7) reported PLEDs in infectious mononucleosis encephalitis. However, to our
PLEDs in Influenza B Encephalopathy

Figure 2. A, B) Axial T2-weighted (TR: 3,540, TE: 104) and FLAIR (TR: 10,002, TE: 152) MR images on the 32nd hospital day demonstrated an area of abnormally high signal intensity in the left hippocampal region, whereas T1-weighted images (not shown) demonstrated an area of low signal intensity.

Knowledge no report has documented PLEDs in influenza-associated encephalopathy. Her right hemiconvulsion was consistent with PLEDs in the left hemisphere. While PLEDs are sometimes associated with focal hypoxic brain damage following seizures (6), it is unlikely, because the patient was intubated and ventilated immediately after the respiratory arrest following the seizure at the emergency clinic.

The cause of the high signal intensity lesions that appeared on T2-weighted and FLAIR images of MRI on the 32nd hospital day is unclear. When the MRI was obtained, the patient was free of neurologic or psychiatric symptoms, and the EEG had become normal. No hypoxic event was documented after admission. A second MRI 1 month later showed regression of the high signal intensity. These observations suggest that the MRI lesion is unlikely to reflect acute inflammation, focal brain edema, petechiae, necrosis (8), or focal hypoxic brain damage following seizures (9). Kimura et al (10) has reported similar MRI changes in two children with influenzal encephalitis. In those patients, abnormal high signal intensity lesions on T2-weighted images were observed in the cortex more than 20 days after the onset of the influenzal infection but the lesions spontaneously resolved 7 to 10 days later. The authors called these lesions “postinfectious focal encephalitis” and, on the basis of the elevated levels of thrombin anti-thrombin III (TAT) complexes, attributed them to angiopathy. In recent reports of influenzal encephalitis/encephalopathy, hypodense areas on CT or high signal intensity areas on T2-weighted images on MRI have been documented in the thalamus (8, 10), brainstem (8), and parietal cortex (10). Except for the complete recovery, the present patient showed clinical features quite similar to that of herpes simplex encephalitis, i.e., disturbance of consciousness, hemiconvulsions, PLEDs, and abnormal MRI signal intensity changes in the unilateral temporal lobe, while the MRI changes were not directly related to the PLEDs or hemiconvulsions. Influenza-associated encephalopathy should be included in the differential diagnosis of acute encephalopathy or encephalitis characterized by hemiconvulsions and PLEDs.

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