Journal of Zhejiang University SCIENCE B
ISSN 1673-1581
http://www.zju.edu.cn/jzus
E-mail: jzus@zju.edu.cn

# A case of overlapping Bickerstaff's brainstem encephalitis and Guillain-Barré syndrome

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Received Aug. 3, 2005; revision accepted Nov. 13, 2005

**Abstract:** Objective: There is no report on Bickerstaff's brainstem encephalitis (BBE) patients in China. We here report the first case of BBE in China. Methods: Clinical features, results of electromyography, electroencephalography (EEG), magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) examination were studied to clarify the characteristics of this syndrome. Results: A 44-year-old man presented himself at our inpatient department with somnolence and dizziness as his initial symptoms. He developed multiple cranial nerves paralysis especially internal and external ophthalmoplegia, ataxia and tetraparesis within 1 week. His condition rapidly deteriorated, and he experienced coma. Electromyography showed indications of peripheral nerve dysfunction, electroencephalography revealed loss of basic rhythm, MRI demonstrated high-intensity abnormalities on $T_2$-weighted images of medulla oblongata, and CSF albuminocytological dissociation was defined abnormally as high protein. Ten months later, he almost completely recovered. Conclusion: BBE, fisher syndrome (FS) and Guillain-Barré syndrome (GBS) are similar clinically; BBE and FS were proposed to be the variant of GBS.

**Key words:** Bickerstaff's brainstem encephalitis, Fisher syndrome, Guillain-Barré syndrome
**doi:**10.1631/jzus.2006.B0138 **Document code:** A **CLC number:** R745.4[+]3

## INTRODUCTION

Bickerstaff's brainstem encephalitis (BBE) is characterized by acute onset of ophthalmoplegia, ataxia, disturbance of consciousness, hyperreflexia or Babinski's sign (Bickerstaff, 1957; Al-Din *et al*., 1982). Most of the patients generally have a good outcome. Only a small proportion of the patients die or show incomplete remission with residual symptoms (Odaka *et al*., 2003). Because of its rarity, there has been no report on BBE patients in China. We here report the first case of BBE in China, with dizziness and somnolence the initial symptoms. The patient developed multiple cranial nerves paralysis especially internal and external ophthalmoplegia, ataxia and tetraparesis within one week. His condition rapidly deteriorated, and he experienced coma. After ten months following up, he almost completely recovered.

## CASE REPORT

A 44-year-old man presented at our Department of Neurology, saying that he appeared acute dizziness, nausea and vomiting, and that three days earlier he had a sore throat, experienced fatigue and drunk alcohol in moderate amount. His vomits were gastric content, and he also suffered mild fever. Two days later he was hospitalized in the Department of Gastroenterology. He denied he was alcoholic and exposure to poison. The results of his serum and urinary amylase concentration, full blood count, urinalysis, routine test of stool, plasma electrolyte levels, liver and kidney function tests were within normal limits. Color duplex Doppler sonography showed "fatty liver

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and polyploidy lesions of gallbladder". Abdominal computed tomography performed was normal. Gastroscopy revealed "esophagitis and biliary reflex gastritis". On the forth day after the onset of disease, he developed somnolence, limb weakness and numbness. His speech was slurred. Because these symptoms worsened continuously, he was transferred to the Neurological Department on day 6. He could speak a little, when aroused by language stimulation. His slurred speech was accompanied by dysarthria. Several water blisters of burning could be seen on his right hand. Neurological examinations showed bilateral blepharoptosis. His pupils were fixed (about 5 mm diameter) and light reflexes were absent. He could not gaze upward; his horizontal gaze and downward gaze were mildly limited. Corneal reflex and orbicularisoculi reflex were intact. Bilateral facial paralysis was detected. Mild dysphasia and limitation of gag reflex were observed. Limb strength in the arms and legs was 3 on the MRC scale. His muscular tension was diminished. All tendon jerks were absent. Bilateral abdominal reflexes disappeared. However, when the lower ribs were struck, contraction of the abdominal muscles and movement of the umbilicus towards the stimulus could be observed. Pathological reflexes were lacking. Finger-to-nose test and rapid alternating supination pronation test were ataxic. Defect of pain and thermal sensation over the limbs below elbows and patellas were observed. Vibration and position senses were impaired. Neck stiffness and Kernig sign were not present. The concentrations of serum sodium, potassium and chloride were 118.7 mmol/L, 3.3 mmol/L and 98 mmol/L respectively. Results of serological examination for rheumatism, systemic lupus erythematosus, toxicants including lead and mercury were negative. Electromyography showed distal motor and sensory nerve conduction velocities from the upper and lower limbs were reduced, and their amplitudes were diminished. Brainstem auditorily evoked potentials (BAEP) had obscured I and III waves on the left sides. Visually evoked potential (VEP) and somatosensorily evoked potentials (SEP) were normal. Magnetic resonance imaging (MRI) scan showed high-intensity abnormalities on $T_2$-weighted images of medulla oblongata (Fig.1). Chest radiographs suggested "a fusiform shade in oblique fissure on right lung, suspected as interlober pleural effusion". Cerebrospinal fluid (CSF)

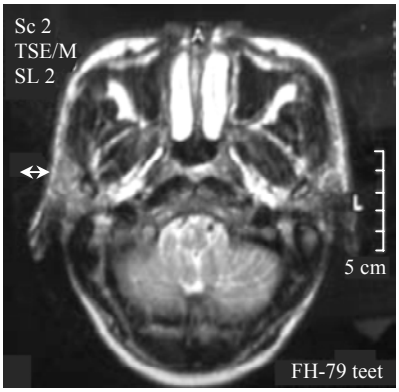


**Fig.1 MRI scan demonstrated high-intensity abnormalities on $T_2$-weighted images of medulla oblongata**

pressure was 120 mm$H_2O$, its appearance was clear and colorless. CSF protein was 98 mg/dl and the cell count was 15 $mm^{-3}$, reflecting predominantly mononuclear leukocytes. He was given vitamin $B_1$, $B_6$, $B_{12}$, and antibiotic treatment, as well as fluid electrolyte management. His condition rapidly deteriorated, and he experienced coma on the 9th day following onset. His pupils were dilated (8 mm diameter) and light reflexes were absent. Corneal reflexes were sluggish. Oculocephalic movement (including upward and horizontal movement) disappeared. Because of tachypnea, he was transferred to the intensive care unit. His blood oxygen saturation remained normal all the time, so he never received assisted respiration. The basic frequency of EEG was lost. He received 0.4 g/(kg·d) intravenous immunoglobulin for 5 d. Twenty-three days after the onset of the symptom, he recovered from coma, and his breath was stable. Chest radiographs became normal. EEG showed $\alpha$ activity with some $\theta$ waves and $\delta$ waves. He was fully alert and returned to the neurological department on day 24. His voice was hoarsen and slurred. His pupils were 5.5 mm diameter, light reflexes and corneal reflexes were sluggish. Lateral gaze and upward gaze were limited apparently. Left facial weakness and bilateral palatal palsy were observed. Limb strength was 4 on the MRC scale. Finger-to-nose test and rapid alternating supination pronation test remained ataxic. His paresthesia was still present; he said he always felt something crawling on the skin of his arms and legs. Lumbar puncture was performed again. CSF pressure was 140 mm$H_2O$, appearance was mildly yellow, cell count was 5 $mm^{-3}$,

Pandy test was positive. The patient was discharged from the hospital on day 32. The patient's follow-up evaluation was conducted 10 months later and showed that he was nearly normal. He could walk and work without support. Photophobia was the only residual symptom. Neurological examinations showed bilateral pupils were 5 mm in diameter, and constricted slowly to 4 mm diameter in response to intensive light. The clinical diagnosis was overlapping GBS and BBE.

## DISCUSSION

Diagnosis of our patient's illness was difficult. Initially, he was diagnosed as GBS because of his rapidly progressive multiple cranial nerves paralysis, limb weakness and absent tendon reflexes after infection. Electromyography showed positive peripheral nerves dysfunction. CSF albuminocytological dissociation was detected. Within one week, his condition had rapidly deteriorated to coma and completely ophthalmoplegia. These findings were not compatible with GBS. Moreover, his bilateral abdominal reflexes were completely lacking. However, the lower ribs were struck, contraction of the abdominal muscles could be observed. This sign indicated pyramidal injury. Furthermore, EEG showed basic rhythm lost. All these clinical and electrophysiological findings indicated existing central nervous system involvement. Thereafter, his brain MRI revealed abnormal images of medulla oblongata, which proved the brainstem injury. When considering the electrolyte disorders appearing in the middle course of the disease, central pontine myelinolysis should be clinically suspected. This patient's electrolyte disorders appeared following the conscious disturbance; the clinical symptoms and signs went beyond medulla oblongata injury; no underlying causes of central pontine myelinolysis were found in this patient. Therefore, central pontine myelinolysis could not be diagnosed. When his muscle strength improved to near normal level, his limbs and trunk ataxia became the outstanding sign. After ten months follow-up observation, he recovered almost completely. Thus, BBE overlapping GBS is a reasonable diagnosis.

Bickerstaff and Cloake (1951) reported 3 cases of drowsiness, ophthalmoplegia and ataxia, and proposed that the lesion responsible for these clinical signs was in the midbrain. Bickerstaff (1978) reviewed the syndrome for "*the Handbook of Clinical Neurology*" under the title "brainstem encephalitis" (BBE). The diagnostic criteria for BBE were: (1) progressive, relatively symmetric ophthalmoplegia and ataxia by 4 weeks; (2) either consciousness disturbance (coma, semicoma, or stupor) or pyramidal signs (hyperreflexia or pathological reflexes); (3) limb strength of 5 or 4 on the Medical Research Council scale. Patients showing limb weakness (3 or less on the Medical Research Council scale) were diagnosed as having overlapping BBE and GBS (Susuki *et al*., 2001). The clinical symptom of BBE is similar to that of FS, because of evidence of ophthalmoplegia, ataxia and CSF albuminocytological dissociation. Hence, BBE should be differentially diagnosed with FS (Al-Din *et al*., 1982). BBE must have consciousness disturbance or pyramidal signs, which reflect serious brainstem lesion. While, FS must have none of these characteristics. BBE also has other clinical features. Its male:female ratio is about 3:2. The most frequent preceding symptom is upper respiratory infection, others include fever, headache and diarrhea. All the patients have ophthalmoplegia (external and internal) and ataxia. Upward gaze and horizontal gaze disability, pupillary abnormalities and nystagmus are frequent. Our patient's initial symptoms were partially internal ophthalmoplegia and upward gaze difficulty. He developed completely internal and external ophthalmoplegia, and internal ophthalmoplegia was the only residual sign. All his clinical symptoms were compatible with typical BBE. Some other clinical features of BBE are characterized as facial weakness, blepharoptosis, bulbar palsy and long-tract sensory disturbance (Susuki *et al*., 2003). Abnormal lesions (high-intensity areas on $T_2$-weighted images of the brainstem, thalamus, cerebellum and cerebrum) on MRI findings are present in about one-third of BBE patients. These MRI signals may move and regress with the clinical course of the illness (Mondéjar *et al*., 2002). EEG finding could reveal slow-wave activity in the $\theta$ to $\delta$ range. In the electromyography studies, patients with BBE coexisting with limb weakness can show decreased motor nerve conduction velocities, prolonged distal latency, reduced compound muscle action potential

amplitude, F-wave disappearance or its latency prolonged, indicative of motor nerve demyelination and axon degeneration. Several reports suggested that plasmapheresis and IVIg have a beneficial effect on patients with BBE. Moreover, combined therapy of IVIg and high-dose methylprednisolone should be more efficacious therapy. Controlled clinical trials are needed to test this proposal (Fox *et al*., 2000).

The relationship of BBE to FS or GBS remains controversial (Ogawara *et al*., 2002). Serum anti-GQ1b IgG antibody levels can be elevated in all these diseases (Matsuo *et al*., 2004). In pathological investigations showed that human anti-GQ1b antibody strongly stains in the regions of the oculomotor, trochlear but abducent nerves, and weakly stains the deep cerebellar nuclei, the gray matter in the brainstem, spinal cord, and some large dorsal root ganglion cells and muscle spindles. Anti-GQ1b IgG antibody is strongly associated with ophthalmoplegia, and is also closely related to ataxia and areflexia. The etiology of BBE is similar to that of FS and GBS. Moreover, some clinical findings such as areflexia and CSF albuminocytologic dissociation can be detected in all of these diseases. BBE, FS and GBS are similar clinically. It is suspected that BBE, FS and GBS form a continuous spectrum; BBE is a distinct disease entity or a variant of FS and GBS (Ogawara *et al*., 2000; Odaka *et al*., 2001).

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