—Case Reports—

A Case of Acute Encephalopathy Associated with Acute Focal Bacterial Nephritis

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Acute encephalopathy is a syndrome characterized by an acute onset of disturbance of consciousness. Many acute encephalopathies are caused by viral infections; however, they can also be a result of bacterial infections. Acute focal bacterial nephritis (AFBN) can cause neurological symptoms, such as irritation, unconsciousness, and seizures. In some cases, AFBN-associated acute encephalopathy has also been reported. This report describes the first case of acute encephalopathy with AFBN without significant findings on brain MRI. The patient was a 3-year-old male, who had two episodes of febrile seizures at the ages of 1 and 2 years. He developed disturbance of consciousness, irritability, excitability, and neck stiffness on the day after admission. There were no abnormal findings on brain MRI; however, a generalized high-voltage slow wave was noted on electroencephalography (EEG). His urinary sediment count was elevated, and *Morganella morganii* and *Enterococcus faecalis* were detected in the urinary culture. A diagnosis of acute encephalopathy with urinary tract infection (UTI) was made. Intravenous (IV) antibiotics were administered to treat the UTI, while methylprednisolone pulse therapy and IV immunoglobulin were administered to treat acute encephalopathy. Additionally, AFBN was detected in both kidneys on contrast-enhanced CT. The patient received a second course of methylprednisolone pulse therapy due to the persistent high voltage slow wave noted on the EEG on day 8. Furthermore, contrast-enhanced CT revealed AFBN in both kidneys. The final diagnosis was acute encephalopathy with AFBN; however, we had initially diagnosed febrile seizures associated with UTI. It should be noted that acute encephalopathy is associated with AFBN. (J Nippon Med Sch 2022; 89: 640–644)

Key words: acute encephalopathy, urinary tract infection, acute focal bacterial nephritis

Case

The patient was a 3-year-old male with no notable family or perinatal history. Furthermore, his developmental history suggested no complications, and his vaccination regimens had been completed. He had a history of febrile seizures at 1 and 2 years of age. and he had experienced convulsions with fever twice daily prior to hospital admission. The first seizure, a generalized tonic-clonic seizure, occurred 12 hours after the onset of fever; however, his neurological examination revealed normal findings. Additionally, his consciousness was clear between the convulsions. His consciousness was determined to be E2V4M4 according to the Glasgow Coma Scale. He exhibited no symptoms of upper respiratory infection or abdominal pain, and his body temperature was 39.7°C. No seizures occurred; however, irritability, excitability, and neck stiffness were observed 12 hours after admission. Brain magnetic resonance imaging (MRI) results (**Fig. 1**) was normal. Cerebrospinal fluid cell counts, protein, and glucose were normal. However, a generalized high-voltage slow wave was noted on electroencephalogram (EEG) (**Fig. 2a**). Speculum examination of the spinal fluid culture showed no phagocytosis of bacteria or leukocytes. The diagnosis of bacterial meningitis was ruled out because the neck stiffness had disappeared one hour after its initial finding and there were no elevated

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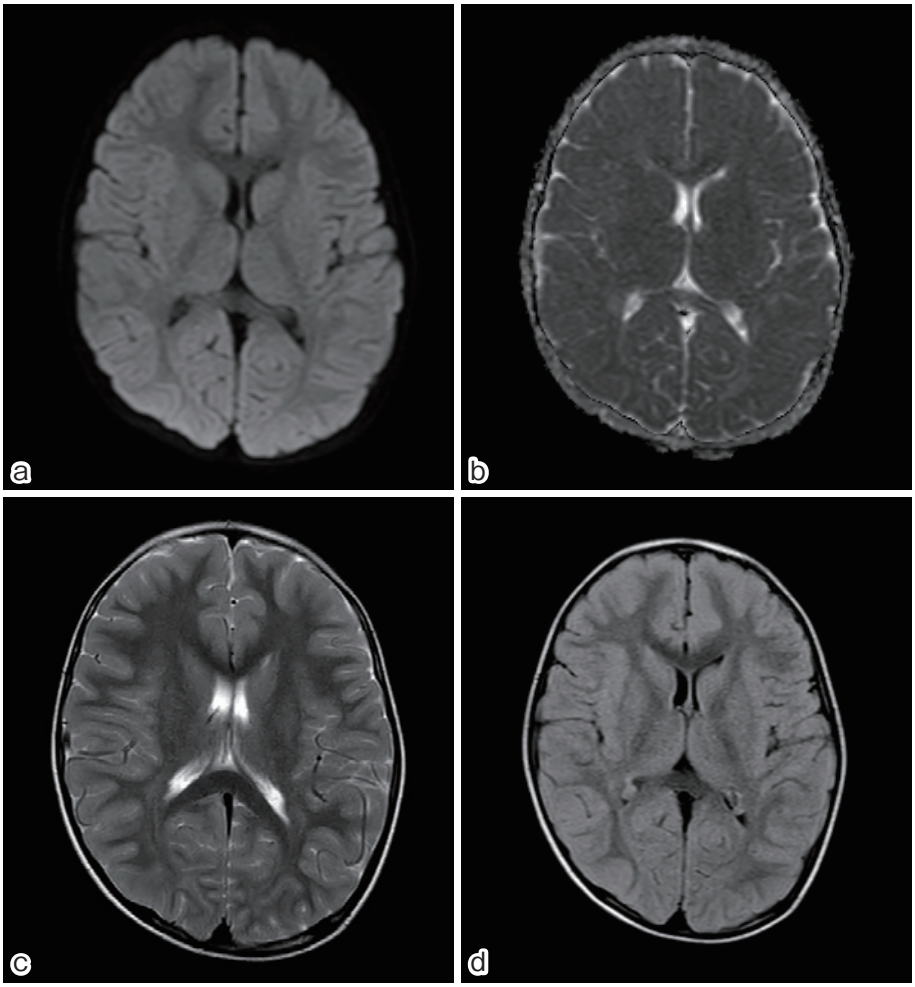

Fig. 1 No abnormal findings on brain MRI: a) DWI, b) ADC map, c) T2WI, d) FLAIR.

cerebrospinal fluid cells and decreased spinal fluid glucose. His laboratory findings revealed a high WBC count (21,400/mm^3) and CRP level (1.38 mg/dL), and urinary sediment result was 30-40/HPF. The patient was diagnosed with acute encephalopathy and urinary tract infection (UTI). Intravenous (IV) ampicillin (300 mg/kg/day) and ceftriaxone (200 mg/kg/day) were administered as treatment for UTI, while methylprednisolone (30 mg/kg/dose, three days) and IV immunoglobulin (1 g/kg/dose) were administered to manage the acute encephalopathy. On day 5, *Morganella morganii* and *Enterococcus faecalis* had counts of up to 10^5 in the urine culture specimens, the samples for which were collected on the day of admission. Ceftriaxone was substituted with cefepime (100 mg/kg/day) on that same day. Other etiologic viral agents causing acute encephalopathy was not detected in CSF and blood. Additionally, contrast-enhanced computed tomography (CT) revealed acute focal bacterial nephritis (AFBN) in both kidneys (**Fig. 3**).

On day 8, a local high-voltage slow wave persisted on the EEG, despite the patient having received the first course of methylprednisolone pulse therapy; thus, a second course was initiated. A follow-up brain MRI revealed no signal changes. EEG findings regarding the natural sleep state had normalized by day 12 (**Fig. 2b**), and the patient was discharged from the hospital on day 19. There were no sequelae at the one-year follow-up, and there was no recurrence of UTI.

Informed consent was obtained from the guardian(s) prior to the manuscript submission.

Discussion

Acute encephalopathy is a syndrome characterized by an acute onset of severe and long-lasting disturbance of consciousness, which is typically observed in previously healthy children[1]. Many acute encephalopathies are caused by viral infections; however, they can also be a result of bacterial infections. Acute encephalopathies can be classified based on the pathogen or MRI findings, according to Japanese guidelines. The most common pathogen to cause acute encephalopathy is the influenza virus, followed by the human herpesvirus 6, rotavirus, and respi-

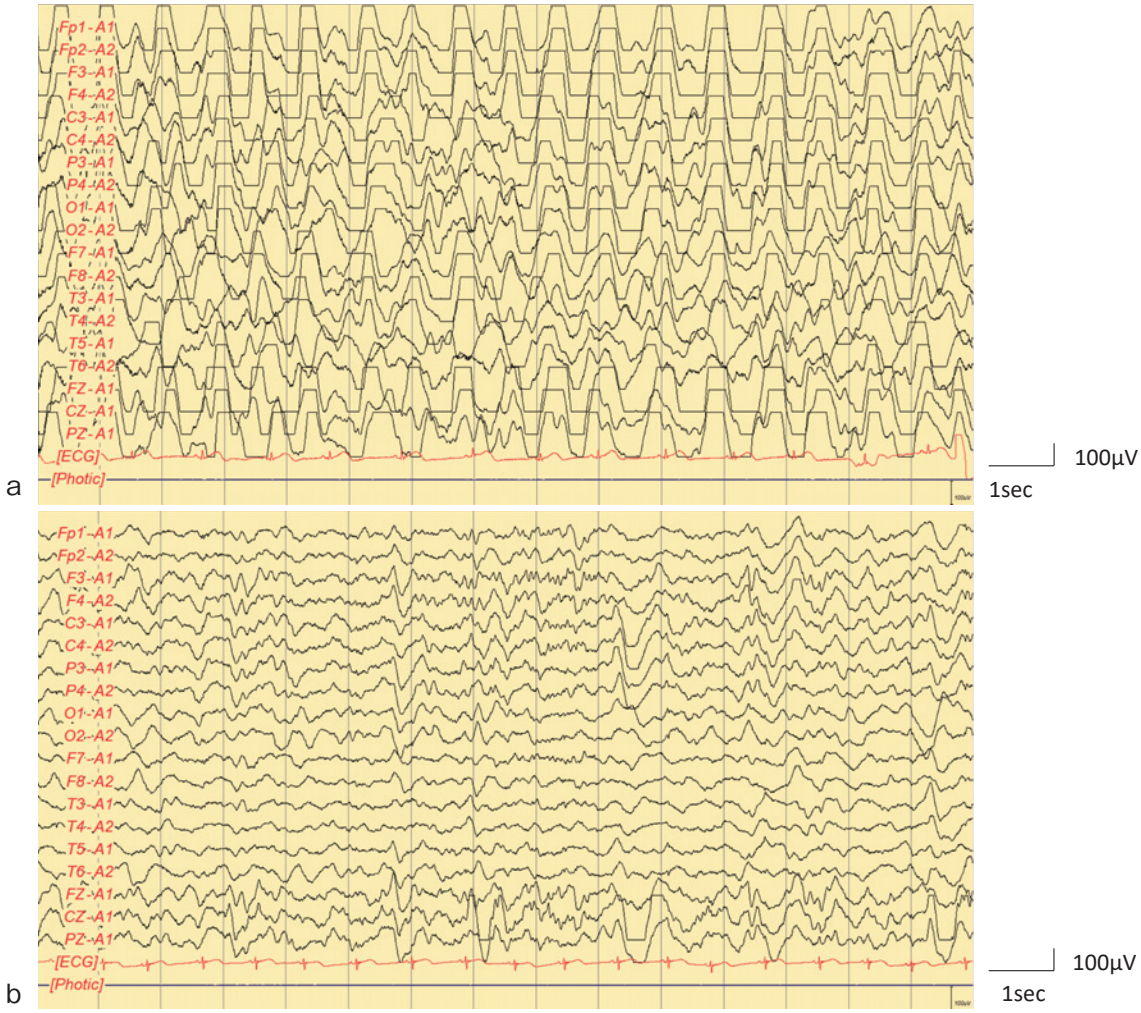

Fig. 2 EEG findings in this case: a) The generalized high voltage on interictal EEG wave upon a disturbance of consciousness on day 2, b) Normal findings whilst in an induced sleep state on day 12.

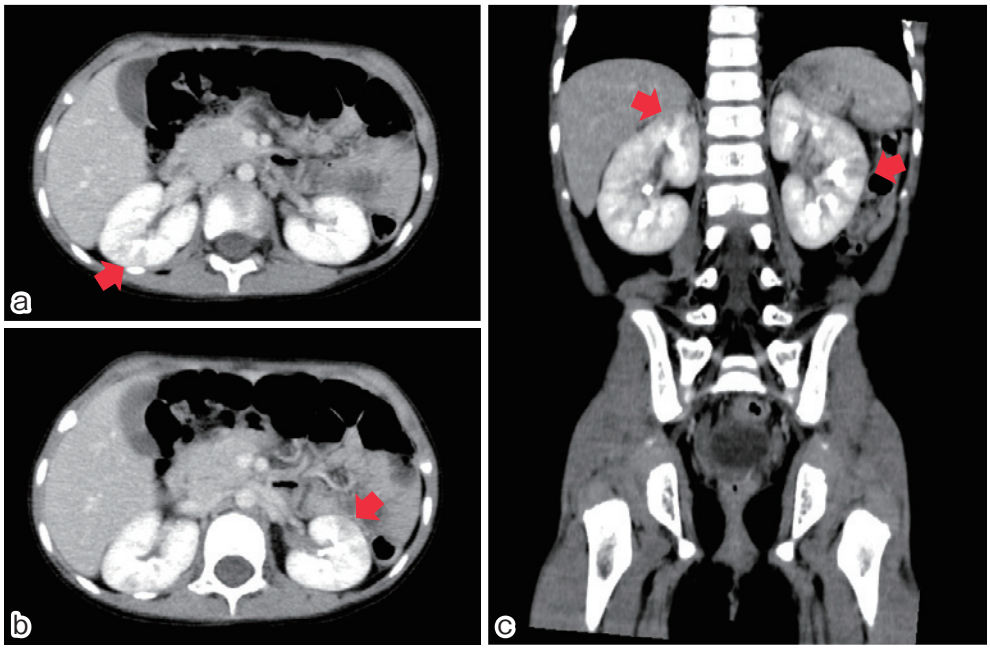

Fig. 3 AFBN in both kidneys noted on abdominal enhanced contrast CT (mark by arrow): a) b) on transverse plane, c) on coronal plane.

ratory syncytial virus[1]. Other etiologic agents of acute encephalopathy include *Bordetella pertussis*, *Salmonella*, enterohemorrhagic *Escherichia coli*, and mycoplasma infections. There have been several reports of UTI or AFBN causing acute encephalopathy; however, alternate diagnoses such as mild encephalitis/encephalopathy with a reversible splenial lesion (MERS), acute encephalopathy with biphasic seizures and late reduced diffusion, and hyperammonemic encephalopathy have been reported[2]. There have been no reports of acute encephalopathy with AFBN without significant findings on brain MRI, such as in this case.

UTI is a common clinical problem in infants and children and usually runs an uncomplicated course. Its more serious forms including AFBN, renal abscess, and pyonephrosis, are uncommon[3]. AFBN sometimes causes neurological symptoms; including meningeal irritation, unconsciousness, and seizures. AFBN-associated acute encephalopathy has also been reported. MERS is a well-known acute encephalopathy-associated UTI that occurs with AFBN[4]. A previous report revealed that AFBN is associated with central nervous system lesions. Similarly, a recent report compared the clinical features of MERS with and without AFBN[5], suggesting that pediatricians should be made aware of the possibility of AFBN in the clinical setting when treating MERS, particularly when the patient exhibits inexplicably high CRP levels. However, our patient was not diagnosed with MERS and had slightly high CRP levels. AFBN as a complication of acute encephalopathy should still be considered, even if a patient does not exhibit elevated CRP levels.

It can be difficult to differentiate between febrile seizures and acute encephalopathy in the early stages. There are a few reports on the differential diagnosis of acute encephalopathy and febrile seizures. Fukuoka et al. reported a predictive factor of acute encephalopathy with biphasic seizures and late reduced diffusion compared with febrile status epilepticus[6]. Tada et al. studied a predictive score for early diagnosis of acute encephalopathy with biphasic seizures and late reduced diffusion. They suggested that age less than 1.5 years and a Glasgow Coma Scale score of 14 or less (Japan Coma Scale score of 1 or higher) were high risk factors for developing acute encephalopathy with biphasic seizures and late reduced diffusion[7]. Another report described significant differences between febrile seizures and acute encephalopathy in terms of serum liver enzyme levels[8]. In regard to the early seizure phase, there are no reports that differentiate between non-prolonged febrile seizures and acute encephalopathy. Initially, we did not suspect this case to be acute encephalopathy, as acute encephalopathy associated with bacterial infections are not common. However, there are multiple reports of acute encephalopathy with bacterial infection, such as those cased by *S.pneumoniae*[9], *S.aureus*[10,11], *E.faecalis*[4], *Yersinia pseudotuberculosis*[12]. It is important to keep these cases in mind and perform careful follow-up even if an initial diagnosis of complex febrile seizures with bacterial infection is made.

Author contribution: HY wrote paper. HY and YM performed the patient care. NS contributed to revising the manuscript. All authors have read and approved the final manuscript.

Conflict of Interest: The authors declare no conflict of interest.

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