Acute encephalopathy with biphasic seizures and late reduced diffusion associated with *Streptococcus sanguinis* sepsis

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Abstract

Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) develops in association with systemic as well as central nervous system (CNS) viral or bacterial infections. AESD is most often noted with influenza or human herpesvirus 6 infection in previously healthy infants. However, AESD has also been reported in an infant with developmental retardation and in a mentally and motor-disabled adolescent. Here, we report the case of a 4-year-old female with significant development delay due to spinal muscular atrophy, who developed AESD during *Streptococcus sanguinis* sepsis with no apparent CNS infection. Although the patient had extremely high serum procalcitonin (45.84 ng/mL; reference; <0.4) on admission indicating a poor prognosis, she was successfully managed for sepsis and AESD.

Introduction

Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD) is a rare encephalopathy that is mostly reported in Japan.1 AESD was originally described as the presentation of clinical biphasic seizures on day 1 and days 4-6 accompanied by radiological findings showing no or mild acute abnormality on days 1-2, followed by magnetic resonance imaging (MRI) findings showing reduced diffusion in subcortical white matter on days 3-9.2 AESD mainly occurs in previously healthy infants, and is associated with viral infections such as influenza3 or human herpesvirus 6 (HHV-6),3 as well as bacterial infections.4-6 AESD has also been reported in an infant with developmental retardation4 and in a mentally and motor-disabled adolescent.7 Here, we report a case of AESD caused by bacterial infection (*Streptococcus sanguinis* [S. sanguinis] sepsis, but not meningitis) in a 4-year-old female with significant developmental delay.

Case Report

The patient was born full term with a birth weight of 3,184 g, and was the second-born child of her family. She was suspected to have developmental delay at the age of 6 months and was diagnosed with spinal muscular atrophy (SMA) at the age of 1 year. It was not determined if she had acute infantile SMA (type I) or chronic infantile SMA (type II).9 She became bed-ridden, could not roll over, and had a weak cough reflex. She had been able to take food with help, but needed biphasic positive airway pressure (BiPAP) apparatus to overcome sleep apnea syndrome until at the age of 4 years and 3 months, when she developed infection-related hemophagocytic lymphohistiocytosis (HLH; for which she fulfilled 5/8 of the clinical diagnostic criteria)10 with significantly abnormal laboratory data (serum brain natriuretic peptide >2,000 pg/mL; aspartate aminotransferase >13,000 U/L; lactate dehydrogenase >10,000 U/L; and ferritin, 7590 ng/mL), and suffered from severe dilated cardiomyopathy (Ejection Fraction, 30%; Mitral Regurgitation grade III).

Fortunately, the patient survived this episode with methylprednisolone pulse therapy and hemodynamic and respiratory support. Eventually, tracheotomy and gastrostomy were performed and she was able to receive home care after discharge. At the age of 4 years and 10 months, she was transferred to the emergency clinic with loss of consciousness associated with severe hypoglycemia (blood glucose, 10 mg/dL). On day 1 of admission, her physical condition was estimated as Japan Coma Scale (JCS) III-200 with blood pressure, 110/62 mmHg; heart rate, 106/min; respiration rate, 30/min; and SpO2, 90% (room air). Along with persistent disturbed consciousness, the patient showed prolonged episodes of facial spasms and one-point stare-type seizures, associated with abnormal electroencephalogram (EEG), which revealed diffuse high-voltage slow wave pattern. No generalized seizures were noted. Her laboratory data were as follows: white blood cell count, 30,000/µL (neutrophils, 89%); Hb, 14.0 g/dL; platelet count, 421 K/µL; serum alanine aminotransferase, 19 U/L; lactate dehydrogenase, 360 U/L; BUN, 33 mg/dL; creatinine 0.16 mg/dL; blood glucose, 10 mg/dL; C-reactive protein (CRP), 0.13 mg/dL; procalcitonin, 45.84 (reference <0.4) ng/mL; and serum ferritin, 85 ng/mL. Blood gas showed a base excess of -8.2 mmol/L. After glucose infusion, cerebrospinal fluid (CSF) was examined, which showed cell counts of 1/µL; protein, 14 mg/dL; and glucose, 60 mg/dL. Tests for viral infections such as influenza A/B and HHV-6 were negative. Blood culture revealed the presence of *S. sanguinis*, thus, the patient was diagnosed as having *S. sanguinis* sepsis; however, clear CSF findings meant that she had no CNS bacterial infections. She was immediately treated with ceftriaxone, midazolam, and fosphenytoin sodium hydrate, and, from days 2 to 5, methylprednisolone pulse therapy. The above measures were effective to control sepsis, to obtain spasmylosis and consciousness recovery. However, the patient lost consciousness again on day 5 in association with similar episodes of facial spasms and one-point stare seizures. This time, intravenous immunoglobulin (2 g) together with midazolam and diazepam was administered. Dextroromethorphan was also given considering its efficacy for encephalopathy.11 The first brain MRI (diffusion weighted imaging, DWI) taken on day 2 of admission showed mild localized
Case Report

Localized high signal intensity in the right temporal lobe (left parietal lobe lesion is not shown in this figure) (A) and, on day 5, showed high signal intensities bilaterally in the cerebral hemispheres (B), indicating a biphasic pattern.

Discussion

We report the case of AESD in a disabled child with SMA, which is a motor neuron disease caused by SMN1 gene mutation. Infants with type 1 SMA, the most severe form, usually die within months or a few years due to respiratory insufficiency and bulbar paralysis.8 Our patient, who had respiratory problems, has survived beyond the age of 4 years; however, during her infancy, she developed severe dilated cardiomyopathy at the time of HLH episode. Since no clear correlation has been confirmed between SMA and cardiac involvement,9 her cardiomyopathy could indicate one of HLH-related organ failures.12 AESD developed in this SMA patient, 7 months after the episode of HLH.

Patients with AESD initially show a prolonged febrile seizure, which is followed by subsequent seizure occurring after several days of interval. Although the initial neu-

Conclusions

This paper describes a unique case of AESD; the patient developed S. sanguinis sepsis-related AESD with underlying SMA,
and fully recovered. However, since the eventual outcome of AESD is thought not to be bright,\textsuperscript{1} we plan to carry out long-term follow-up of mental and physical development in this patient.

References