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Case Report

An unusual manifestation of Sjögren syndrome encephalitis

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Abstract

Sjögren syndrome (SS) is a systemic inflammatory and autoimmune disease characterized by systemic disorders of the exocrine glands, predominantly the salivary and lacrimal glands. Here, we report a 4-year-old boy who presented with the repetition of generalized tonic-clonic seizures for 1–2 min. Initially, he was diagnosed with idiopathic autoimmune encephalitis and was treated with steroids. He was eventually diagnosed with SS based on the examination results, such as inflammatory cell infiltration into the minor salivary glands and positive serum anti-SSA/Ro antibody. Although central nervous system complications are rare in pediatric SS, this condition should be considered in the differential diagnosis when a patient presents with idiopathic autoimmune encephalitis of unknown cause. Furthermore, SS can occur in relatively young children and can present without imaging abnormalities.

Keywords: Sjögren syndrome; Seizure; Steroid; Encephalitis; Epilepsy

1. Introduction

Sjögren syndrome (SS) is a chronic inflammatory and autoimmune disease characterized by systemic disorders of the exocrine glands, predominantly the salivary and lacrimal glands. SS is a common autoimmune disease in adults, but it occasionally affects children. However, central nervous system (CNS) complications associated with SS are rare in both adults and children. The epidemiology, diagnostic criteria, and pathophysiology of SS encephalitis still remain unknown. Most patients with SS reported in previous cases were older than the patient in our case and the youngest previously reported patient with SS encephalitis was 9 years old. Moreover, patients with SS encephalitis generally show some abnormal findings on computed tomography (CT) or magnetic resonance imaging (MRI). Herein we report an unusual case of a relatively young patient with SS encephalitis who did not show imaging abnormalities.

2. Case report

A 4-year-old boy with no past medical history was admitted to our hospital because of a seizure clustering. One day before admission, he experienced generalized tonic convulsions for 3 min. Subsequently, he was lethargic and had fecal incontinence. On the day of admission, he experienced a tonic seizure that lasted for 2 min, and he was transferred to a nearby hospital. He continued to experience generalized tonic-clonic seizures for 1–2 min despite administration of anticonvulsants such as diazepam 0.2 mg/kg, phenobarbital

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suppository 5 mg/kg, carbamazepine 4 mg/kg and midazolam 0.1 mg/kg/hr. Thus, he was transferred to our hospital. On arrival, he was on continuous intravenous midazolam administration, and he appeared lethargic. There were no specific signs on physical examination except for his level of consciousness. Laboratory data were normal apart from a high ketone body level (1238 μmol/l). Polymerase chain reaction analysis of plasma and cerebrospinal fluid showed negative results for herpes simplex virus 1 (HSV-1), human herpes virus 6 (HHV-6), and human herpes virus 7 (HHV-7). Cerebrospinal fluid examination showed mild pleocytosis (15/μl with 80% monocular cells) and a high neopterin level (222.4 ng/ml), which indicated the possibility of autoimmune diseases. The serum neopterin level was normal. Head CT and MRI revealed no abnormalities. Electroencephalography (EEG) showed generalized high amplitude slow waves (Fig. 1A). Intravenous midazolam administration was continued under mechanical ventilation for 3 days. According to his clinical manifestations and examination results, the patient was diagnosed with idiopathic encephalitis of unknown cause. Pulsed steroid (30 mg/kg/day) was administered for 3 days.

On the third day of admission, his serum amylase level increased to 1729 IU/l. We suspected mumps encephalitis, but the level spontaneously decreased to 392 IU/l on the following day. His serum tested negative for anti-mumps IgM antibody. Additionally, mumps virus was not detected in his cerebrospinal fluid and

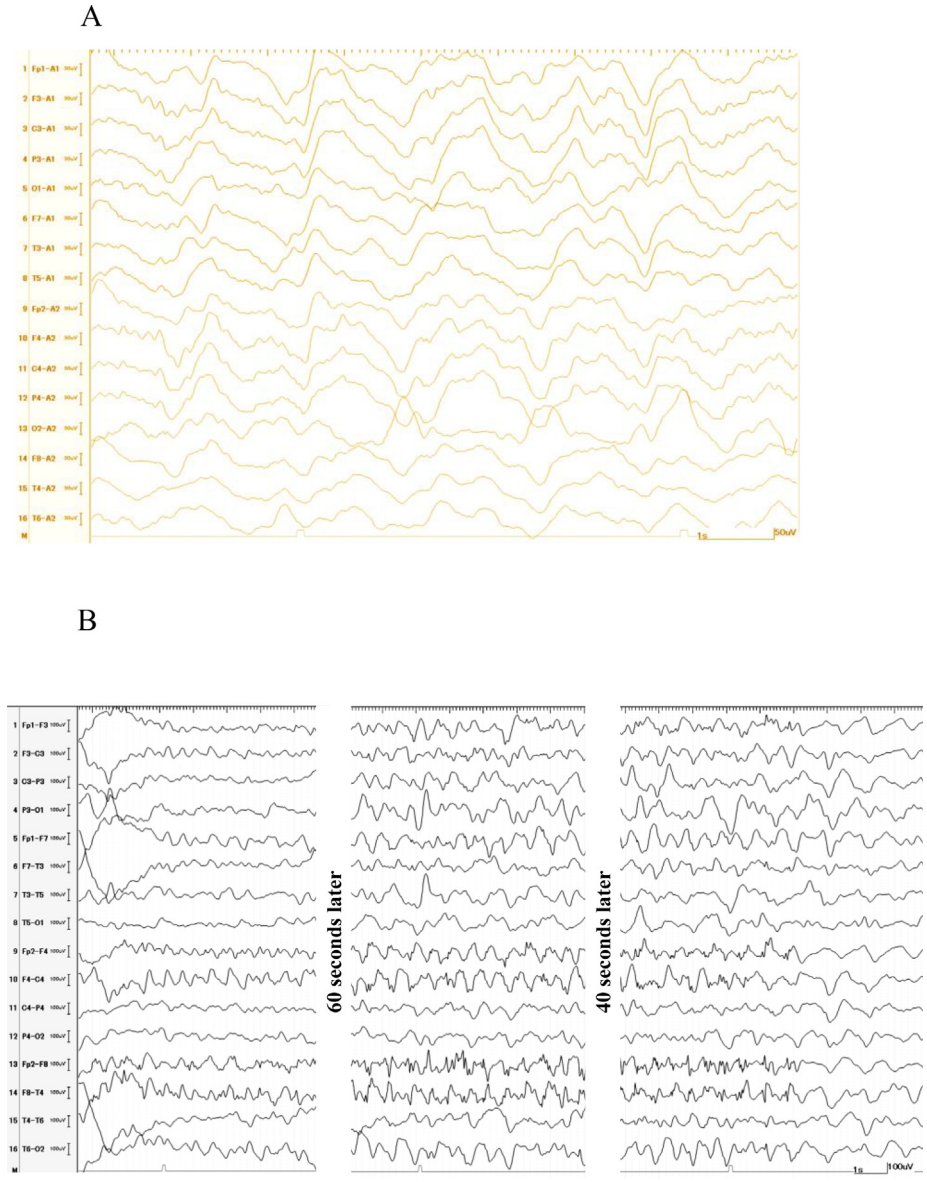

Fig. 1. A Electroencephalography (EEG) shows diffuse delta activity on admission. B Ictal EEG shows focal rhythmic waves originating from the right front-temporal region 5 days after neurological onset.

stool. Thus, the possibility of mumps meningitis was excluded.

His general condition had gradually stabilized after multiple administrations of administration of pulsed steroids, and the dose of steroids was tapered until the 33rd day of admission when he developed a fever of 104°F. Moreover, his submandibular and parotid glands were swollen on both sides. His serum amylase level increased to 1628 IU/l. Contrast-enhanced cervical CT also showed swollen submandibular glands and parotid glands on both sides (Fig. 2A and B). Anti-SSA/Ro antibody was positive, and the erythrocyte sedimentation rate and amyloid level were elevated. Additionally, he showed a dry mouth. Salivary gland biopsy showed sialoadenitis (Fig. 3). These findings met the diagnostic criteria of SS proposed by the American College of Rheumatology.

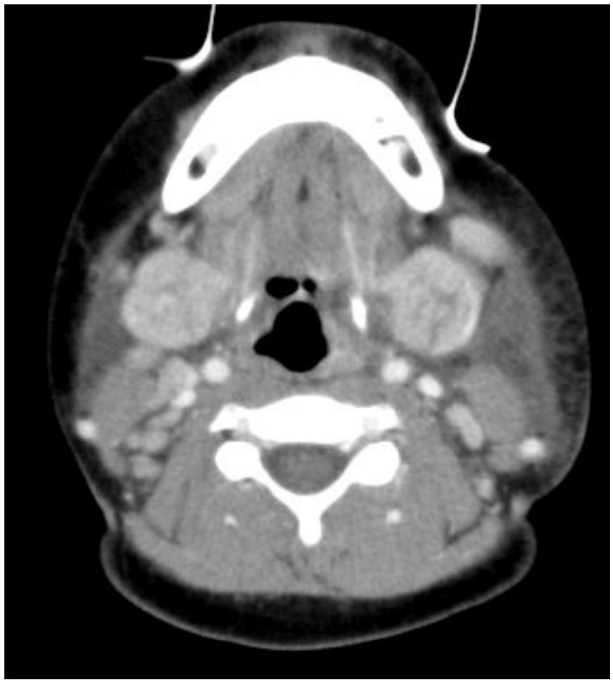

Fig. 2. A Contrast-enhanced cervical computed tomography (CT) shows swollen submandibular and parotid glands on both sides. B Contrast-enhanced cervical CT shows swollen parotid glands on both sides.

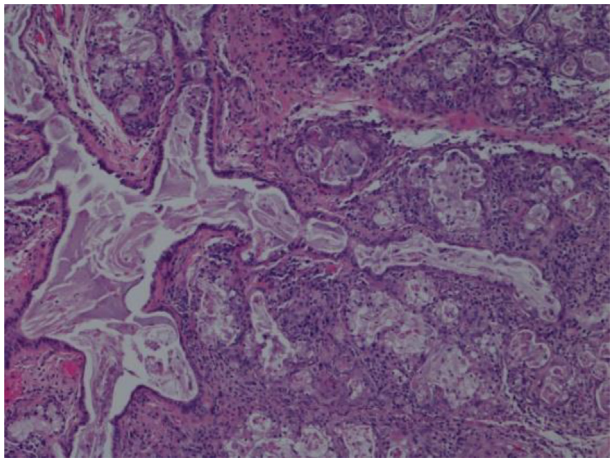

Fig. 3. Minor salivary gland biopsy shows inflammatory cell infiltration into the salivary gland.

On tapering the dose of steroids, his epileptic seizures worsened and he was then treated with cyclosporine in combination with steroids. An EEG during a seizure showed revealed focal rhythmic waves originating from the right front-temporal region (Fig. 1B). Although we performed the MRI every time his symptoms worsened, we did not identify any abnormalities. He is currently on anticonvulsants and steroids because of the epileptic seizures. In addition to epileptic seizures, he was diagnosed with attention deficit hyperactivity disorder in the course of follow-up

3. Discussion

We described an unusual case of a 4-year-old boy who initially had seizure clustering and was later diagnosed with SS encephalitis. We made two important clinical findings. First, SS encephalitis can occur in patients younger than 5 years. Second, patients with SS encephalitis can show no imaging abnormalities.

Our patient was relatively young compared with not only patients who have CNS complications but also those with SS in general [1,2]. Yokogawa *et al* reported that the mean age of 26 children with SS was 12.4 years [3]. In addition, Matsui *et al* reviewed 10 cases of childhood SS with CNS complications and found that the

youngest patient was 9 years old [2]. The present patient was 4 years old, and to the best of our knowledge, our case is the first to report the youngest patient with SS encephalitis. Based on the present case, we believe that SS encephalitis can occur in relatively young patients aged around 5 years. Moreover, although several types of CNS complications of SS have been reported to date [2–4], this is the first case to initially present with seizure clustering. Although the treatments for CNS complications of SS have been reported primarily comprise immunosuppressive agents including steroids [5], there is inadequate evidence on the treatment of protracted cases, such as this case. Careful dose adjustment of the steroids and occasional addition of other agents are required depending on the symptoms of patients. Regarding the prognosis, although there is no definite evidence of the prognosis of SS encephalitis, the neurologic symptom of this patient is predicted to be persistent based on the current condition and previous report [2].

Our patient was diagnosed with SS encephalitis, although he lacked abnormalities on imaging studies, including MRI. Matsui *et al.* have previously reported 10 cases of central nervous system complications in childhood SS, and all patients showed neuroimaging abnormalities [2]. In the present case, we performed head MRI including diffusion-weighted imaging, every time the symptoms worsened. However, neuroimaging abnormalities were not detected. Thus, even if a patient does not show any findings on CT or MRI, SS encephalitis should not be ruled out.

In conclusion, although encephalitis is rare in pediatric cases of SS, it should be considered in the differential diagnosis when a patient presents with idiopathic autoimmune encephalitis of unknown cause, regardless of age. Moreover, we should recognize that SS encephalitis can occur in a relatively young patient and can present without any abnormal findings on imaging studies. The pathophysiology of SS encephalitis is yet to be elucidated; however, the association between anti-N-methyl-D-aspartate receptor subunit NR2A/B antibody and SS encephalitis has recently been pointed out [6]. Thus, further reports need to be accumulated to determine the demographics of SS encephalitis.

4. Disclosure

The authors have no financial or personal relations that could pose a conflict of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.braindev.2018.08.004.

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