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Case report

# A case of acute encephalitis with refractory, repetitive partial seizures, presenting autoantibody to glutamate receptor Gluε2

Hiromichi Ito[a,*], Kenji Mori[a], Yoshihiro Toda[a], Mayumi Sugimoto[a], Yukitoshi Takahashi[b], Yasuhiro Kuroda[a]

[a]*Department of Pediatrics, Institute of Health Biosciences, The University of Tokushima Graduate School, 3-18-15, Kuramoto-Cho, Tokushima 770-8503, Japan*

[b]*Department of Pediatrics, Shizuoka Medical Institute of Neurological Disorders, Shizuoka, Japan*

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**Abstract**

An 11-year-old male was admitted to our hospital because of high-grade fever, repetitive seizures, and prolonged impairment of consciousness (Glasgow coma scale E1, M5, V1). His seizures were repetitive complex partial seizures that expanded from the unilateral face to the corresponding side of the body. He sometimes developed secondary generalized seizures. While most seizures lasted 1 or 2 min, intractable seizures also frequently (about 5 times/h) occurred. We diagnosed him as encephalitis/encephalopathy, and treated him with artificial respiration, thiamylal sodium, mild hypothermia therapy, steroid pulse therapy, massive γ-globulin therapy, etc. Afterwards, he had sequelae, such as post-encephalitic epilepsy (same seizures continued to recur), hyperkinesia, impairment of immediate memory, change in character (he became sunny and obstinate), dysgraphia, and mild atrophy of the hippocampus, amygdala, and cerebrum. However, he could still attend a general junior high school. He was diagnosed as acute encephalitis with refractory, repetitive partial seizures (AERRPS). In this case, he was positive for autoantibody to glutamate receptor Gluε2 IgG or IgM in an examination of blood and spinal fluid, and we presumed that this may have influenced his sequelae. In this case, a combination of mild hypothermia therapy, steroid pulse therapy, and massive γ-globulin therapy was effective.


*Keywords:* Autoantibody to glutamate receptor Gluε2; Acute encephalitis with refractory, repetitive partial seizures (AERRPS); A peculiar type of post-encephalitic/encephalopathic epilepsy; Mild hypothermia therapy; Massive γ-globulin therapy; Steroid pulse therapy

## 1. Introduction

A peculiar type of post-encephalitic/encephalopathic epilepsy was first reported by Awaya et al. [1]. It is characterized by epilepsy with the same repetitive intractable partial seizures from the acute phase to the convalescence phase. However, it is not known when epileptogeneity is acquired. Soon thereafter, Shiomi et al. reported a similar case of encephalitis accompanied by frequent seizures in Japan. Sakuma et al. proposed the terminology acute encephalitis with refractory, repetitive partial seizures (AERRPS), which satisfied the following five criteria: (1) a prolonged acute phase of more than 2 weeks, (2) partial seizures with the same symptoms persisting from the acute phase to the convalescence phase, (3) seizures frequently evolving into status convulsivus, especially during the acute phase, (4) marked intractability of seizures, and (5) exclusion of related disorders such as known viral encephalitis or metabolic disorders [2], based on these two previous reports. On the other hand, it was reported that autoantibody to glutamate receptor Gluε2 was often positive in Rasmussen's encephalitis [3] and in acute encephalitis/encephalopathy. It is possible that autoantibody to glutamate receptor Gluε2 may cause persistent excitation of glutamate receptor Gluε2 and may be associated with seizures and impairment of the central nervous system. We report here a case of AERRPS, presenting autoantibody to glutamate receptor Gluε2. To the best of our knowledge,

* Corresponding author. Tel.: +81 88 633 7135; fax: +81 88 631 8697.
*E-mail address:* moriken@clin.med.tokushima-u.ac.jp (H. Ito).

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this is the first report of AERRPS presenting autoantibody to glutamate receptor Gluε2. It is possible that autoantibody to glutamate receptor Gluε2 may be associated with the pathophysiology of AERRPS.

## 2. Case report

An 11-year-old male was admitted to our hospital because of high-grade fever, repetitive seizures, and prolonged impairment of consciousness (Glasgow coma scale E1, M5, V1). His seizures were repetitive complex partial seizures that expanded from the unilateral face to the corresponding side of the body. He sometimes developed secondary generalized seizures. While most seizures lasted 1 or 2 min, intractable seizures also frequently (about 5 times/h) occurred. The family history and past history were not marked. On admission, he showed no abnormal neurological findings except for impairment of consciousness and intractable seizures. On blood examination, he showed no abnormality except for FDP and ALT (16 μg/ml (1–12 μg/ml), 53 U/l (5–40 U/l), respectively). On spinal fluid examination, leukocyte count was 25 $mm^3$. Brain computed tomography (CT) and magnetic resonance imaging (MRI) with T2-weighted imaging (T2-WI) showed no abnormality (Fig. 1(A)). There was no significant increase in any virus antibody titer. His clinical course after admission is described in Fig. 2. On day 1 of admission, he was administered glycerol (5 ml/kg × 4 times/day), acyclovir (5 mg/kg × 3 times/day), γ-globulin (250 mg/kg/day for 3 days), steroid pulse therapy (methylprednisolone 25 mg/kg/day for 3 days), and midazolam (0.1 mg/kg/h) for his encephalitis and seizures. On day 2, since he had repetitive seizures, the dose of midazolam was increased and he was administered lidocaine hydrochloride. On day 3, artificial respiration was begun along with thiamylal sodium at 3 mg/kg/h because of intractable seizures. Afterwards, we treated him with thiamylal sodium at 8 mg/kg/h because of intractable seizures and mild hypothermia therapy. He was given an intravenous injection of phenytoin (5 mg/kg × 2 times/day) during treatment with thiamylal sodium, but this was not effective. Interictal electroencephalogram (EEG) on day 8 showed slow spike and wave predominantly in the frontal and central region (Fig. 3(A)). Ictal EEG on day 8 showed rhythmic spikes in the left frontal–central–temporal region with antecedent spikes (Fig. 3(B)). At this time, he was treated with thiamylal sodium at 6 mg/kg/h because of repetitive seizures. Interictal EEG on day 10 showed a burst-suppression pattern and spikes were present during the burst phase (Fig. 3(C)). He was then treated with mild hypothermia therapy and thiamylal sodium at 8 mg/kg/h, and the seizures stopped. On day 10, the leukocyte count was 3 $mm^3$ and IgG was 10.2 mg/dl (reference value, 0.2–0.6 mg/dl) on spinal fluid examination. Since we thought that a mechanism of abnormal immunity may be involved in his encephalitis because of the increase in IgG on spinal fluid examination, massive γ-globulin therapy (400 mg/kg/day over 5 days) was performed again on day 12. On day 12, we discontinued treatment with thiamylal sodium and began treatment with massive phenobarbital suppository therapy (20 mg/kg/day) because of an impairment of liver function on blood examination. In association with a decrease in thiamylal sodium, his EEG findings worsened. However, EEG spikes almost disappeared following treatment with

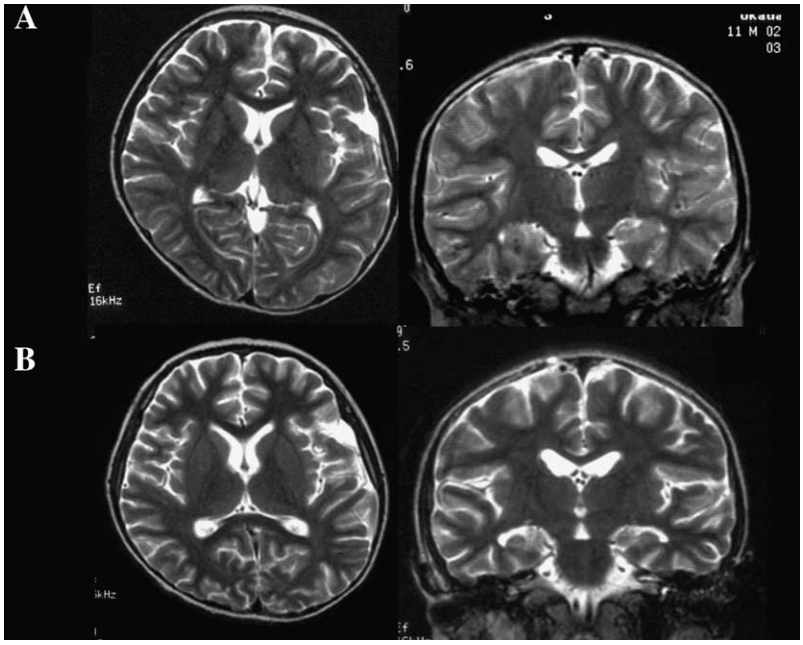


Fig. 1. (A) Brain MRI T2-WI on admission showed no abnormality. (B) Brain MRI on day 36 showed mild atrophy of the hippocampus, amygdala, and cerebrum.