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Case Report

The association of anti-glutamic acid decarboxylase antibodies with different neurological findings in childhood

Mehpare Ozkan [a,*], Ayşe Aksoy [a], Funda Çenesiz [b], Nilgün Erkek Atay [c], Deniz Yüksel [a]

[a] Department of Pediatric Neurology, Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, Ankara, Turkey
[b] Department of Pediatrics, Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, Ankara, Turkey
[c] Department of Pediatric Intensive Care, Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, Ankara, Turkey

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ABSTRACT

Glutamic acid decarboxylase antibodies can rarely be associated with various neurological syndromes, which are usually present in adults. Here, we present 2 affected children. Our first patient had a diagnosis of epilepsy and presented with continuous involuntary movements and multifocal myoclonic seizures following an infection at the age of 9 months. Anti-glutamic acid decarboxylase antibodies were found in the serum and cerebrospinal fluid. A partial response was obtained from intravenous immunoglobulin, steroid, and plasmapheresis treatment. The other patient presented with a clinical picture of acute cerebellar ataxia and mutism at the age of 6 years and recovered fully following intravenous immunoglobulin treatment. Neurological findings due to anti-glutamic acid decarboxylase antibodies may be more common in children than previously thought, and achieving an early diagnosis can be important for prompt treatment.

1. Introduction

Glutamic acid decarboxylase (GAD) is the enzyme involved in the synthesis of gamma-aminobutyric acid (GABA), which is the major inhibitory neurotransmitter in the central nervous system. Antibodies against glutamic acid decarboxylase (anti-GAD-Ab) are associated with various neurological conditions such as cerebellar ataxia, limbic encephalitis, epilepsy, myasthenia gravis, and stiff person syndrome, all described mainly in adults [1–3]. There are also a few reports in children with these conditions [4–6]. Limbic encephalitis is characterized by acute or subacute onset of cognitive and/or memory deficits, seizures, and psychiatric symptoms [7]. Although limbic encephalitis usually presents in a paraneoplastic form [1,8], many cases with non-paraneoplastic form and with specific anti-GAD-Ab have been reported [9,10].

Herein, we report two children who developed different neurologic syndromes associated with anti-GAD-Ab.

2. Case reports

1. Case 1

A nine-month-old boy was referred with status epilepticus and involuntary movements following an upper respiratory infection 2 weeks before admission. He had been delivered normally from a 22-year-old woman following a full-term and an uncomplicated gestation and labor. The seizures had started at the age of 2 months, and early developmental milestones had been delayed. He had approximately 10 brief myoclonic seizures per day, which were treated with clobazam and topiramate up until the last 15 days. After the upper respiratory tract infection, he had started having continuous involuntary movements and multifocal myoclonic seizures involving the hand, face, and leg, which had continued over the last 15 days. An electroencephalogram (EEG) showed frequent bilateral occipital spikes and posterior slow waves (Fig. 1). The magnetic resonance imaging (MRI) scan was normal on admission. He was started on antiepileptic drugs. Then, he was intubated and midazolam coma induction was used due to status epilepticus, but no effect was observed on the seizure frequency or involuntary movements. Intravenous immunoglobulin (IVIG) was given at a dose of 0.4 g/kg/d for 5 days. Acyclovir was used for 4 days starting on admission, but was discontinued when the polymerase chain reaction for herpes simplex virus was found to be negative. The metabolic tests, including lactate, pyruvate, ammonia, urinary organic acid, urinary and blood amino acids, and tandem mass were unremarkable. Thyroid functions, antithyroglobulin antibody, thyroid peroxidase antibodies, anti-islet antibodies, amylase, lactate dehydrogenase, liver enzymes, quantitative immunoglobulins, neuron-specific enolase, and alpha fetoprotein were also within normal limits. Cerebrospinal fluid (CSF) examination revealed normal protein and cellular content together with the presence of oligoclonal bands. Plasmapheresis was started on day 10 (1 exchange/d for 5 consecutive days) for the presumed diagnosis of limbic encephalitis. Plasmapheresis consisted of single-volume plasma exchanges with fresh frozen plasma as replacement fluid

* Corresponding author at: Dr. Sami Ulus Children's Health and Diseases Training and Research Hospital, Babür Cd. Altındağ, 06090, Ankara, Turkey. Fax: +90 312 3170353.
E-mail address: mehparekafali@gmail.com (M. Ozkan).

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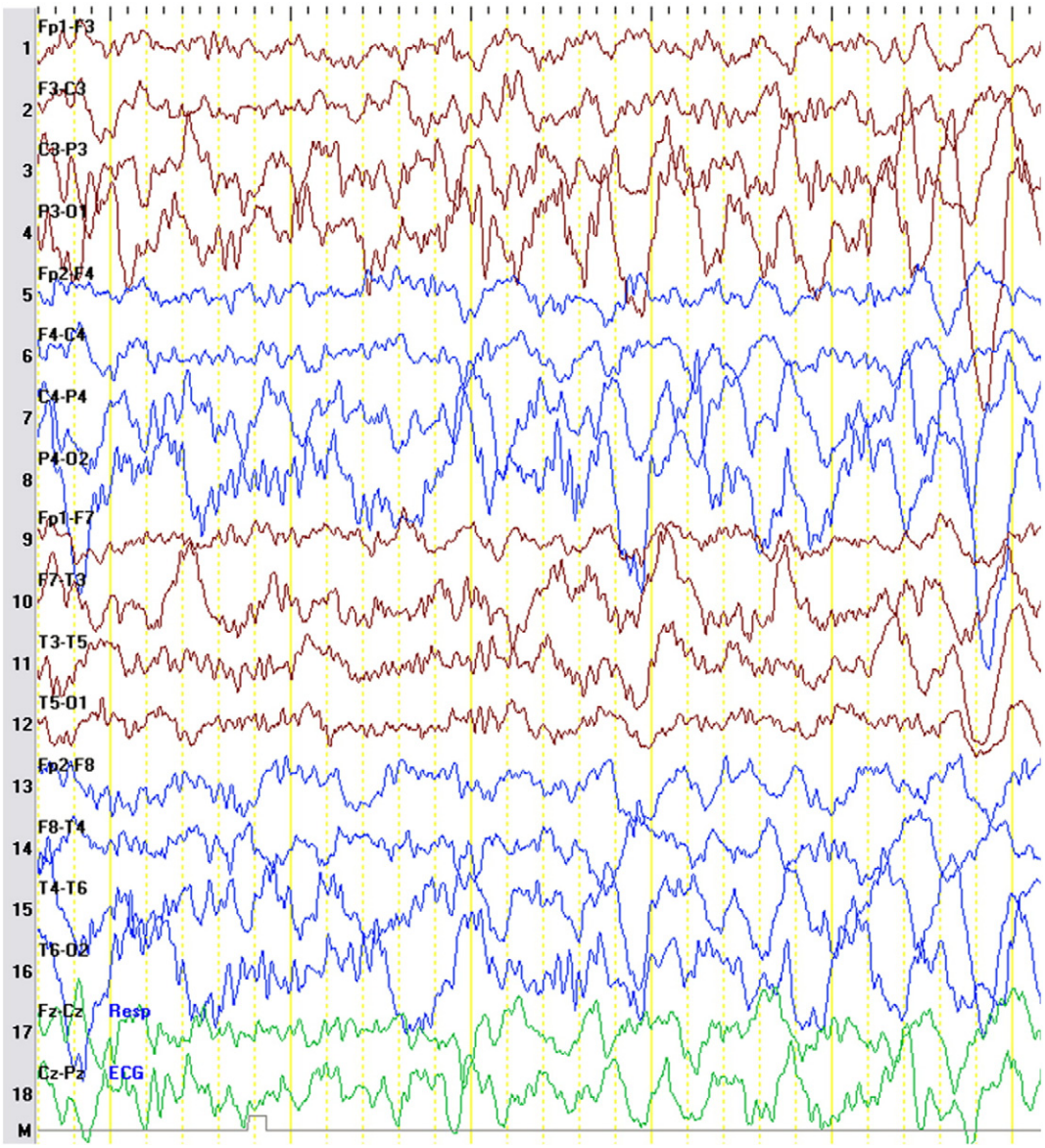

Fig. 1. Bilateral occipital spikes and posterior slow waves.

(Prismaflex-Gambro membrane filtration system, TPE-1000). A three-day course of intravenous methylprednisolone at the dose of 30 mg/kg/d was initiated, and then the patient was given oral prednisone at 2 mg/kg/d. The seizure frequency and involuntary movements decreased after the plasmapheresis and steroid treatment. Oral prednisone was tapered to 1 mg/kg/d. The serum anti-GAD-Ab level was 1.79 U/mL (reference, <1 U/mL) and the CSF anti-GAD-Ab level was 2.16 U/mL (reference, <1 U/mL) using the Immunotec GAD kit for radioimmunoassay. Additional diagnostic evaluation did not suggest the possibility of an infection, neoplasm, or any metabolic etiology. Testing for the neuronal ceroid lipofuscinosis type 1 mutation was negative and muscle biopsy was unremarkable. The patient became seizure free and was able to communicate within 2 months. The MRI scan, 2 months later, was still normal. The serum anti-GAD-Ab titer was 1.99 U/mL 2 months later and 1.49 U/mL 5 months later. The patient continued to be treated with a combination of IVIG (1 g/kg/d for 2 days every 4 weeks) and oral prednisone (0.75 mg/kg/d). Despite showing marked improvement, the patient was still experiencing involuntary movements at 5 months after disease onset.

2. Case 2

This six-year-old boy was born at term after an unremarkable pregnancy. Early developmental milestones were normal. Vomiting and dizziness had started 2 days before presentation, and there had been no seizures or fever. His speech had decreased the next day and the gait became unbalanced. He presented to our hospital's emergency department the next day when he was unable to walk unsupported. The neurological examination on presentation revealed that he could obey commands but responded only rarely to questions and used single words. The patient had an ataxic gait with support. There was no focal neurological deficit, and the rest of the neurological examination was normal. There was no history of trauma, infection, vaccination, or drug use within the last 2 months. The toxicology screen was negative. A full blood count, C-reactive protein (CRP), electrolytes, and hepatic and renal function tests were normal, as was the brain computed tomography scan. CSF examination was unremarkable. Vasculitis screening including lupus anticoagulant, antinuclear antibodies, anti-DNA antibodies, and rheumatoid factor