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Case Report

A case of anti-NMDAR encephalitis presented hypotensive shock during plasma exchange

Akihiko Miyauchi [a], Yukifumi Monden [a,*], Hitoshi Osaka [a], Yukitoshi Takahashi [b], Takanori Yamagata [a]

[a] Department of Pediatrics, Jichi Medical University, Japan
[b] National Epilepsy Center, Shizuoka Institute of Epilepsy and Neurological Disorders, Shizuoka, Japan

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Abstract

We are reporting on a case of pediatric anti-NMDAR encephalitis with autonomic instability. The patient showed little response to first-line treatment of steroid and IVIG. We initiated plasma exchange, also a first-line treatment. This worsened his autonomic instability, resulting in hypotensive shock. He responded well to rituximab and cyclophosphamide, second-line therapies.

Anti-NMDAR encephalitis is often accompanied by autonomic instability. Our and other reported cases, raise the question of plasma exchange as a first-line therapy for pediatric NMDAR encephalitis, which is frequently accompanied by autonomic instability. Plasma exchange should be performed cautiously in such patients.

Keywords: Anti-NMDAR encephalitis; Plasmapheresis; Autonomic instability; Rituximab; Cyclophosphamide

1. Introduction

Encephalitis associated with N-methyl-D-aspartate receptor (NMDAR) antibodies is caused by autoimmune mechanisms associated with antibodies [1,2]. Anti-NMDAR encephalitis has been increasingly reported since 2007, and is the second most frequent cause of pediatric encephalitis after acute demyelinating encephalomyelitis [1,3]. More than one-third of anti-NMDAR encephalitis cases present flu-like prodromal symptoms (headache, vomiting, fever) followed by altered consciousness, seizures, cognitive dysfunction, movement disorder, autonomic instability and central hypoventilation [1,4].

Current first-line treatment strategies recommend the initiation of steroids, intravenous immunoglobulins (IVIG) and plasma exchange, which is effective in up to 48% of cases. In cases refractory to first-line treatments, the administration of rituximab, cyclophosphamide, or both is recommended as second-line treatment [1]. However, there are few reports on their use for pediatric anti-NMDAR encephalitis. Here, we report on a child with anti-NMDAR encephalitis. The patient did not respond to steroid and IVIG treatments, and exhibited hypotensive shock during plasma exchange. He responded well to rituximab and cyclophosphamide.

* Corresponding author at: Department of Pediatrics, Jichi Medical University, 3311-1 Yakushiji, Shimotsuke-city, Tochigi, Japan. Tel.: +81 285 58 7710; fax: +81 285 44 8329.
E-mail address: mon4441977319@jichi.ac.jp (Y. Monden).

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2. Case report

The patient (11-year-old male; no past or family medical history) initially presented with high-grade fever and delirium-like psychiatric symptoms (shouting, agitation, abnormal behavior). Laboratory tests on admission were normal (white blood cell count: 6700/μl; C-reactive protein: 0.02 mg/dl). Cerebrospinal fluid (CSF) revealed an elevated cell count (116/mm^3; polycyte 2 mm^3, monocyte 114 mm^3), elevated protein levels (64 mg/dl) and normal glucose (80 mg/dl). The CSF culture was negative. Serum viral antibodies for the human immunodeficiency virus and varicella zoster virus were negative. Herpes simplex virus (HSV)-DNA was negative in the CSF by PCR. Interictal electroencephalogram (EEG) showed laterality, 2–4 Hz slow waves on the right side and mostly low voltage on the left side (Fig. 1). Brain magnetic resonance imaging showed no abnormalities (Fig. 2). Tumor screening for thoraco-abdominal computed tomography and tumor markers was negative (AFP 1 ng/ml, HCG-β < 0.1 ng/ml).

We suspected anti-NMDA encephalitis and initiated corticosteroids (1000 mg/day for 3 days, 3 cycles) from day 5 to 26 and IVIG (0.4 g/kg for 5 days) from day 13 to 17, with no effectiveness. On day 21 post-admission, the patient developed generalized convulsions, uncontrollable with phenytoin and midazolam. Interictal EEG focal spikes were observed mainly in the frontal and anterior temporal lobe (Fig. 1). In addition, he exhibited central apnea, and autonomic instability such as urinary incontinence, hypersalivation, episodic bradycardia and intermittent hypo- and hypertension. These autonomic symptoms continued for two weeks, but did not lead to hypotensive shock. An ELISA analyses of anti-NMDA glutamate receptor antibodies revealed that serum and CSF were positive for anti-glutamate receptor ε2 and δ2 antibodies on admission (serum: 1.192 (normal: 0.52 ± 0.23); CSF: 0.935 (0.22 ± 0.08)). In addition, a cell-based assay using GluRζ1 N/R+ GluRε2 N/R, expressed at the HEK293T cellular membrane, also proved the presence autoantibodies in serum and CSF [5].

Plasma exchange was initiated from day 35 for refractory convulsions and psychiatric symptoms. One hour after initiation of the second treatment, the patient developed a rapid decrease in blood pressure, which resulted in shock, consisting of bradycardia (50 beats/min) and hypotension (50/30 mmHg) within 5 min. The procedure was stopped; he was treated with intravenous epinephrine (0.5 mg) and hydrocortisone (100 mg). In addition, administration of normal saline and 25% albumin bolus followed by continuous infusions of noradrenaline were required to control blood pressure. Anaphylaxis was not suspected as he was devoid of urticaria and wheezing. His neurological status was not improved with plasma exchange, which was discontinued. On day 42 we started weekly administration of rituximab (375 mg/m^2/week for 4 weeks) and cyclophosphamide (750 mg/m^2/month for 6 months), the recommended second-line treatment, due to lack of improvement with first-line treatments [1,6,7]. Within days of initiating second-line treatment, the patient's clinical symptoms, including convulsions, autonomic instability and central apnea, markedly

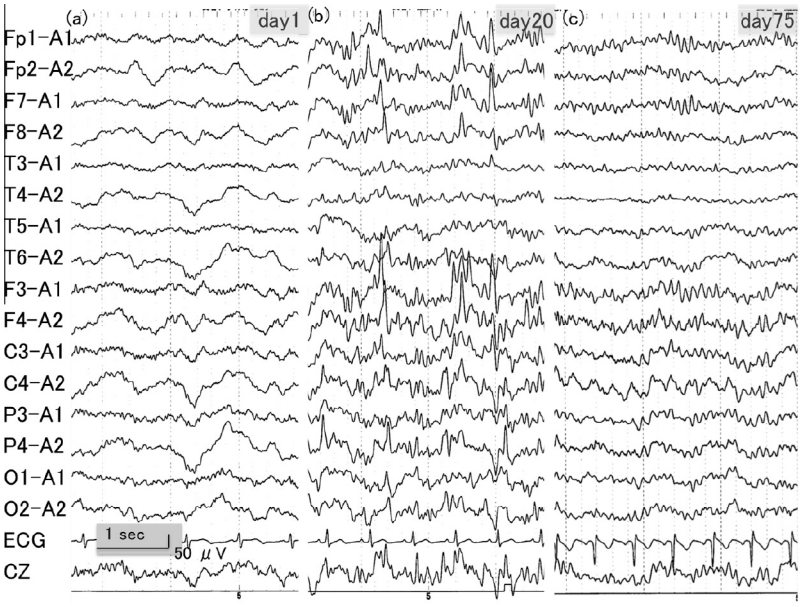

Fig. 1. Interictal electroencephalogram. (a) 2–4 Hz slow waves on the right side and mostly low voltage on the left side were seen before first-line treatment. (b) Focal spikes were observed mainly in the frontal and anterior temporal lobe. (c) After second-line treatment was introduced, abnormal findings were improved.