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Case report

# Anti-aquaporin 4 antibody-positive acute disseminated encephalomyelitis

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**Abstract**

*Objective:* To describe the clinical and neuroimaging features of a young female patient with acute disseminated encephalomyelitis associated with anti-aquaporin-4 antibodies.

*Methods:* The patient had mild encephalopathy 14 days after influenza vaccination. Cerebrospinal fluid analysis revealed an increased cell count and a marked increase in myelin basic protein. Magnetic resonance imaging (MRI) demonstrated multiple lesions in the juxtacortical white matter. The patient was diagnosed with acute disseminated encephalomyelitis and treated with methylprednisolone pulse therapy. She recovered in 1 month. However, right retrobulbar optic neuritis appeared 2 months after discharge, and serum anti-aquaporin 4 antibodies were measured with a cell-based assay.

*Results:* Anti-aquaporin 4 antibodies were present in the patient's serum. She was treated with a prolonged course of oral prednisolone. The patient was negative for serum anti-aquaporin 4 antibodies 8 months after the second clinical event, and prednisolone was discontinued 13 months after the second clinical event. Serum anti-aquaporin 4 antibodies remained negative 4 months after the discontinuation of prednisolone. There was no evidence of relapse at 9 months after discontinuation of steroids.

*Conclusions:* This case will expand the spectrum of anti-aquaporin-4 antibody-related central nervous system disorders. The measurement of anti-aquaporin 4 antibody may be considered in patients with a clinical diagnosis of acute disseminated encephalomyelitis and a second clinical event within a short interval.


*Keywords:* Anti-aquaporin 4 antibody; Acute disseminated encephalomyelitis; Optic neuritis; Steroids; Vaccination

## 1. Introduction

Neuromyelitis optica (NMO), the coexistence of optic neuritis with myelitis, was recognized in the 19th century and had long been considered a variant of multiple sclerosis (MS) [1]. In 2004, Lennon et al. reported the presence of a circulating IgG autoantibody specific to

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NMO [2]. The astrocyte water channel protein aquaporin 4 (AQP4) was identified as the target of NMO autoantibodies [3]. At present, anti-AQP4 antibody-positive NMO is distinguished as a clinical entity independent from MS [4]. Thus, serological identification of anti-AQP4 antibodies is currently included as an additional diagnostic criterion for NMO [5].

Optic neuritis and/or spinal cord lesions are frequent clinical manifestations of anti-AQP4-mediated central nervous system (CNS) disorders. However, the spectrum of anti-AQP4-mediated CNS disorders has not been sufficiently elucidated, especially in children. We encountered a young female patient with acute disseminated encephalomyelitis (ADEM) in whom anti-AQP4 antibodies were detected. Here, we report the clinical course and neuroimaging findings of this patient.

## 2. Patient report

A previously healthy 4-years-old female was admitted to our hospital due to reduced consciousness and difficulty ambulating. She was the first child of nonconsanguineous healthy parents. Her past and family histories were unremarkable, and her psychomotor development was within normal limits. She received an influenza vaccine containing the A/California/7/2009 (H1N1) pdm09, A/Victoria/210/2009 (H3N2), and B/Brisbane/60/2008 strains 14 days before the onset of neurological symptoms. Three days before admission, somnolence and behavioral changes such as irritability were observed in association with a low-grade fever of approximately 38 °C.

Meningitis was suspected because she had nuchal rigidity. On admission, her body temperature was 37.0 °C, heart rate was 96 beats per minute, respiration rate was 24 per minute, and blood pressure was 98/58 mmHg. She was oriented but mildly somnolent. Physical examination was remarkable for nuchal rigidity, and neurological examination demonstrated hyperreflexia in both legs. Cerebrospinal fluid (CSF) analysis revealed an elevated cell count of 109 cells/μl, with normal protein and glucose levels. Laboratory data were otherwise unremarkable. A marked increase (>2000 pg/ml) in myelin basic protein was found in the CSF on admission; no measurement of oligoclonal bands and glial fibrillary acidic protein was performed. Virological studies were negative for influenza virus (rapid antigen test), cytomegalovirus (enzyme-linked immunosorbent assay), herpes simplex virus (enzyme-linked immunosorbent assay), and Epstein–Barr virus (enzyme-linked immunosorbent assay). Electroencephalogram showed mild slowing of background activity. Cranial magnetic resonance imaging (MRI) demonstrated multiple high-intensity areas in the juxtacortical white matter on T2-weighted imaging and fluid-attenuated inversion recovery (Fig. 1). No lesions were found in the corpus callosum, periventricular white matter, or deep gray matter, including the hypothalamus, cerebellum, brainstem, and cervical spinal cord. No abnormalities were recognized on funduscopic examination.

The patient was diagnosed with ADEM and treated with methylprednisolone pulse therapy, intravenous acyclovir, and mannitol. Her somnolence resolved on the third day of admission, and neurological abnormalities resolved on the ninth day of admission. An enhance MRI on the tenth day of admission revealed a reduction in brain lesions and no contrast enhancement (Fig. 1). Oral prednisolone was prescribed at a dose of 1 mg/kg/day for 1 week, followed by 0.5 mg/kg/day for 2 weeks. The patient was discharged from our hospital on day 13. An MRI at 1 month after the onset of the first clinical event showed that the cerebral lesions had disappeared (Fig. 1).

Two months after discharge, the patient's mother noticed disconjugate eye movements. Ophthalmological examination revealed retrobulbar optic neuritis of the right eye. MRI demonstrated swelling and increased intensity in the proximal portion of the right optic nerve on T2-weighed imaging (Fig. 1) but no brain or spinal lesions. The patient was again treated with methylprednisolone pulse therapy. The right optic nerve lesion resolved 9 days after the initiation of methylprednisolone pulse therapy (Fig. 1).

Serum anti-AQP4 antibodies were detected in the patient's serum during the second clinical event using cell-based assays [6]. Once anti-AQP4 antibodies were detected, the patient was prescribed a prolonged course of oral prednisolone with a gradual taper. After methylprednisolone pulse therapy, 2 mg/kg/day of prednisolone was given for 1 week. The dose of prednisolone was then reduced every 1–2 months. The patient tested negative for serum anti-AQP4 antibodies 8 months after the second clinical event. Prednisolone was discontinued 13 months after the second clinical event. The patient's serum again tested negative for anti-AQP4 antibodies 4 months after the discontinuation of prednisolone. There was no evidence of relapse at 9 months after the discontinuation of steroids. The patient's psychomotor development and growth were normal at the last follow-up at 79 months of age.

## 3. Discussion

Our patient initially presented with the typical features of ADEM, which was followed by optic neuritis after the discontinuation of steroids. Serum anti-AQP4 antibodies were present during the acute period and disappeared after long-term treatment with oral steroids. This case will expand the spectrum of anti-AQP4 antibody-related CNS disorders.

A revised consensus definition of ADEM was proposed by the International Pediatric Multiple Sclerosis