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Case Report

Rituximab was effective for acute disseminated encephalomyelitis followed by recurrent optic neuritis with anti-myelin oligodendrocyte glycoprotein antibodies

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Abstract

Background: The effect of rituximab on acute disseminated encephalomyelitis (ADEM) followed by recurrent optic neuritis (ON) is not yet known.

Patient: We are reporting the case of a 4-year-old Japanese girl who was diagnosed with anti-myelin oligodendrocyte glycoprotein (MOG) antibody positive ADEM followed by recurrent ON. She developed altered mental status, left facial paralysis, left paresis, and experienced three episodes of ON. She was treated with rituximab and azathioprine (AZA) as prevention for recurrent ON. She relapsed under treatment with AZA when CD19 cells reappeared 6 months after the first rituximab infusion. However, she has not relapsed since her CD19 count was reduced and kept low with rituximab infusion.

Conclusions: It is conceivable that anti-MOG antibodies are involved in the pathology of "ADEM followed by recurrent ON," and that the early introduction of rituximab, which is involved in the suppression of antibody production and has effects on CD20 T lymphocytes, may be a feasible treatment for ON. Due to the small number of patients, additional reports on prospectively followed patients are needed.

Keywords: ADEM; ON; MOG; Rituximab

1. Introduction

Acute disseminated encephalomyelitis (ADEM) is a monophasic inflammatory demyelinating disorder of the central nervous system (CNS) [1–3]. Previous studies report ADEM followed by recurrent optic neuritis (ON) as a currently non-classifiable phenotype [2–4]. There is no established treatment protocol. Rituximab or azathioprine (AZA) are therapeutic options for demyelinating diseases, but there are no reports on the use of rituximab for ADEM followed by recurrent ON (ADEM-rON). To our knowledge, only one paper has

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reported the use of AZA, an immunosuppressive antimetabolite pro-drug, for this purpose [5].

Autoantibodies targeting myelin oligodendrocyte glycoprotein (MOG), glycoprotein localized on the outer surface of the myelin sheath, and oligodendrocytes in the CNS are reported to relate to demyelinating diseases [2,4,5]. Here we describe a case with anti-MOG antibody positive ADEM-rON in which rituximab was effective and AZA was ineffective.

2. Case report

The patient was an 8-year-old Japanese girl with no past medical history or family history. At 4 years 7 months of age, she developed an altered mental status four days after an influenza vaccination. Neurological and cerebrospinal fluid (CSF) examinations revealed nothing abnormal. Magnetic resonance imaging (MRI) at 1 day from onset with fluid-attenuated inversion recovery (FLAIR) and T2 revealed high signal intensity in the subcortical white matter of the frontal lobe and temporal lobe (Fig. 2a, b); thus, she was diagnosed with ADEM and treated with steroid pulse therapy (SPT, intravenous 30 mg/kg/day, methylprednisolone) for 3 days followed by tapered oral prednisolone (OP) (Fig. 1).

Thirty-seven days after initial onset, two weeks after the cessation of OP, the patient experienced left facial paralysis, left paresis and developed altered mental status. Barre's sign was present on the left side and left deep tendon reflex was exaggerated. MRI revealed no new lesions. She was treated with two courses of SPT followed by tapered OP.

Three months after onset, the patient developed sudden visual loss (right eye). Decimal visual acuity (VA) was 0.05 (right) and 1.0 (left), and the right pupil was dilated to 10 mm. Ophthalmoscopy revealed papilledema (right eye). MRI revealed high signal intensity in her right optic nerve on a magnetization prepared rapid acquisition with gradient echo (MP-RAGE) sequence and no new cerebral lesions (Fig. 2c). She was diagnosed with right ON and treated with two courses of SPT followed by rituximab (intravenous 375 mg/m^2/week for 4 weeks) and followed by tapered OP. One week after the first intravenous rituximab therapy, the lymphocytic CD19 count was 0.88×10^6 cells/L, and was maintained at $\leqq 1 \times 10^6$ cells/L for the following 6 months (Fig. 1).

Twenty-three months after onset, the patient developed limited VA bilaterally (decimal VA: 5 cm/counting

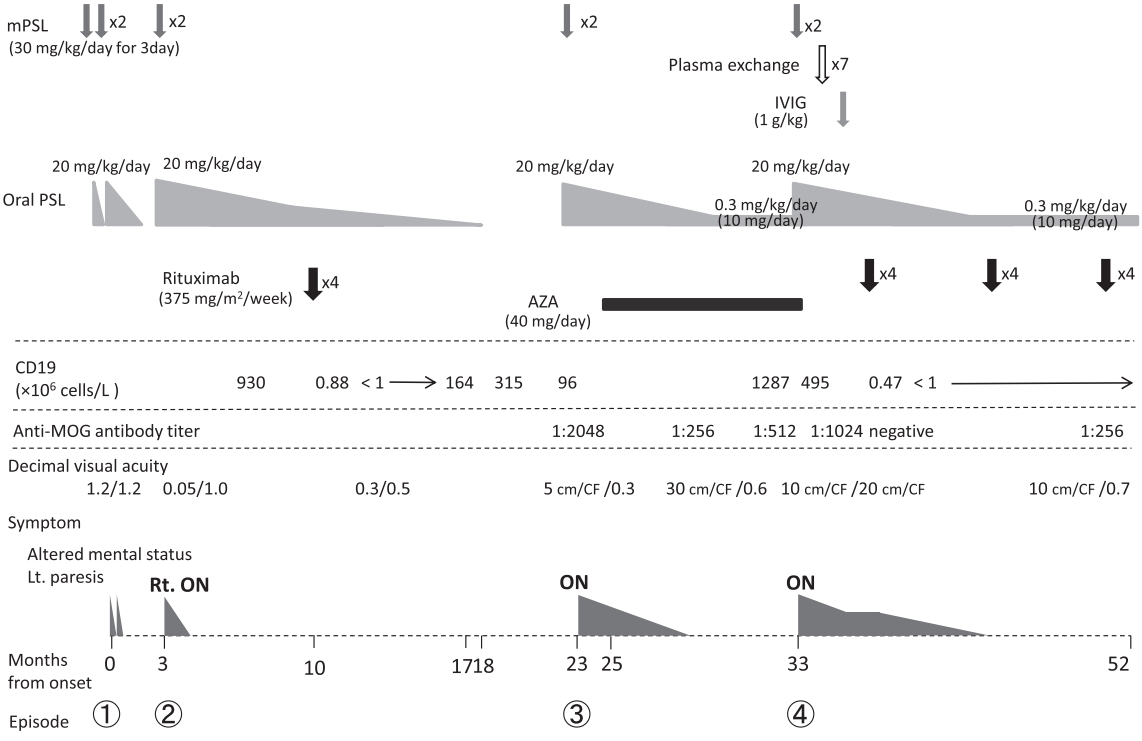

Fig. 1. Clinical course. The patient developed altered mental status, left facial paralysis, left paresis, and experienced three episodes of ON. She was first treated with steroid pulse therapy and therapeutic plasma exchange and IVIG were added at the fourth episode. She was treated with rituximab to prevent recurrent ON but she relapsed when CD19 cells reappeared. AZA was not effective. She has not relapsed since her CD19 count was reduced with rituximab infusion. Anti-MOG antibodies were positive with titers ranging up to 1:2048. In the last measurement, CD19 count and anti-MOG antibodies were $\leqq 1 \times 10^6$ cells/L and positive with titers ranging up to 1:256. mPSL, methylprednisolone; IVIG, intravenous immunoglobulin; PSL, prednisolone; AZA, azathioprine; MOG, myelin oligodendrocyte glycoprotein; CF, counting finger; Lt.,Left; Rt., Right; ON, optic neuritis.

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