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Case Report

Post-vaccination MDEM associated with MOG antibody in a subclinical *Chlamydia* infected boy

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Abstract

The mechanism of post-vaccination acute disseminated encephalomyelitis (ADEM) has been hypothesized as resulting from vaccination-injected antigens cross-reacting with myelin components, however, a precise etiology has been uncertain. In this report, we describe the case of a 6-year-old Japanese boy who had multiphasic disseminated encephalomyelitis (MDEM), and was positive for both anti-myelin oligodendrocyte glycoprotein (MOG) antibodies and *Chlamydophila pneumoniae* antibodies. After vaccinations that were the second one for measles and rubella, and the booster immunization for Japanese encephalitis, the patient presented with fever, headache, vomiting, and a change in personality. He was treated with a high-dose of intravenous methylprednisolone in the diagnosis of ADEM. However, these symptoms recurred with different magnetic resonance imaging lesion, and he was diagnosed as MDEM. Retrospective testing for pathogens revealed *C. pneumoniae* IgM and IgG antibodies, and it was considered that he was infected with *C. pneumoniae* subclinically. The patient's serum indicated a positive response for the anti-MOG antibody from the onset of the ADEM diagnosis and in all recurrent episodes. *Chlamydia* species infection has been known to play a role in demyelinating diseases. It is also known that the anti-MOG antibody may be present but not exhibit its pathogenesis in the absence of a cell-mediated inflammatory response; however, the precise mechanism of action of the anti-MOG antibodies is not yet determined. We propose the possibility that post-vaccination demyelinating disease may result from the synergistic effects of a preceding anti-MOG antibody, possibly produced in response to a subclinical *Chlamydia* species infection.

Keywords: *Chlamydia*; Multiphasic disseminated encephalomyelitis (MDEM); Myelin oligodendrocyte glycoprotein (MOG); Vaccine

1. Introduction

Acute disseminated encephalomyelitis (ADEM) is often associated with infection and less frequently with vaccination [1]. With the refinement of vaccines, a signif-

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icant decrease in the prevalence of post-vaccination ADEM had been observed, however it still exists after the removal of *in vivo* infected tissues [2]. Although ADEM is usually a monophasic disease, the diagnosis becomes challenging when the patients have relapses with other demyelinating events [3]. In such a situation, a chronic disorder, such as multiple sclerosis may be considered [4]. Here we describe a case of post-vaccination multiphasic disseminated encephalomyelitis (MDEM) that is associated with anti-myelin oligodendrocyte glycoprotein (MOG) antibody, possibly produced in response to a subclinical *Chlamydophila pneumoniae* infection.

2. Case report

A 6-year-old Japanese boy presented with fever, headache, and vomiting (day 1), 2 days after vaccination. These vaccines were the second vaccination for measles and rubella, and the booster immunization for Japanese encephalitis. The patient's white blood cell count was measured at 14,400/μL (4000–8000/μL) and C-reactive protein was 7.97 mg/dL (less than 0.4 mg/dL). He was hospitalized in Seikeikai Hospital due to persistent fever and headache (day 5). At that point he exhibited neck stiffness and a change in personality, such as being easily angered. Examination of the cerebrospinal fluid (CSF) showed pleocytosis (99/mm^3; normal range, less than 5/mm^3, 49% mononuclear cells) and elevation of myelin basic protein (446 pg/mL; normal range, less than 102 pg/mL). The appearance of oligoclonal IgG bands only in the CSF was determined to be positive. Serum anti-aquaporin-4 antibody was negative and the IgG index was in the normal range. On the electroencephalogram, the background showed slow wave activity. Although there was no abnormality on the brain magnetic resonance imaging (MRI), taking into consideration the time between vaccination and the disturbance of consciousness, he was suspected of having post-vaccination ADEM (day 10). He was treated with a high-dose of intravenous methylprednisolone (IVMP, 30 mg/kg/day) on days 11–13, and 20 mg of prednisolone (1 mg/kg/day) was prescribed. The symptoms resolved completely by day 15. The prednisolone was tapered to 5 mg within 2 weeks. However, on the day following tapering to 5 mg (day 26), these symptoms soon recurred and novel brain lesions, seen with MRI, appeared in the cerebellum and the left temporal lobe (Fig. 1A and B). Therefore, on the next day, 20 mg of oral prednisolone was re-initiated (day 27). Two days after increasing the prednisolone, his symptoms were relieved. On day 38, the MRI-imaged brain lesions disappeared. He was discharged on day 44 and the oral prednisolone was discontinued on day 75. However, on day 92 (second admission), his fever, and headache reappeared, along with diplopia. At this time, he did not have a disturbance of consciousness or change in personality. A novel lesion in the dorsal midbrain was seen with MRI (Fig. 1C and D). At that point he was tentatively diagnosed with MDEM due to recurrence of different central nervous system manifestations. Thereafter, a 10–20 mg daily maintenance dose of prednisolone was continued for 2 years, since oral prednisolone at less than 10 mg daily (0.4 mg/kg) could not prevent minor exacerbations, such as headache (Fig. 1E). Retrospective analyses of pathogens (day 14) were tested for *Chlamydia* species, *Mycoplasma pneumoniae*, herpes simplex virus, cytomegalovirus and Epstein-Barr virus. The patient's serum was positive for *C. pneumoniae* IgM and IgG antibodies. These were entrusted with SRL, Inc. (Tokyo, Japan). The IgM antibody levels were found to be negative, but the IgG antibody was persistently detected. In Tohoku University, the serum anti-MOG IgG antibody titer was measured visually using a cell-based assay with full-length human MOG cDNA transfected HEK293 cells by serial dilution. The detection limit of this assay was 1:128 [5]. The serum anti-MOG antibody titer was found to be elevated to 1:16,384 (day 26), but had decreased to 1:8,192 by day 35. A high titer of the serum anti-MOG antibody remained for the subsequent days. Although the serum anti-MOG antibody titer had decreased to 1:1,024 by day 731, the titer re-elevated to 1:2048 (day 779) (Fig. 1E).

3. Discussion

In exploring the possible etiology of this patient's MDEM, we searched for the presence of pathogen and measured the serum anti-MOG antibody. Judging from the change in the *C. pneumoniae* antibody titers, the patient was suspected to have a subclinical *C. pneumoniae* infection prior to vaccination. Although the patient was affected with MDEM after vaccination, we speculated the involvement of the preceding, subclinical *C. pneumoniae* infection. On the other hand, the anti-MOG antibody has been identified in a subgroup of pediatric patients with inflammatory demyelinating disease of the central nervous system [6], and correlated with the relapsing course of demyelination [7]. Therefore, the anti-MOG antibody has been considered to be useful in monitoring the disease progression. In the acute period, the anti-MOG antibody titer rose to 1:16,384 (day 26), and then decreased to 1:8192 by day 35. The anti-MOG antibody titer re-elevated to 1:4096 coincident with recurring headache on day 387. Two years after the onset of the disease, minor exacerbations appeared, and the anti-MOG antibody titer was found to have risen again to 1:2048 (Fig. 1E). Although the ratio of children developing MS following ADEM, has been reported as 6% in a 9-year follow up [4], we should pay attention to his disease progression.