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Short Communication

Optic Neuritis Following Aseptic Meningitis Associated with Modified Measles: a Case Report

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SUMMARY: In this study, we report the case of a 35-year-old woman with modified measles complicated by aseptic meningitis and subsequent optic neuritis. Although her initial manifestations were only flu-like symptoms without any Koplik's spots or skin rashes, virological testing confirmed an acute measles infection. Subsequently, right optic neuritis appeared after aseptic meningitis and was completely resolved following steroid pulse therapy. In general, modified measles is believed to be associated with mild symptoms and few neurological complications; however, our present observations demonstrated that modified measles can cause rapid neurological complications.

The measles virus is known to cause various neurological complications such as measles encephalitis and/or encephalopathy, which reportedly occur in 1 of 1,000 cases (1). Measles is an acute infectious disease, typically characterized by flu-like symptoms, conjunctivitis, Koplik's spots, and a maculopapular rash, although optic neuritis associated with measles has also been reported (2). In addition, mild symptoms sometimes occur with measles infection in a manifestation referred to as modified measles, resulting from waning of maternally conferred or acquired immunity, or incomplete development of immunity. Although, modified measles is difficult to diagnose because of the absence of typical symptoms during outbreaks (3,4), it is generally considered a mild illness in which patients only rarely develop neurological complications. Nonetheless, such complications are possible; therefore, it is important for clinicians to recognize these potentially serious symptoms of modified measles. In this study, we present a case of modified measles complicated by meningitis and optic neuritis.

A 35-year-old woman was admitted to our hospital because of a headache and pyrexia that persisted for 2 weeks. She had a history of natural measles infection when she was 20 years old. One week before the onset of her symptoms, her children (a 4-year-old girl and a 1-year-old boy) developed rashes with fever and were diagnosed with measles infection. A general physical examination on admission was unremarkable except for pyrexia. Neither Koplik's spots nor rashes on the limbs or trunk were observed. A neurological examination revealed no particular abnormal findings other than a stiff neck.

A general blood examination revealed no abnormalities except for mild leukocytosis. Cerebrospinal fluid (CSF) examination revealed high opening pressure (245 mmH_2O), pleocytosis with a mononuclear cell predominance (290 cells/mm^3; monocytes, 92.4%), increased protein level (58.0 mg/mL), and elevated immunoglobulin (Ig) G index (0.76). Serological tests using an enzyme immunoassay (EIA; Denka Seiken Co., Tokyo, Japan) revealed elevated serum levels of measles-specific IgM (3.04 antibody index; cut-off level, <0.8 antibody index) and IgG titers (114 EIA value; cut-off level, <2.0 EIA value). The CSF sample was negative for measles-specific IgM (0.25 antibody index; cut-off level, <0.8 antibody index) and positive for measles-specific IgG (1.06 EIA value; cut-off level, <0.2 EIA value) using EIA kits (Denka Seiken) but negative for the other virus-specific antibodies. Cranial magnetic resonance imaging (MRI) revealed no obvious abnormalities.

The patient was treated with intravenous fluid supplementation and acetaminophen, and the pyrexia and headache improved within 7 days after admission. A follow-up examination revealed that the patient's serum measles-specific IgG level (highest value, 223 EIA value) and CSF (highest value, 2.72 EIA value) further increased. Reverse transcriptase-polymerase chain reaction (RT-PCR) analysis was negative for measles virus RNA in the serum and CSF. A diagnosis of aseptic meningitis associated with modified measles was made on the basis of the high level of measles-specific IgG with a significant response in the follow-up examination because low positivity for measles-specific IgM EIA antibodies has no definite diagnostic value. Upon follow-up, the CSF cell counts were normalized, but the CSF protein level was elevated (155 mg/mL). Myelin basic protein and oligoclonal bands were negative on a follow-up CSF examination.

On day 15 of hospitalization, the patient began to

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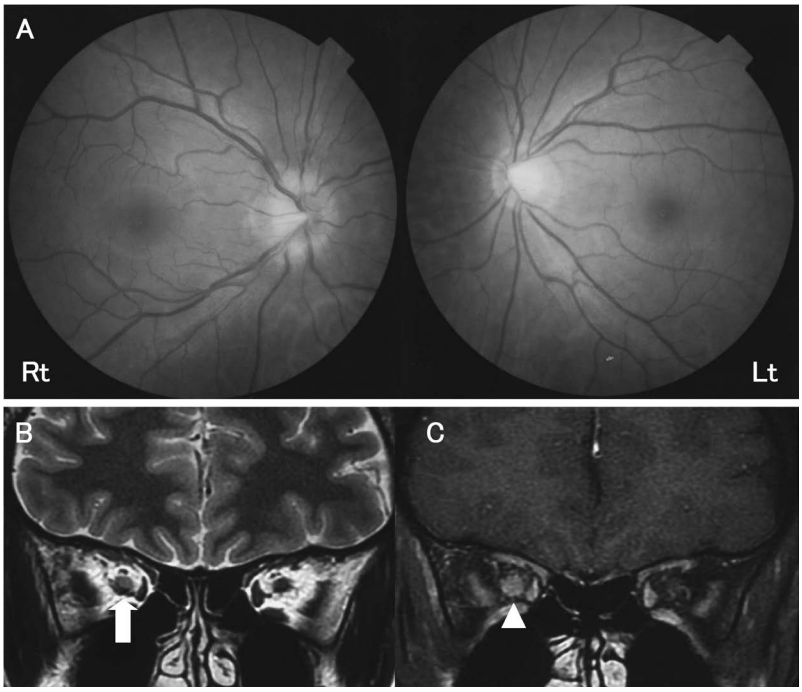

Fig. 1. A funduscopic photograph and orbital magnetic resonance images indicating acute visual loss. Note the edema of the right optic disc (A). Coronal T_2-weighted image on acute visual loss (B). Note the high signal intensity of the right optic nerve (arrow). Contrast-enhanced coronal T_1-weighted image on acute visual loss (C). Note the abnormal enhancement and swelling of the right optic nerve (arrowhead).

experience discomfort in her right eye followed by an oppressive feeling of the right eyelid, color blindness, and reduced visual acuity. The light reflex was sluggish in the right eye. The mean central critical flicker fusion frequency decreased (18.0 Hz) on the right side, and optic disc edema was observed using funduscopy (Fig. 1A). T_2-weighted orbital MRI revealed a high-intensity signal in the right optic nerve with abnormal enhancement on T_1-weighted MRI (Figs. 1B and 1C). Brain and spine MRI examinations were also unremarkable. Her serum was negative for anti-aquaporin-4 antibodies. Therefore, a diagnosis of right optic neuritis was made. Subsequently, she was treated with methylprednisolone (1000 mg/day) for 3 days, and the visual acuity, eyelid pain, and color blindness were ameliorated by 5 days following steroid pulse therapy. On a CSF examination performed 7 days after the steroid therapy, the protein levels returned to the normal range (30 mg/mL) and measles-specific IgG level notably decreased (0.61 EIA value; cut-off level, <0.2 EIA value). She was discharged on 37th day of hospitalization without any neurological deficits.

We reported rare manifestations of meningitis and optic neuritis in a patient with modified measles, which is generally considered a mild illness. Optic neuritis associated with measles has been reported with and without central neurological complications (2,5–14), in which all of the reported patients exhibited typical rashes similar to those seen in measles. However, measles-associated optic neuritis without rashes, as seen in the present patient, has rarely been reported in the literature.

As in the present patient, it may be difficult to completely clarify the pathogenesis of aseptic meningitis. In this study, RT-PCR for measles virus in CSF was negative; therefore, direct evidence for the viral infection was lacking. However, aseptic meningitis was probably caused by measles infection within the central nervous system, as indicated by the increased measles-specific IgG level in CSF on the follow-up examination. Alternatively, an immune-mediated reaction, secondary to measles infection, may have provoked a central neurological complication. Thus, we believe that our patient's prolonged pyrexia may have reflected an inflammatory response to aseptic meningitis.

The MRI of the central nervous system did not display any lesions except the involvement of the right optic nerve in our patient, and anti-aquaporin-4 antibodies were not detected. Therefore, a clinical diagnosis of multiple sclerosis, neuromyelitis optica, or acute disseminated encephalomyelitis was unlikely. Hence, a final diagnosis of optic neuritis following aseptic meningitis associated with modified measles was made.

Measles-associated optic neuritis is a rare complication of measles infection, and demyelination may be a causative mechanism because of autoimmune responses, rather than direct viral invasion because of the delayed onset after infection and the relatively good prognosis of the impaired visual acuity (15,16). While the incidence of optic neuritis following full measles infection remains unclear, the reported incidence of optic neuritis after measles encephalitis is 7.5% (17). In contrast to the surprisingly high percentage of optic neuritis after measles encephalitis, measles-associated optic neuritis without rashes is considerably rare, which may be, at least in part, owing to the difficulty or inaccuracy in diagnosis of modified measles because of atypical clinical manifestations.

The diagnosis of modified measles is difficult based on clinical symptoms alone, and virological tests are,

therefore, necessary for an accurate diagnosis. Although modified measles is generally believed to be associated with mild symptoms, some patients may develop rapid neurological complications, as seen in the present patient. Therefore, physicians should make meticulous efforts, including careful medical interviews, to promptly detect modified measles in patients with flu-like symptoms.

Conflict of interest None to declare.

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