MRI Findings from a Case of Fulminating Adult-onset Measles Encephalitis

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Abstract

We report a rare case of fulminating adult-onset measles encephalitis. A 34-year-old man developed a comatose state after measles eruptions and ultimately akinetic mutism. Titers of anti-measles IgM antibodies were elevated in both serum and cerebrospinal fluid. Brain magnetic resonance imaging (MRI) 3 months after onset revealed widespread hyperintense lesions in the periventricular white matter and marginal hyperintense lesions in the brainstem on fluid-attenuated inversion recovery and diffusion-weighted images. The marginal lesions in the brainstem are similar to subpial demyelinating lesions seen in postinfectious encephalomyelitis. This case of encephalitis may be related to an autoimmune-mediated process triggered by measles infection.

Key words: adult-onset, brainstem, diffusion-weighted imaging, measles encephalitis, MRI, subpial demyelination

Introduction

With the institution of a measles vaccine, the infection rate of measles has plummeted. However, in many Asian and African countries many people still become infected with the measles virus and some patients die from the infection, because the vaccine has not been widely available. Encephalitis carries the highest mortality rate of all complications associated with measles infection. The measles virus is now known to be the cause of three forms of encephalitis: acute measles encephalitis, subacute sclerosing panencephalitis, and subacute measles encephalitis (measles inclusion body encephalitis in the immunosuppressed). Acute measles encephalitis occurs from direct viral-induced cellular damage or from an autoimmune-mediated process of tissue damage, usually in non-immunocompromised patients, most of whom are children and adolescents (1-3). Few reports are available on magnetic resonance imaging (MRI) of adult-onset cases of acute measles encephalitis (4, 5). We report a rare case of fulminating adult-onset measles encephalitis that reveals a characteristic finding in the brainstem on fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted (DW) images.

Case Report

A 34-year-old man became febrile and after five days developed cutaneous eruptions suggestive of measles. On the sixth day he experienced a severe headache (day 1 of encephalitis). On day 2 of encephalitis he became drowsy and was admitted to our hospital. The patient had received a routine measles vaccination during infancy and had atopic dermatitis since childhood. Upon admission his pulse rate was 78 and blood pressure was 140/78 mm Hg. He had a fever of 38.5°C and was drowsy with meningeal signs. He did not display any cranial nerve palsies and his tendon reflexes were normal without pathologic reflex. The result of serologic testing for HIV was negative and the CD4 lymphocyte count was 453/mm³ (with a total lymphocyte count of 1,115/mm³), indicating normal cellular immunity. Cerebrospinal fluid (CSF) on day 2 showed 1,533 white blood...
cells/mm³ (18.1% polymorphonuclear, 81.9% lymphocytes), protein 270 mg/dL, and glucose 68 mg/dL. Intrathecal production of IgG was also revealed (IgG index was 1.33). Both oligoclonal IgG banding and myelin basic protein were positive. Titers of anti-measles IgM antibodies, measured using an enzyme-linked immunosorbent assay (ELISA), were elevated in both serum and CSF (Table 1). CSF bacterial culture and polymerase chain reaction (PCR) for herpes simplex virus (HSV) DNA polymerase gene were negative. An electroencephalogram (EEG) on day 6 showed diffuse slowing of background activity (four- to six-cycle-per-second theta wave), indicating moderate diffuse cerebral dysfunction. A brainstem auditory evoked potential (BAEP) test on day 8 revealed decreased amplitude of wave III and the absence of wave V, indicating middle to upper brainstem dysfunction. Brain MRI on day 7 consisted of T1-weighted, T2-weighted, and FLAIR images. In this study including the brainstem, no remarkable abnormalities were observed (Fig. 1).

When the patient was admitted, treatment with acyclovir and glycerin was initiated since the possibility of herpes simplex encephalitis could not be excluded. However, his consciousness gradually declined and he fell into respiratory failure. On day 8, he required intubation and mechanical ventilation. He also received a 3-day course of pulse-dose intravenous methylprednisolone, which did not improve his clinical status. CSF examination on day 9 revealed elevated protein levels (114 mg/dL) with mild lymphocytic pleocytosis (9/mm³). The patient remained on mechanical ventilation and displayed akinetic mutism (Fig. 2).

An EEG on day 42 showed diffuse slowing of background activity (low-voltage delta wave), indicating severe diffuse cerebral dysfunction. BAEP on day 55 revealed the absence of waves III and V, indicating severe brainstem dysfunction including the lower portion of the brainstem. Anti-measles antibodies in the serum on day 89 showed decreased IgG and IgM (Table 1). CSF analysis at this time revealed a normal cell count, protein level, and IgG index. Anti-measles antibodies in the CSF showed increased IgG and decreased IgM (Table 1). The diagnosis of acute measles encephalitis was made based on the patient’s clinical course, CSF findings, and changes in anti-measles antibody titers in the serum and CSF.

Brain MRI on day 90 consisted of T1-weighted, T2-weighted, FLAIR, and DW images. T1-weighted images from MRI findings showed marked and diffuse cerebral atrophy mainly due to ventricular dilatation. T1-weighted images after contrast administration showed no abnormally enhanced lesions. T2-weighted, FLAIR, and DW images demonstrated widespread hyperintense lesions around the lateral ventricles. In addition, FLAIR and DW images revealed marginal hyperintense lesions in the brainstem (Fig. 3).

Table 1. Serial Anti-measles Ig Titers in the Serum and Cerebrospinal Fluid

<table>
<thead>
<tr>
<th>Anti-measles antibodies (ELISA)</th>
<th>Day 2</th>
<th>Day 36</th>
<th>Day 89</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum IgM</td>
<td>12.75 (+)</td>
<td>5.02 (+)</td>
<td>0.72 (-)</td>
</tr>
<tr>
<td>Serum IgG</td>
<td>1.710 (4+)</td>
<td>1.070 (3+)</td>
<td>0.298 (1+)</td>
</tr>
<tr>
<td>CSF IgM</td>
<td>13.72 (+)</td>
<td>NE</td>
<td>0.26 (-)</td>
</tr>
<tr>
<td>CSF IgG</td>
<td>NE</td>
<td>NE</td>
<td>1.301 (4+)</td>
</tr>
</tbody>
</table>

CSF: cerebrospinal fluid, NE: not examined

Figure 1. Brain MRI 6 days after the onset of neurological symptoms. MRI studies were performed using a 0.5-T MR unit (Vectra Horizon LX; GE Medical Systems, Milwaukee, WI) equipped with a conventional head coil. FLAIR imaging [6,000/100 (TR/TE); TI, 1,700] shows no remarkable abnormalities.

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Discussion

We report here a rare case of fulminating adult-onset measles encephalitis. Interestingly, the present case revealed marginal hyperintense lesions in the brainstem in addition to the periventricular white matter lesions on FLAIR and DW images during the chronic phase of the illness (3 months after the onset). The distribution of these marginal hyperintense lesions is similar to that of marginal subpial demyelinations, which have been described as a characteristic pathological finding during the acute phase of postinfectious encephalomyelitis (6). Such a peculiar MRI finding in the brainstem may indicate the presence of perivascular gliosis, fibrosis of perivascular spaces, and perivascular rarefaction of myelinated tissue following marginal subpial demyelinations. The pathomechanism of acute measles encephalitis is thought to be direct viral-induced cellular damage or an autoimmune-mediated process in the central nervous system (7-10). We find it difficult to believe that direct viral-induced cellular damage was responsible for the MRI findings in the brainstem. Subacute sclerosing panencephalitis, or chronic neuronal degeneration caused by measles virus, has never shown subpial demyelination in the brainstem, either neuroradiologically or neuropathologically. Thus, the presence of these marginal lesions in the brainstem suggests that the pathomechanism of the present case is demyelination related to an immunologic reaction triggered by the measles infection, in addition to positive oligoclonal IgG banding and myelin basic protein in the CSF and the presence of the periventricular white matter lesions. MRI findings associated with subpial demyelination in the brainstem were reported neither at the acute phase nor at the chronic phase of the encephalitis. The MRI studies of reported cases of adult-onset measles encephalitis have consisted of only T1-weighted and T2-weighted images (4, 5). The encephalitis of the present case caused such severe perivascular gliosis following subpial demyelinations in the brainstem that we could detect it as marginal hyperintense lesions in the brainstem on FLAIR and DW images during the chronic phase of the illness, although our case showed no remarkable abnormalities on MRI during the acute phase.

Most patients with measles are children and adolescents. Acute measles encephalitis is reported to occur in only 0.5-1.0 case per 1000 estimated total cases of measles. Thus, acute measles encephalitis in adults is very rare (1-3). All of the patients with adult-onset measles encephalitis reported recently were women, two of whom were pregnant (4, 5). Pregnant women have a lower resistance to some viral infections, because immunosuppression occurs during pregnancy. However, our patient was a healthy young man with normal immunity, who had received a routine measles vaccination during infancy. He had not had contact with measles patients before the onset of measles and no factors associated with second vaccine failure were observed. Thus, it is unknown why he caught measles and developed encephalitis. The existence of some immune imbalance was suspected to induce fulminant encephalitis of our patient.

Although some reports state that steroid pulse therapy can improve the clinical status of patients with acute measles encephalitis (5), the efficacy of steroid pulse therapy for acute measles encephalitis has never been established (4). In the present case, we hesitated and delayed steroid therapy at the acute phase of measles encephalitis because his encephalitis might have occurred from direct viral-induced cellular damage. We started a 3-day course of pulse-dose intravenous...
methylprednisolone from day 12 of encephalitis, which did not improve his clinical status. The timing of steroid therapy for acute measles encephalitis needs further consideration. The general prognosis of the patients with acute measles encephalitis is still poor. It has been reported that 10-25% of cases with acute measles encephalitis die and 25-60% suffer from long-term disability, including mental retardation, seizures, severe behavioral disorders, hemiplegia, and paraplegia (1, 2, 11). About 25% of patients with adult-onset acute measles encephalitis are reported to die of this disorder (2). To prevent such fulminant cases, a total eradication of measles with a vaccination program is desirable.

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References