INTRODUCTION

Kawasaki disease (KD) is an acute febrile illness of childhood seen worldwide, with the highest incidence in children of Asian background. The six principal clinical criteria for KD are as follows: fever persisting at least 5 days; conjunctival hyperemia; oral and pharyngeal erythema with strawberry tongue; cracked lips; edema and erythema of the hands and feet; rashes of various forms; and cervical lymphadenopathy. KD is a systemic vasculitis with a predilection for the coronary arteries, and approximately 20-25% of untreated patients experience coronary artery abnormalities, including aneurysms (1). The prevalence of coronary disease is reduced to only 2-4% in those treated with intravenous immunoglobulin (IVIg) and aspirin within the first 10 days of illness (1).

Subclinical asymptomatic myocarditis has been found in more than 50% of KD cases (2). On the other hand, myocarditis severe enough to require treatment is a rare complication of KD. Significant irritability is common, and is particularly prominent in infants, likely due to aseptic meningitis. However, myocarditis/encephalopathy is extremely rare in KD (3). To the best of our knowledge, only six cases of KD complicated by severe myocarditis and encephalopathy have been reported (1, 2, 4, 5). All six cases were treated with IVIg and/or aspirin and showed left dilatation or aneurysms in coronary arteries. We reported a case of KD with serious myocarditis/encephalopathy successfully treated using steroid and IVIg without showing any abnormalities in the coronary arteries.

CASE REPORT

Early combined treatment with steroid and immunoglobulin is effective for serious Kawasaki disease complicated by myocarditis and encephalopathy

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Abstract: Severe-type Kawasaki disease (KD) complicated by serious myocarditis and encephalopathy can be successfully treated without abnormality of the coronary arteries by steroid pulse treatment and intravenous immunoglobulin (IVIg). A 4-year-old Japanese girl was diagnosed with KD due to a 6-day history of fever, rash, flushed lips, conjunctival hyperemia, palmar edema, and cervical lymphadenopathy. The day after initiation of IVIg and aspirin, cardiac gallop rhythm was identified. Cardiac ultrasonography revealed severe left ventricular dysfunction. Disturbance of consciousness, hallucinations, and slurred speech were also observed. Magnetic resonance imaging showed no abnormalities, but electroencephalography revealed high-voltage slow waves. Despite this serious disease, cardiac function and neurological abnormalities showed complete recovery without dilatation of the coronary arteries by steroid pulse treatment and additional IVIg. Follow-up at 15 months revealed no abnormality of the coronary arteries. In conclusion, we suggest that early combined treatment with steroid and IVIg is effective for serious KD complicated by myocarditis and encephalopathy. J. Med. Invest. 63: 140-143, February, 2016

Keywords: Kawasaki disease; myocarditis; encephalopathy; steroid
**DISCUSSION**

To the best of our knowledge, only 16 cases of KD complicated by severe myocarditis have been reported (4). Clinical symptoms with myocarditis are severe, but respond well to treatment. However, coronary artery aneurysm (CAA) is often seen in KD with severe myocarditis despite IVlg and aspirin treatment, with giant aneurysm in 30%, small to moderate aneurysms in 30%, dilatation in 10%, and normal findings in 20% (2). Patients with KD complicated by encephalopathy also show CAA at a high rate (about 30%) (5) with IVlg and aspirin alone. Only 6 patients with KD complicated by both severe myocarditis and encephalopathy have been described (Table 1). Such severe-type KD appears associated with a high rate of coronary artery abnormalities, and 5 of these 6 patients (83%) developed CAA despite IVlg treatment, while the remaining patient exhibited mild dilatation of a coronary artery. Steroid was not used in any of these 6 patients. On the other hand, the present case recovered completely without any abnormal findings for the coronary arteries during the course. We started steroid pulse treatment as soon as we diagnosed cardiomyopathy, because we were afraid of volume overload resulting from additional IVlg. One possibility is that steroid pulse helped to suppress systemic vasculitis early, including in the coronary arteries. Although steroid use for KD has been controversial, Kobayashi et al. (6) recently reported that combined treatment with steroid and IVlg significantly reduced the risk of CAA in a high-risk group showing a lack of responsiveness to IVlg. According to the procedure described by Kobayashi et al., the predictive score for the present case would be 5 points, suggesting a high risk of IVlg resistance, and steroid therapy would thus have been started 1 day earlier. We suggest that steroid treatment should be started as early as possible when myocardial damage is identified.

The etiology of encephalopathy associated with KD has yet to be elucidated. Hyponatremia, aseptic meningitis due to IVlg, cytokine...
storm, and vasculitis have been considered responsible in previous reports (4, 5). In the present case, we considered systemic vasculitis as the likely cause of encephalopathy. First, we identified severe hyponatremia and hypoalbuminemia, which are suggested to reflect increased vascular permeability associated with vasculitis. Severe hyponatremia and hypoalbuminemia are common features in previous reports of myocarditis/encephalopathy complicating KD (2). Second, no other alternatives besides systemic vasculitis appeared plausible. After correcting serum sodium levels, disturbance of consciousness continued. Aseptic meningitis was ruled out as a complication after normal results were obtained from CSF examination. The normal level of IL-6 in CSF indicated that levels of this cytokine were unrelated to encephalopathy in this case. Accordingly, we considered systemic vasculitis as most likely associated with progressive encephalopathy in this case.

In conclusion, we have reported a case of KD complicated by severe myocarditis and encephalopathy. We suggest that early steroid pulse treatment combined with IVIg for such severe-type KD may inhibit formation of aneurysms in coronary arteries. Further investigation is required to confirm the effectiveness of this treatment strategy.

CONFLICTS OF INTEREST

None

REFERENCES

1. Itamura S, Kamada M, Nakagawa N: Kawasaki disease complicated with reversible splenial lesion and acute myocarditis. Pediatr Cardiol 32 : 696-9, 2011

Table 1. Kawasaki disease complicated by severe myocarditis and encephalopathy

<table>
<thead>
<tr>
<th>Year</th>
<th>Age (years)</th>
<th>Sex</th>
<th>SF (%)</th>
<th>Neurological findings</th>
<th>MRI</th>
<th>Treatment</th>
<th>Coronary findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>6</td>
<td>F</td>
<td>18</td>
<td>altered consciousness</td>
<td>N.D.</td>
<td>IVIg + aspirin</td>
<td>dilatation</td>
</tr>
<tr>
<td>2006</td>
<td>7</td>
<td>M</td>
<td>16</td>
<td>altered consciousness</td>
<td>N.D.</td>
<td>IVIg + aspirin</td>
<td>CAA</td>
</tr>
<tr>
<td>2011</td>
<td>14</td>
<td>F</td>
<td>25</td>
<td>visual hallucination</td>
<td>MERS</td>
<td>IVIg</td>
<td>CAA</td>
</tr>
<tr>
<td>2012</td>
<td>4</td>
<td>M</td>
<td>20</td>
<td>GCS 10</td>
<td>normal</td>
<td>IVIg</td>
<td>CAA</td>
</tr>
<tr>
<td>2012</td>
<td>3</td>
<td>M</td>
<td>23</td>
<td>GCS 14</td>
<td>normal</td>
<td>IVIg</td>
<td>CAA</td>
</tr>
<tr>
<td>2012</td>
<td>4</td>
<td>M</td>
<td>20</td>
<td>GCS 12</td>
<td>normal</td>
<td>IVIg</td>
<td>CAA</td>
</tr>
<tr>
<td>2014</td>
<td>4</td>
<td>F</td>
<td>19</td>
<td>GCS 12</td>
<td>normal</td>
<td>Steroid + IVIg</td>
<td>Normal</td>
</tr>
</tbody>
</table>

(SF, shortening fraction; MRI, magnetic resonance imaging; CAA, coronary artery aneurysm; IVIg, intravenous immunoglobulin; GCS, Glasgow Coma Scale).

The last case is the present case.
unexpected etiology of shock and multiple organ dysfunction syndrome. Intensive care medicine 38: 872-8, 2012
