Case Report

Hemophagocytic Lymphohistiocytosis Induced by Severe Pandemic Influenza A (H1N1) 2009 Virus Infection: A Case Report

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After early outbreaks in North America in April 2009, the pandemic influenza A (H1N1) virus spread rapidly around the world, and even some patients developed certain severe complications. We reported one case of hemophagocytic lymphohistiocytosis (HLH) induced by severe pandemic influenza A (H1N1) virus infection. A 17-year-old girl had acute onset of fever, dry cough, rhinorrhea, and sore throat. Her family members and close friends also had the similar symptoms. Anti-infection treatment with penicillin was given after 8 days of the onset of symptoms in the local hospital, and her chest radiograph showed consolidation of the left lung. Then, she was sent to the People’s Hospital of Guizhou Province in China and endotracheal intubation underwent on the ninth day for acute hypoxic respiratory failure. She was diagnosed with HLH induced by severe pandemic influenza A (H1N1) 2009 virus. Oseltamivir, steroids, immunoglobulin, and plasmapheresis were given immediately after admission. After being treated in the People’s Hospital of Guizhou Province for 16 days, she was discharged. This experience shows that HLH may be a life-threatening complication for severe pandemic influenza A (H1N1) 2009 virus infection and responds well to therapy.

1. Introduction

The first case of human infection with pandemic influenza A (H1N1) 2009 virus was identified in Mexico in April 2009. The first three cases of confirmed pandemic virus in China were reported in May 2009 [1].

Hemophagocytic lymphohistiocytosis (HLH) is a rare clinical-pathological condition, which is characterized by the activation of the mononuclear phagocyte system, along with the hemophagocytosis in the reticuloendothelial systems. The rare case of HLH induced by pandemic influenza A (H1N1) 2009 virus infection was reported, and it was successfully treated.

2. Case Presentation

After catching a cold, a 17-year-old, 160 cm height, 40 kg weight, previously healthy girl had acute onset of fever, fatigue, sore throat, and rhinorrhea for 3 days. Then, she was sent to the emergency department of a local hospital for medical help on January 6, 2010. Though conventional medications were given to the patient, no obvious symptomatic relief was obtained. The next day, she was sent to the emergency department of the People’s Hospital of Guizhou Province on account of persistent fever.

On examination, she was conscious and well oriented. Her temperature was 40°C–40.5°C, respiratory rate was 38
Table 1: Laboratory test results of the case on different days.

<table>
<thead>
<tr>
<th>Variable</th>
<th>01/07/2010</th>
<th>01/08/2010</th>
<th>01/14/2010</th>
<th>01/20/2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days in the People’s Hospital of Guizhou Province</td>
<td>1</td>
<td>2</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>Pandemic influenza A (H1N1) 2009 virus (RT-PCR)</td>
<td>—</td>
<td>Positive</td>
<td>Negative</td>
<td>—</td>
</tr>
<tr>
<td>White blood cell (cells/L)</td>
<td>$2.17 \times 10^9$</td>
<td>$3.82 \times 10^9$</td>
<td>$13.24 \times 10^9$</td>
<td>8.88</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>116</td>
<td>75</td>
<td>103</td>
<td>127</td>
</tr>
<tr>
<td>Platelet (cells/L)</td>
<td>$46 \times 10^9$</td>
<td>$19 \times 10^9$</td>
<td>$102 \times 10^9$</td>
<td>$122 \times 10^9$</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>158.30</td>
<td>175.50</td>
<td>16.20</td>
<td>9.2</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>30.3</td>
<td>18.8</td>
<td>38.1</td>
<td>36.9</td>
</tr>
<tr>
<td>Triglyceride (mmol/L)</td>
<td>—</td>
<td>3.13</td>
<td>1.76</td>
<td>1.68</td>
</tr>
<tr>
<td>Creatinine (umol/L)</td>
<td>190.7</td>
<td>332.8</td>
<td>82.6</td>
<td>66.1</td>
</tr>
<tr>
<td>Urea nitrogen (mmol/L)</td>
<td>8.4</td>
<td>21.3</td>
<td>10.8</td>
<td>6.5</td>
</tr>
<tr>
<td>Alanine transaminase (u/L)</td>
<td>52</td>
<td>56</td>
<td>32</td>
<td>14</td>
</tr>
<tr>
<td>Direct bilirubin (mol/L)</td>
<td>12.7</td>
<td>11.9</td>
<td>5.9</td>
<td>5.0</td>
</tr>
<tr>
<td>NK-cell activity</td>
<td>—</td>
<td>2%</td>
<td>7.5%</td>
<td>20%</td>
</tr>
<tr>
<td>Blood cultures</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>

*— Denotes no data.

The next day, the retest of throat swab specimens for pandemic influenza A (H1N1) 2009 virus by RT-PCR was negative. On January 19, her temperature dropped to 38.2°C, while platelet increased to $108 \times 10^9$ cells/L and triglycerides decreased to 1.20 mmol/L. All the results suggested that her HLH had already improved, indicating that HLH might be induced by H1N1 infection. She was transferred to the respiratory department for left small pleural effusion after her fever has improved and left lung consolidation resolved. On January 23, the patient almost recovered and was discharged.

3. Discussion

This case was diagnosed as pandemic influenza A (H1N1) 2009 virus infection by RT-PCR at the 10th day after...
symptom onset. Soon after, she had several conditions such as fever, splenomegaly, cytopenias, hypertriglyceridemia, haemophagocytosis in her bone marrow, and low NK-cell activity. According to the diagnostic criteria made by Histiocyte Society, HLH is defined by the presence of at least five of the following criteria: (1) fever, (2) splenomegaly, (3) bicytopenia, (4) hypertriglyceridemia and/or hypofibrinogenemia, (5) haemophagocytosis, (6) low/absent NK-cell activity, (7) hyperferritinemia, and (8) high-soluble interleukin-2 receptor levels [3]. The last two parameters cannot be determined in our hospital, but the present case met the former 6 criteria, so she could be diagnosed with HLH. Since this case did not have other risk factors which may be associated with HLH except for pandemic 2009 H1N1, she was finally diagnosed with HLH induced by severe pandemic 2009 H1N1 virus infection.

HLH is a life-threatening condition, which can be classified into genetic HLH and secondary HLH. Both types can occur at any age and are associated with increased mortality. Autosomal gene defects can cause genetic HLH or other immune deficiencies, such as Chediak-Higashi syndrome, X-linked lymphoproliferative syndrome, and Griscelli syndrome [4]. Secondary HLH is associated with exogenous agents (including viruses, bacteria, fungi, parasites, and toxins), endogenous products (including those resulting from tissue damage, metabolic products, and free radical stress), rheumatic diseases, and malignant diseases [5]. HLH induced by viral infection was first described in 1979 [6]. Apart from H1N1 virus, others such as human immunodeficiency virus (HIV), cytomegalovirus (CMV), and Epstein-Barr virus (EBV) have been reported to trigger the disorder [7–9].

The pandemic H1N1 virus is a triple-reassortant influenza virus containing genes from human, swine, and avian influenza viruses. Unlike typical seasonal flu patterns, the pandemic H1N1 virus caused high levels of summer infections in the northern hemisphere and then even higher levels of activity during cooler months in this part of the world [8]. The study launched by Cao et al. showed that 21.4% of activity during cooler months in this part of the world [9]. Apart from H1N1 virus, others such as human immunodeficiency virus (HIV), cytomegalovirus (CMV), and Epstein-Barr virus (EBV) have been reported to trigger the disorder [7–9].

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There may be several ways to treat secondary HLH. High-dose corticosteroids are commonly used due to the inflammatory nature of the condition. Intravenous immunoglobulin can enhance humoral immunity as an immunomodulator, which appears to be more effective in infection-mediated HLH. Plasmapheresis, which was first used to further decrease the cytokine storm in 1982, [12], was an effective therapeutic tool for HLH. Apart from cytotoxic chemotherapy, the comprehensive therapy mentioned above had been carried out, and a rare hematological complication of pandemic H1N1 virus infection was successfully cured.

In conclusion, if febrile patients with pandemic H1N1 virus infection are associated with cytopenia, a bone marrow aspiration is recommended. Once confirmed as HLH cases, they should be given directed therapy as early as possible.

References


