Three Cases of Avian-origin Influenza A (H7N9) Virus Infection in Zhejiang Province, China: Case Report and Literature Review

Weizhong Jin, Limin Wang, Junbo Xia and Jian Ye

Abstract

This report provides information on the clinical characteristics and treatment of three patients with avian influenza A (H7N9) virus treated in Zhejiang Province, China. The infection was characterized by respiratory symptoms, fever, rapid progression, and significant hypoxemia. Laboratory tests showed a low level or decrease in leukocytes. It is recommended that neuraminidase inhibitors be administered at early stage of the disease.

Key words: avian influenza, H7N9, pneumonia

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Introduction

Following the first wave of infections last spring, more than 226 new H7N9 influenza infections have been reported this year in China. With confirmed H7N9 cases on the rise, avian-influenza A is posing a significant threat to the global public health. However, our knowledge about the clinical characteristics of this disease are still very limited (1), though Gao and coauthors recently reported the clinical features of 111 cases in China (2).

In the first wave, we admitted three patients with laboratory-confirmed avian influenza A (H7N9) virus infection in Zhejiang Province, China. We herein summarize the preliminary findings of these three cases, including clinical features and treatment experience, which may help us to understand the natural history and full spectrum of H7N9 infection.

Case Reports

Case 1

A 69-year-old man presented at our hospital complaining of chill, fever, pharyngalgia, and fatigue for 5 days and productive cough, bloody sputum, and diarrhea for 1 day. The patient had previously been exposed to poultry 10 days before onset (Table 1).

Physical examination revealed a maximum body temperature of 39.0°C, cyanotic lips, heart rate (HR) of 118 beats/min, respiratory rate (RR) of 20 times/min, and moist and dry rales were present in both lungs. The blood test on admission showed a WBC count of 4.8×10^9/L, N% of 75.7%, L% of 19.7%, platelet (PLT) 152×10^9/L, and C-reactive protein (CRP) of 125 mg/L. Chest X-rays showed infiltration of the left lower lobe of the lung (Fig. 1A).

The patient was diagnosed with pneumonia and was treated with 3.0 g sulperazone every 8 hours and 40 mg methylprednisolone once daily, but no improvement was noted. The patient’s shortness of breath was aggravated the following day, with blood gas analysis showing hypoxemia (partial pressure oxygen (PO2) of 53 mmHg, 91% saturation of arterial oxygen (SaO2) with an oxygenation index 252), not alleviated by supplemental oxygen, and a body temperature up to 40.2°C with a RR of 33 times/min. Subsequent chest X-rays showed worsened bilateral lung infiltration 7 days after onset of illness (Fig. 1B). The patient was then intubated following mechanical ventilation with 10 cm H2O positive end-expiratory pressure (PEEP). Meanwhile, blood tests showed a low level of leukocytes (Table 2) and PO2 of
Case 2

A 42-year-old man complained of 3-day history of chill, fever, cough, and bloody sputum. The patient had a history of renal extracorporeal shock wave lithotripsy ten years prior, but no history of poultry contact. The patient’s body temperature rose to 39°C and a chest CT was taken (Fig. 2A). Routine blood tests indicated a WBC count of 4.2×10^9/L, N% of 84.6%, L% of 11.4%, and CRP of 123 mg/L at disease onset. The patient was treated with 0.5 g oseltamivir twice daily and 4.5 g piperacillin sodium every 8 hours together with supportive therapy for 7 days after onset. After transfer to another hospital designated by the government, however, the patient’s overall condition progressively deteriorated, and he died of multiple-organ failure 9 days after disease onset.

Case 3

A previously healthy 37-year-old man complained of cough for 20 days and chest pain for 4 days before admission. His chest oppression and pain aggravated when coughing but could be relieved after rest. The patient had a temporary syncope attack at the waiting room. Routine blood test at that time showed a WBC count of 4.3×10^9/L, N% of 66.0%, and CRP of 8 mg/L, with normal myocardial enzymes level, while electrocardiogram showed the ST segment increased.

His physical examination showed a body temperature of 39.8°C, HR of 87 beats/min, RR of 20 times/min, BP of 115/56 mmHg, cyanotic lips, and wet rales were present in the lower lobe of the right lung. Chest X-ray and CT images are shown in Fig. 3.

The patient was diagnosed with suspected viral myocarditis and CAP and treated with 4.5 g piperacillin sodium every 8 hours and other supportive treatment. The following day, his temperature fell to 37.9°C, with a lowered WBC count (Table 2). Collected throat swabs were positive for H7N9 6 days after disease onset. The patient was transferred to another hospital, and eventually discharged from the hospital 22 days after admission.

Discussion

In this report, we described the clinical characteristics and treatment regimen of three patients who presented with H7N9 infection in Zhejiang Province, China. One patient in this report had a clear history of direct poultry contact before disease onset while the others did not. Based on this report alone, it is hard to draw the conclusion that animal-to-human transmissibility is higher for H7N9 compared to H5N1 (3), although national survey suggests that over 80% of patients infected with H7N9 are connected with live poultry markets. Though extensive monitoring of patient contacts did not find evidence of human-to-human transmission last year (4), it has been noted that H7N9 is transmitted from a first-infected person to a second, but transmission from a second-infected person to a third has not been noted. Unlike the H7N7 cases in 2003 (5), which mainly presented with conjunctivitis, the H7N9 infections detected thus far featured respiratory symptoms and rapidly progressive lung radiographic infiltrate. Early clinical presentation included fever and airway syndromes that were not distinguishable from the “influenza syndrome” associated with other human influ-

### Table 1. Demographic, Complications, Treatment, and Clinical Outcomes of Three Patients Infected with H7N9 Virus

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>69</td>
<td>42</td>
<td>37</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Occupation</td>
<td>Retired</td>
<td>Unemployed</td>
<td>Worker</td>
</tr>
<tr>
<td>Underlying conditions</td>
<td>Healthy</td>
<td>Renal calculus</td>
<td>Healthy</td>
</tr>
<tr>
<td>BMI</td>
<td>22.5</td>
<td>23.1</td>
<td>22.4</td>
</tr>
<tr>
<td>Exposure to poultry in</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>past 10 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic shock</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>ARDS</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>consciousness</td>
<td>Clear-headed, obstruction</td>
<td>Transient syncope</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Oxygen therapy</td>
<td>Mechanical ventilation</td>
<td>Mask</td>
<td>Mask</td>
</tr>
<tr>
<td>Antiviral agent</td>
<td>Oseltamivir &amp; Aciclovir</td>
<td>Oseltamivir</td>
<td>Oseltamivir</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Died of MODS 9 days after onset</td>
<td>Discharged on 21 days after onset</td>
<td>Discharged on 40 days after onset</td>
</tr>
</tbody>
</table>

MODS: multiple organ dysfunction syndrome, BMI: body mass index

104 mmHg, 92% SaO₂ with an oxygenation index 160. A throat swab was collected and sent to the Hangzhou Center for Disease Control and Prevention for nucleic acid tests; results came back positive for H7N9. Meanwhile, the patient was treated with 75 mg oseltamivir twice daily, 4.5 g tazo-cin every 8 hours, and 10 g gamma globulin once daily together with supportive therapy for 7 days after onset. After transfer to another hospital designated by the government, however, the patient’s overall condition progressively deteriorated, and he died of multiple-organ failure 9 days after disease onset.

In this report, the clinical characteristics and treatment regimen of three patients who presented with H7N9 infection in Zhejiang Province, China. One patient in this report had a clear history of direct poultry contact before disease onset while the others did not. Based on this report alone, it is hard to draw the conclusion that animal-to-human transmissibility is higher for H7N9 compared to H5N1 (3), although national survey suggests that over 80% of patients infected with H7N9 are connected with live poultry markets. Though extensive monitoring of patient contacts did not find evidence of human-to-human transmission last year (4), it has been noted that H7N9 is transmitted from a first-infected person to a second, but transmission from a second-infected person to a third has not been noted. Unlike the H7N7 cases in 2003 (5), which mainly presented with conjunctivitis, the H7N9 infections detected thus far featured respiratory symptoms and rapidly progressive lung radiographic infiltrate. Early clinical presentation included fever and airway syndromes that were not distinguishable from the “influenza syndrome” associated with other human influ-
Laboratory tests showed that these three cases all presented with a low level or decrease in leukocytes. A blood gas analysis showed significant hypoxemia, and chest imaging showed rapidly progressive infiltration in both lungs. Previous studies have shown severe obesity to be a risk factor for hospitalizations for the H1N1 influenza (7) and severe influenza outcomes (8), but our three H7N9 patients were all of healthy weight. Gastrointestinal symptoms are common in H1N1 and H3N2 infections but rare in H2N2 and H5N1 infections. In this report, patient 1 had diarrhea three times daily on admission. The findings in our patients may not represent the whole spectrum of disease in the community where mild disease may remain unrecognized. However, the high mortality in patients admitted to the hospital with severe disease is very unusual and merits attention.
The platelet counts in our patients were within the normal ranges, compared to 73% of patients who had thrombocytopenia as reported by Li et al. (4), though it is difficult to measure percentage based on only three cases. Of note, the three patients were all male, consistent with the findings that the majority of H7N9 cases are male patients (2). The underlying mechanism of disease is yet unknown. In contrast to H7N9 cases in Shanghai (9), platelet counts in our patients were within the normal ranges, as was liver and kidney function, which suggests there might be varying severity of H7N9 infection. The first case in our report also showed a negative throat swab for the nucleic acid test using universal primers. However, the result was positive at 7th day after disease onset.

An H7N9 vaccine is currently in clinical trials, however, it may not be necessary for China to promote the H7N9 flu vaccination this time. As opposed to the 27% mortality reported by Gao et al. (2), two of the three patients eventually recovered in the present report, although it is difficult to measure mortality based on the findings of only three cases. We recommend that neuraminidase inhibitors be administered as soon as possible. Though glucocorticoid has no beneficial effect on acute respiratory distress syndrome caused by H5N1 infection in mice (10), it still remains controversial as to whether or not methylprednisolone can be used short term in H7N9 infections to reduce the excessive inflammatory reaction associated with pneumoniedema. Currently, there is no scientific basis for treatment of H7N9 with anti-infective drugs. However, the empirical use of antibiotics is initially recommended while trying to determine the underlying etiology of severe pneumonia followed by re-evaluation according to any evidence or suspicion of nosocomial infections. Given the small number of patients in this report, the effect of oseltamivir on disease outcome was not conclusive. In regards to immunoglobulin, Hong et al. showed cross-reactive neutralizing antibody against pandemic 2009 H1N1 influenza A virus in intravenous immunoglobulin preparations (11).

However, it is not known if immunoglobulin has any cross-reactivity against H7N9. The only passive immunity that may be useful for H7N9 is convalescent plasma, which was used for H5N1 (12) and pandemic H1N1 infections in 2009 with favorable outcomes (13).

Severe H7N9 virus infections, characterized by high fever and severe respiratory distress symptoms, may pose a serious risk to human health. To date, there is a paucity of detailed clinical data and appropriate counter measures on optimal clinical management of patients with H7N9 infection. Further clinical research is needed to improve the clinical care of H7N9 virus-infected patients.

The authors state that they have no Conflict of Interest (COI).

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References