Case Report

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Analysis of the clinical characteristics and treatment of two patients with avian influenza virus (H7N9)

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Summary **Avian influenza is one of the most dangerous contagions in poultry worldwide, and avian influenza A viruses are the major pathogens responsible. Outbreaks of H7N9, a strain of the avian influenza A virus H7 subtype, have increasingly been reported in several countries since 2007. This spring, H7N9 broke out in China and has thus far caused 24 cases of infection and 7 deaths. Recently, we treated two patients with H7N9 infection. The infection was characterized by respiratory symptoms, fever, rapid progression, and significant hypoxemia. Laboratory tests showed a low level or decrease in leukocytes, a drop in blood platelets, and an increase in myocardial enzymes and aspartate aminotransferase. Oseltamivir, anti-infective drugs, and immunoglobulin were administered. Supplemental oxygen or non-invasive mechanical ventilation helped to relieve symptoms. This report provides information on the clinical characteristics and treatment of two Chinese patients with H7N9.**

Keywords: Avian influenza virus, H7N9, China

1. Introduction

Over the past decade, avian influenza derived from animal reservoirs has become a major challenge (*1*). Recent outbreaks detected in fowl and wild birds in many Asian, European, and African countries are devastating to the poultry industry and also to public health (*2*). Among the avian influenza viruses, only *Orthomyxoviridae Influenzavirus* A is known to infect birds, so it has been termed avian influenza A virus as a result. Type A influenza viruses are classified into 16 hemagglutinin (HA) subtypes and 9 neuraminidase (NA) subtypes (*3*). Influenza A viruses are further divided into low-pathogenic avian influenza (LPAI) and high-pathogenic avian influenza (HPAI) viruses based on their pathogenic properties in chickens. Infection of fowl with the H7 subtype is of great concern because of its high pathogenicity (*4*). Fowl were infected with avian influenza A (H7) viruses in Italy in 2000, Chile in 2002, the Netherlands in 2003, British Columbia, Canada in 2004, and Saskatchewan, Canada in 2007 (*5*). Unlike other virus subtypes, H7 influenza viruses of both lineages have been predominantly associated with ocular disease in humans, typically in the form of conjunctivitis (*6*). In 2000, human infection with the H7N3 subtype of the avian influenza virus was reported in Northern Italy (*7*). In 2003, H7N7 led to 89 cases of human infection and 1 death in the Netherlands (*8*). In 2004, an H7H3 outbreak occurred in humans in Canada (*9*). Within the H7 subtype, the LPAI H7N9 strain, which was collected in the Czech Republic in 2007, appears to have become highly pathogenic after introduction into domestic poultry (*4*). Prior to 2011, H7N9 viruses were reported to cause infections in fowl in many countries such as the Czech Republic, Spain, the US, and Mexico (*10,11*). In the spring of 2013, human infections with H7N9 broke out on the China mainland, and there have been 24 cases of infection and 7 deaths thus far (*12*). The current report describes the clinical characteristics and treatment of two patients with avian influenza virus (H7N9).

2. Case report

Since February 2013, three patients from Shanghai

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and Anhui Province, China were infected with avian influenza virus (H7N9); two of the patients died but one survived. H7N9 was successfully isolated from these patients by the Chinese Center for Disease Control and Prevention on the afternoon of March 29th. To date, there have been 19 or 20 confirmed cases of patients infected with H7N9 in China, six of whom had already died. On April 6th, two patients were admitted and were confirmed to be infected with H7N9 by the Shanghai Public Health Clinical Center.

Case I: This case involved a 74-year-old male who had previously been exposed to poultry. The patient had a cough, fever, and shortness of breath for 7 days before being admitted to hospital (Figure 1). The patient indicated that the cough, fever, and shortness of breath began on March 31, 2013 after a cold. Examination revealed a maximum body temperature of 39.3°C, WBC of 5.5 × 10^9/L, N% of 79.6%, Cr of 157 μmol/L, and BUN of 12.1 mmol/L. Chest CT revealed inflammation of the lower lobe of the left lung. The patient was treated with ceftazidime for 3 days to fight the infection, but no improvement was noted. On April 5, 2013, another examination was conducted and the results revealed WBC of 2.95 × 10^9/L, N% of 80.4%, and large areas of inflammatory cell infiltrates in both lungs. On the second day, the patient's blood pressure decreased (89/49 mmHg) and the patient developed hypoxemia (arterial oxygen 7.47 kPa) and hyponatremia (122 mmol/L). The patient's respiratory secretions were sent to the Shanghai Center for Disease Control and Prevention for nucleic acid tests, which suggested positivity for H7N9. The patient was treated with oseltamivir to fight the virus and moxifloxacin to fight infection. The patient was also administered methylprednisolone 40 mg/d. Non-invasive mechanical ventilation and symptomatic and supportive treatment were provided to prevent spasms, loosen phlegm, and correct the patient's electrolyte imbalance. Afterwards, the patient's body temperature returned to normal and his shortness of breath improved. On April 6, 2013, a third examination was conducted and the results indicated WBC of 5.41 × 10^9/L and N% of 90.30%. Serology and blood gas analysis indicated an SpO_2 of 99.30% ↑, Pa of 20.10 KPa ↑, AST of 86.00 U/L ↑, LDH of 886.00 U/L ↑, BUN of 16.20 mmol/L ↑, Cr of 159.60 umol/L ↑, CK of 170.00 U/L, and CKMB of 18.00 U/L.

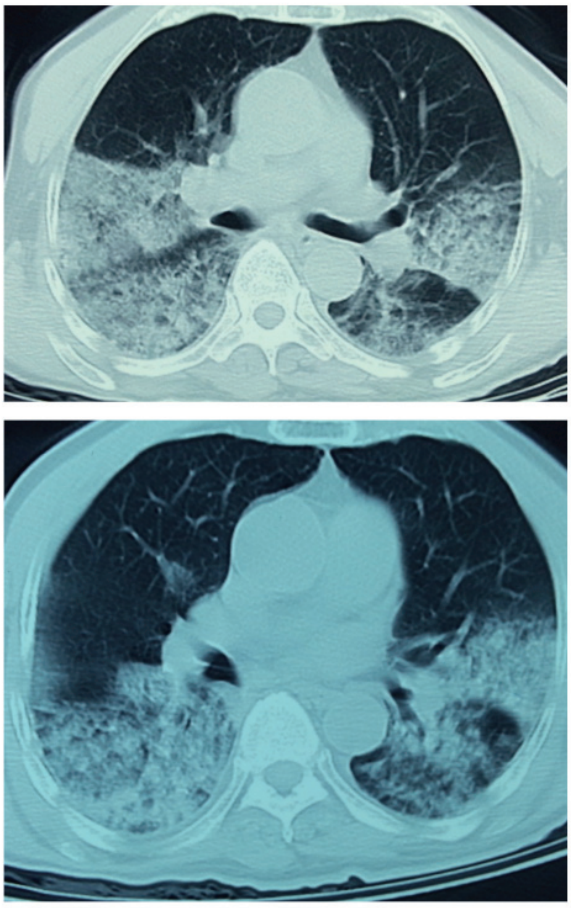

Figure 1. Chest CT of a 74-year-old male patient on April 5th, 2013.

Past history: Coronary disease and liver disease due to schistosomiasis.

Physical examination: Temperature of 35.6°C, pulse of 98 beats/min, respiratory rate of 30 breaths/min, and BP of 148/85 mmHg. The patient was alert and oriented and appeared fatigued. The patient had a very sickly appearance, shortness of breath, cyanotic lips, and a barrel chest. Moist rales were present in both lungs. The patient had a regular rhythm, soft abdomen, and no dropsy in the lower limbs.

Diagnosis upon admission: Viral pneumonia (H7N9), acute respiratory failure, coronary disease, class III cardiac function, and renal insufficiency.

Anti-infective therapy: Sulperazon, moxifloxacin, and oseltamivir. Noninvasive assisted ventilation and symptomatic therapy and supportive treatment were used.

The treatment improved the patient's level of consciousness and the patient's overall condition. The patient's lips were no longer cyanotic. The patient occasionally coughs, producing a small amount of white phlegm, and he breathes somewhat heavily after activity. The patient did not develop a fever or chest pain again. Physical examination: heart rate of 70 beats/min, respiratory rate of 28 breaths/min, SPO_2 of 98%, and BP of 116/70 mmHg. Coarse breath sounds and moist rales were heard in both lungs while the patient was helped with a non-invasive ventilator.

Case II: This case involved a 65-year-old male who had a fever for 5 days and a cough for 2 days (Figure 2). The patient began to feel dizzy and have chills and a fever after paying respect to deceased relatives on March 31, 2013. The patient's body temperature was 38.0°C and the patient had no coughing or sputum. The patient described being admitted to a local hospital on April 2, 2013 and undergoing symptomatic treatment

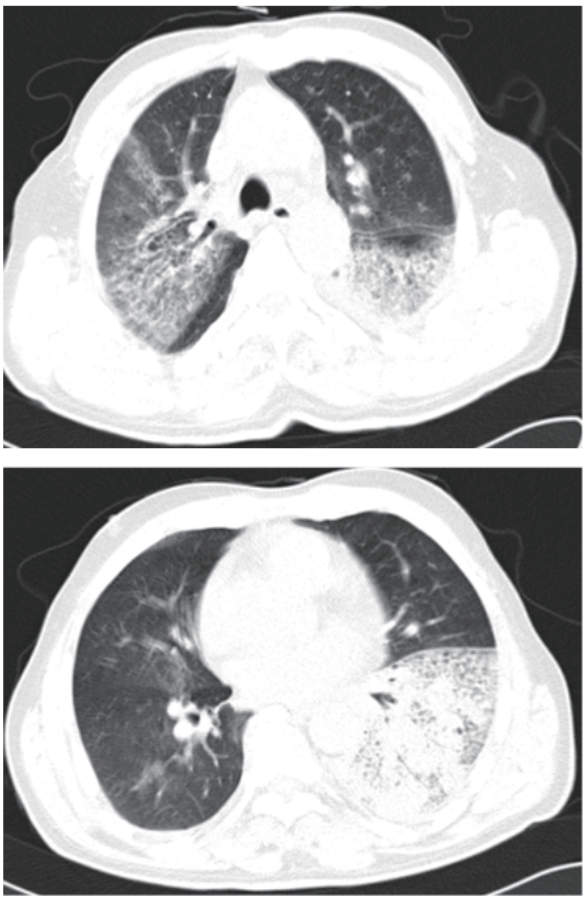

Figure 2. Chest CT of a 65-year-old male patient on April 6th, 2013.

for an "upper respiratory infection". On April 3rd, the patient's body temperature rose to 39°C and a chest CT showed inflammatory cell infiltration of the lower lobe of the left lung. A routine blood test indicated WBC of 3.5 × 10^9/L, N% of 72.4% and PLT of 101 × 10^9/L. Anti-inflammatory treatment with penicillin resulted in no improvement. On April 4th, the patient began to cough, producing white, purulent sputum with blood and he gasped after activity. A routine blood test was again conducted, revealing WBC of 2.98 × 10^9/L, N% of 72.1%, Plt of 76 × 10^9/L, and CRP of 66 mg/L. Supplemental oxygen was provided and the patient was given the anti-viral drug oseltamivir and the anti-inflammatory drug ceftriaxone. On April 5th, a chest CT showed improvement in lesions of the lower lobe of the left lung. Serology and blood gas analysis on April 6th indicated PCO_2 of 3.90 KPa, PO_2 of 7.30 KPa, AST of 77.00 U/L, LDH of 492.00 U/L, CK of 1854.00 U/L, and CK-MB of 31.00 U/L. There was significant inflammation in the upper lobe of the right left lung and the lower lobe of the left lung, pleural effusion in both lungs, and lymph node shadows in the mediastinum, suggesting viral pneumonia. Therefore, the patient's respiratory secretions were sent to the Shanghai Center for Disease Control and Prevention for H7N9 nucleic acid tests on April 6th; the specimens were positive for H7N9. Anti-viral, anti-inflammatory, and symptomatic treatments were continued, leading the patient's condition to stabilize.

Past history: The patient had a history of hypertension for 5 years with managed blood pressure.

Physical examination: Temperature of 36.5°C, pulse of 82 beats/min, respiratory rate of 21 breaths/min, and BP of 118/74 mmHg. The patient was alert and oriented and appeared fatigued. Dullness to percussion and weak breath sounds were heard in the lower lobe of the left lung. There were no dry or moist rales in the lungs, heart sounds were strong, and the abdomen was soft. There was no dropsy in the lower limbs.

Diagnosis: Infection with the avian influenza virus (H7N9).

Treatment: The patient received the anti-infective drugs moxifloxacin, cefoperazone sulbactam, and oseltamivir. Supplemental oxygen and symptomatic and supportive treatment were provided.

The patient still coughs, producing a small amount of white phlegm, and he breathes heavily after activity. Physical examination: Oxygen flow of 5 L/min with the help of a nasal catheter, pulse of 86 beats/min, respiratory rate of 32 breaths/min, SPO_2 of 98%, and BP of 126/80 mmHg. The patient's condition improved and his lips are no longer cyanotic. Slightly coarse breath sounds were heard in both lungs, but there were no rales.

3. Discussion

Influenza in birds, or avian influenza, is a viral infectious disease that is highly pathogenic to birds but rarely pathogenic to swine. The avian influenza virus is highly species-specific, but in rare circumstances it will cross the species barrier to cause infection in human beings. The World Health Organization has been concerned about the avian influenza virus since humans were reportedly infected with the avian influenza virus in Hong Kong in 1997. Since then, the disease has broken out sporadically in Asia. Severe outbreaks have occurred in East Asia, primarily in Vietnam, South Korea, and Thailand since December 2003, causing several fatalities in Vietnam. At the present time, countries as far as Eastern Europe have also reported cases. In March 2012, Taiwan garnered attention by first reporting cases of highly pathogenic avian influenza H5N2. On September 18, 2012, the Department of Agriculture of Guangdong Province published a bulletin on highly pathogenic avian influenza occurring in Zhanjiang. This report described a new virus that reassembled the internal genes from the avian influenza virus H9N2 to cause infection in humans.

One of the two patients in the current cases had a clear history of direct contact with poultry and the other did not. Both had respiratory symptoms, fever, rapid progression, and significant hypoxemia. Basic

laboratory tests revealed a low level or decrease in leukocytes, a drop in blood platelets, and an increase in myocardial enzymes and aspartate aminotransferase. The patients were confirmed to have H7N9 infection, and oseltamivir, anti-infective drugs, and immunoglobulin were administered for symptomatic and supportive treatment. Supplemental oxygen or non-invasive mechanical ventilation helps to relieve symptoms (*13*). Thus far, there are no grounds for the use of hormone treatment.

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