RESPIRATORY CARE Paper in Press. Published on September 17, 2013 as DOI: 10.4187/respcare.02634

Management of the First Confirmed Case of avian Influenza A H7N9

Jian-ge Qiao MB[a], Lu Zhang MB[a], Ya-hui Tong MB[a], Wei Xie MB[a],
Jin-dong Shi MM[b$], Qing-min Yang MM[a$]

[a] Department of Nursing, the Fifth People's Hospital of Shanghai, Fudan University, Shanghai, China.

[b] Department of Respiratory Medicine, the Fifth People's Hospital of Shanghai, Fudan University, Shanghai, China.

Funding: This work was partially funded by the Young Scholars foundation of Shanghai Municipal Health Bureau, China (2010Y036) and the Shanghai Minhang District Committee of science and technology, China(2010MHZ018).

Conflict of Interest: The authors have disclosed no conflicts of interest.

[$] Corresponding author: The Fifth People's Hospital of Shanghai, Fudan University, Shanghai 200240, China.

E-mail address: yangqingmin2001@yeah.net or shijd8@163.com

Abstract

In March 2013, the first patient infected with H7N9 avian influenza virus was identified in China. The infection progressed rapidly, and the patient died of acute respiratory distress syndrome. During hospitalization, the patient was suspected of having respiratory infectious disease, and contingency plans for public health emergencies were promptly started. When the viral infection was identified, strict procedures for disinfection and protection were carried out. None of the health care workers involved in the management of the patient were infected.

Key words: avian influenza virus; H7N9; human; nursing

RESPIRATORY CARE Paper in Press. Published on September 17, 2013 as DOI: 10.4187/respcare.02634

Introduction

In the last few years, many cases of H7 subtypes of avian influenza virus infection, generally associated with mild symptoms, have been reported.[1] However, only 1 case of death due to human infection with H7N7 has been reported.[2] In March 2013, a novel avian influenza A (H7N9) virus was identified,[3-5] with no known cases of infection in humans. Since April 27, 2013, a total of 121 cases of H7N9 infection were identified in China, and 23 of the infected patients died.

On February 25, 2013, the world's first human patient with H7N9 infection was admitted to the Fifth People's Hospital of Shanghai, Fudan University. Because of the rapid course of progression and clinical features of the illness, we suspected that the patient had respiratory virus infection. Subsequently, we isolated the H7N9 virus from throat swab specimens.[3]

Case report

Clinical Presentation

An 87-year-old man, who had a cough with sputum for 5 days and fever for 1 day, was admitted to the Fifth People's Hospital, Fudan University, Shanghai, on February 25, 2013 (Day 1). He had a history of chronic bronchitis for the past 7–8 years and a history of hypertension for more than 10 years.

Physical examination at admission showed an increased respiratory rate (28 breaths/min) and fever (body temperature, 39.9°C). Blood tests showed a normal white blood cell (WBC) count (4.66×10^9/L), but a decreased lymphocyte count (0.53×10^9/L). A chest radiography showed slightly vague, higher-density patches in both lung fields and the heart on the right side**,** suggesting lung inflammation and dextrocardia (Fig1.A). The patient was administered anti-infection treatment with ceftriaxone (2 g/day) and levofloxacin (0.5 g/day) together with oxygen therapy and other supportive treatments. Because of the similar clinical presentations of his 2 sons, who were also admitted to our hospital, we suspected that the patient had influenza. Therefore, the patient was administered oseltamivir (150 mg/day) and maintained in an isolation ward. Although initial tests failed to show infection by a novel virus, we

RESPIRATORY CARE Paper in Press. Published on September 17, 2013 as DOI: 10.4187/respcare.02634

sent the blood, sputum, and throat swab specimens to Shanghai Public Health Center of Fudan University for examination.

The patient's family did not agree to invasive mechanical ventilation, and on Day 3, we started non-invasive mechanical ventilation applied through a full-face mask with an oxygen flow of 8 L/min and positive end-expiratory pressure of 8 mmHg and administered methylprednisolone for the treatment of aggravated dyspnea and worsening hypoxemia (Table 1). On the evening of Day 4, the patient exhibited irritability, delirium, and other psychiatric symptoms and refused to use mechanical ventilation. On Day 5, blood tests showed leukocytosis, and we treated the patient with antibiotics, piperacillin/tazobactam (4.5 g/8 hours), and levofloxacin (0.5 g/day). However, the patient's condition deteriorated, and he died from severe pneumonia and acute respiratory distress syndrome (ARDS) on Day 8. Subsequently, the patient's throat swab sample showed positivity for influenza A universal primers, and a novel multiple reassortant avian influenza virus was isolated. Its 2 gene segments, HA and NA, were highly homologous with the H7 subtypes of avian influenza, and the 6 internal genes (NP, NS1, PB1, PB2, PA, and M) came from H9N2 avian influenza. Thus, the first case of H7N9 avian influenza was confirmed on March 30, 2013.[3]

Fig1. Chest Radiographs

Chest radiographs taken on Day 1 shows the patient's heart on the right side and mild ground-glass opacity (panel A). Chest computed tomography performed on Day 2 indicate substantial bilateral ground-glass opacity and consolidation (panel B). Chest radiographs taken on Day 4 indicate bilateral progressive exudative lesions and right pleural effusion (panel C).

Care and Precautionary Management

Based on the patient's condition, we suspected the presence of a respiratory infectious disease, which could have been contagious. We reported the case to the hospital authority and carried out isolation and protection procedures. The prompt

RESPIRATORY CARE Paper in Press. Published on September 17, 2013 as DOI: 10.4187/respcare.02634

reporting facilitated effective communication and medical treatment.

Immediate expert consultations were organized to formulate the care strategy. The Department of Respiratory Medicine reinforced the professional training of the deployed professional and technical nurses entering the isolation room to take care of the patient, by providing further training in the management of infectious diseases and self-protection such as the proper use of isolation clothes and hand disinfection.

The patient was isolated in a separate ward in the Respiratory Medicine Department. The ward temperature was maintained at 22–24°C, with 50–60% humidity, and the ward facilities including the floor were disinfected in a timely fashion. The disposable medical supplies were collected by specialized staff and incinerated. The patient's secretions and excretions were treated with bleach and soaked in a stamped container for 2 hours before discarding them into the sewage disposal system. Items used by the patient were sealed in double yellow medical garbage bags and disposed as special medical waste. Collected specimens were sealed in sterile containers and placed in a clean plastic box. People who were exposed to the virus undertook 3-level protection steps.[6-8]

The nurses followed the standards of intensive care rigorously. We carefully recorded the patient's vital signs and peripheral oxygen saturation, performed suction when necessary, and kept the airways unobstructed. We provided an appropriate level of psychological support to the patient to alleviate his anxiety and fear. Following non-invasive ventilation, the patient was given a pen and paper to allow him to communicate with us. The family members were routinely informed of any changes in the patient's condition and the treatment approach and progress.

After the patient died, nurses performed post-mortem care. The body was scrubbed with disinfectant, and each orifice was filled with disinfectant cotton balls. The corpse was wrapped with a bed sheet, encased in an opaque bag, and marked with infection markers. Good isolation and protection guidelines were followed during the transportation process.[6-8]

Discussion

RESPIRATORY CARE Paper in Press. Published on September 17, 2013 as DOI: 10.4187/respcare.02634

H7N9 is an avian influenza virus subtype.[3] All the 25 strains of H7N9 viruses identified prior to March 2013 infected only birds. H7N9 has low pathogenicity and causes mild symptoms in infected birds. Thus far, there have been no reported human cases of H7N9 infection.[9] The H7N9 virus found in our patient is a novel recombinant avian influenza virus.[3] The understanding of this virus is limited, and the general population lacks immunity against it. Therefore, the diagnosis, treatment, and management of the first patient infected with H7N9 virus were difficult. For a novel influenza virus, rapid detection is a challenging task and a critical component of national efforts in infection prevention.[10] We now know that H7N9 avian influenza virus is similar to H5N1 in terms of its clinical symptoms, disease progression, and lethality and can be treated.[11,12] Early diagnosis is important to initiate the antiviral treatment on time, provide barrier precautions, and influence the natural course of the disease favorably.[12]

In general, patients infected with the H7N9 virus have flu-like symptoms. The infection progresses rapidly and can lead to life-threatening ARDS.[13] Our patient had no influenza-like symptoms, but had a high fever, cough with sputum, and significantly increased blood creatinine kinase and lactate dehydrogenase levels. The patient's WBC count was normal, and the lymphocyte count decreased significantly in the early stages of the disease. This was followed by an increase in the WBC count accompanied with bacterial infection. Computed tomography showed alveolar consolidation in the lungs (Fig1.B). The disease progressed rapidly, leading to hypoxemia and ARDS. In addition, the patient's advanced age and previous diseases such as chronic obstructive pulmonary disease and hypertension aggravated his condition.

Despite the patient's death, we provided adequate medical care and carried out thorough laboratory investigations. Therefore, we identified the world's first human case of avian influenza A H7N9 virus infection. When we first admitted this patient, there were no health care guidelines that we could follow. Even in the absence of a definite diagnosis of influenza infection, we actively carried out isolation protection in accordance with the standard hospital infection-protection protocols while closely

RESPIRATORY CARE Paper in Press. Published on September 17, 2013 as DOI: 10.4187/respcare.02634

coordinating the activities of different departments and ensuring the protection of the medical supplies. In addition, we organized the training for respiratory infectious disease protection in the nursing department. We believe that first-line health care providers should be highly aware of the appropriate infection-prevention measures before determining whether the pathogen has the capability for human-to-human transmission.[10] Finally, we found no evidence of clinical infection in the health care workers involved in the management of this patient in our hospital.

Isolation, non-invasive ventilation, and other disease complications are known to be psychologically traumatic for patients. Our patient was given appropriate psychological care and treated respectfully. We also ensured the comfort and safety of the given airway care. Although the patient ultimately died, the family appreciated the treatment and care provided. Most importantly, we gained extensive experience in the management and prevention of viral infectious diseases, which will be useful in the treatment of future cases of H7N9 virus infections.

ACKNOWLEDGMENTS

The authors would like to thank the Fifth People's Hospital of Shanghai and Shanghai Public Health Clinical Center, Fudan University for providing medical resources.

REFERENCES

1. Belser JA, Davis CT, Balish A, Edwards LE, Zeng H, Maines TR, et al. Pathogenesis, transmissibility, and ocular tropism of a highly pathogenic avian influenza A (H7N3) virus associated with human conjunctivitis. J Virol 2013; 87(10):5746-5754.

2. Kemink SA, Fouchier RA, Rozendaal FW, Broekman JM, Koopmans M, Osterhaus AD, Schneeberger PM. A fatal infection due to avian influenza-A (H7N7) virus and adjustment of the preventive measures. Ned Tijdschr Geneeskd 2004; 148(44):2190-2194.

3. Gao R, Cao B, Hu Y, Feng Z, Wang D, Hu W, et al. Human infection with a novel avian-origin influenza A (H7N9) virus. N Engl J Med 2013;368(20):1888-1897.

RESPIRATORY CARE Paper in Press. Published on September 17, 2013 as DOI: 10.4187/respcare.02634

4. Liu D, Shi W, Shi Y, Wang D, Xiao H, Li W, et al. Origin and diversity of novel avian influenza A H7N9 viruses causing human infection: phylogenetic,structural, and coalescent analyses. Lancet 2013;381(9881):1926-1932.

5. Liu Q, Lu L, Sun Z, Chen G, Wen Y, Jiang S. Genomic signature and protein sequence analysis of a novel influenza A(H7N9) virus that causes an outbreak in humans in China. Microbes and Infection 2013; 15(6-7):432-439.

6. Chinese Ministry of Health. Technical guidelines for hospital infection: hospital prevention and control of infectious atypical pneumonia (SARS). [2003] No. 308

7. Shanghai CDC. Work plan of prevention and control of Shanghai people infected with highly pathogenic avian influenza (2006 revision). [2006] No. 75

8. Chinese Ministry of Health. Influenza A H1N1 influenza treatment program (2010 edition). [2010] No. 79

9. Bertran K, Perez-Ramirez E, Busquets N, Dolz R, Ramis A, Darji A, et al. Pathogenesis and transmissibility of highly (H7N1) and low (H7N9) pathogenic avian influenza virus infection in red-legged partridge (Alectoris rufa). Vet Res 2011;42(1):24.

10. Tang RB, Chen HL. An overview of the recent outbreaks of the avian-origin influenza A (H7N9) virus in the human. J Chin Med Assoc 2013;76(5):245-248.

11. Wu C, Lu X, Wang X, Jin T, Cheng X, Fang S, et al. Clinical symptoms, immune factors, and molecular characteristics of an adult male in Shenzhen, China infected with influenza virus H5N1. J Med Virol 2013;85(5):760-768.

12. Gao HN, Lu HZ, Cao B, Du B, Shang H, Gan JH, et al. Clinical findings in 111 cases of influenza A (H7N9) virus infection. N Engl J Med 2013;368(24):2277-2285.

13. Chinese National Health and Family Planning Commission of human infection with the H7N9 avian influenza treatment program, 2nd Edition (2013) [S].2013.

RESPIRATORY CARE Paper in Press. Published on September 17, 2013 as DOI: 10.4187/respcare.02634

Table 1. H7N9 case laboratory findings

Variable	Day 3	Day 5	Day 7	Day 8	Reference value
WBC ($\times 10^9$/L)	4.67	12.87	16.80	NA	4.0–10.0
Neutrophil ($\times 10^9$/L)	4.11	11.62	15.52	NA	2.0–7.0
Lymphocyte ($\times 10^9$/L)	0.53	0.69	0.82	NA	1.0–4.0
PLT ($\times 10^9$/L)	78	121	89	NA	100–400
LDH (U/L)	480	1929	1751	NA	135–215
CK (U/L)	501	311	236	NA	24–192
CK-MB (U/L)	27	28	17	NA	0–25
ALT (U/L)	31	50	58	NA	0–55
AST (U/L)	77	109	73	NA	0–50
pH	7.48	NA	NA	6.96	7.35–7.45
$PaCO_2$ (mmHg)	54	NA	NA	24	35–45
PaO_2 (mmHg)	29*	NA	NA	43#	70–100
SB (mEq/L)	28.2	NA	NA	6.8	22–26

Note: WBC—white blood cell, PLT—blood platelet, LDH—lactic dehydrogenase, CK—creatine kinase, CK-MB—creatine kinase MB isoenzyme, ALT—alanine aminotransferase, AST—aspartate aminotransferase, pH—potential of hydrogen, PaCO2—partial pressure of carbon dioxide,PaO2—partial pressure of oxygen, SB—standard bicarbonate

*Oxygen therapy by nasal catheter (3 L/min) (FiO_2, 33%)

#Oxygen therapy by mask (8 L/min) (FiO_2, 53%)

RESPIRATORY CARE Paper in Press. Published on September 17, 2013 as DOI: 10.4187/respcare.02634