Iranian J Publ Health, Vol. 43, No.2, Feb 2014, pp. 241-246

Case Report

Radiological Features of Human Infection with Avian Influenza A H7N9 Virus: A Report of Three Cases

Dandan WU, Feng XU, *Jin LIU

1. *Dept. of Infectious Diseases, 2nd Affiliated Hospital of Zhejiang University, Hangzhou, China*

***Corresponding Author:** Email: xiaoxiaotianyumi@hotmail.com

(Received 22 Sep 2013; accepted 20 Dec 2013)

Abstract

Human infection with avian influenza A H7N9 virus has emerged in China with high morbidity rates. Patients usually present with severe and rapidly progressive pneumonia. Therefore, radiological findings are important to diagnose and evaluate disease severity. The clinical characteristics of three new cases of H7N9 virus infection were analyzed, especially the radiological findings, and previously published studies regarding H7N9 virus infection were summarized. Ground-glass opacification and areas of consolidation were the most common image features. Although drug resistance has been found in some H7N9 viruses, oseltamivir administration is still recommended as soon as possible. Moreover, timely epidemiological surveillance is needed, and a new vaccine is expected for the management of avian influenza.

Keywords: Human infection, Avian influenza A(H7N9), Radiological findings, China

Introduction

Since March 2013, infection with a novel reassortant avian-origin influenza A H7N9 virus has occurred in China (1). To date, 137 cases of infection have been reported in 10 provinces or municipalities, with 45 deaths (2). As was reported in previous studies, the patients usually presented with a rapidly progressive pneumonia that could result in respiratory failure and acute respiratory distress syndrome (ARDS). Therefore, radiological findings remain the most important information to diagnose and evaluate disease severity. Here, we report three cases of H7N9 virus infection, focusing on the radiological findings.

Case Reports

Case 1

A 65-year-old man came to our hospital complaining of upper abdominal pain and nausea for 6 days. On the same day as symptoms onset, he bought a live hen. He had a history of cholecystitis and cholelithiasis. He was first diagnosed with acute onset cholecystitis and treated for 4 days, including antibiotics, in a primary hospital but still did not feel better. Moreover, his temperature rose to 38.5°C, which forced him to come to our hospital immediately. He had a slight cough and a little sputum without chest pain or dyspnea. Inspiratory crackles were heard in the right lower lung field on auscultation. The oxygen saturation level for room air was 93%. The laboratory results revealed leukopenia and increased myocardial enzyme and aspartate aminotransferase levels (Table 1). High-resolution computed tomography (HRCT) was performed and showed ground-glass attenuation in the right lower lobe and the left upper lobe (Fig. 1). Because of the unexplained pneumonia, his airway secretions were sent to the Zhejiang Center for Disease Control and Prevention for nucleic acid testing. The test results suggested that the patient was infected with the H7N9 virus.

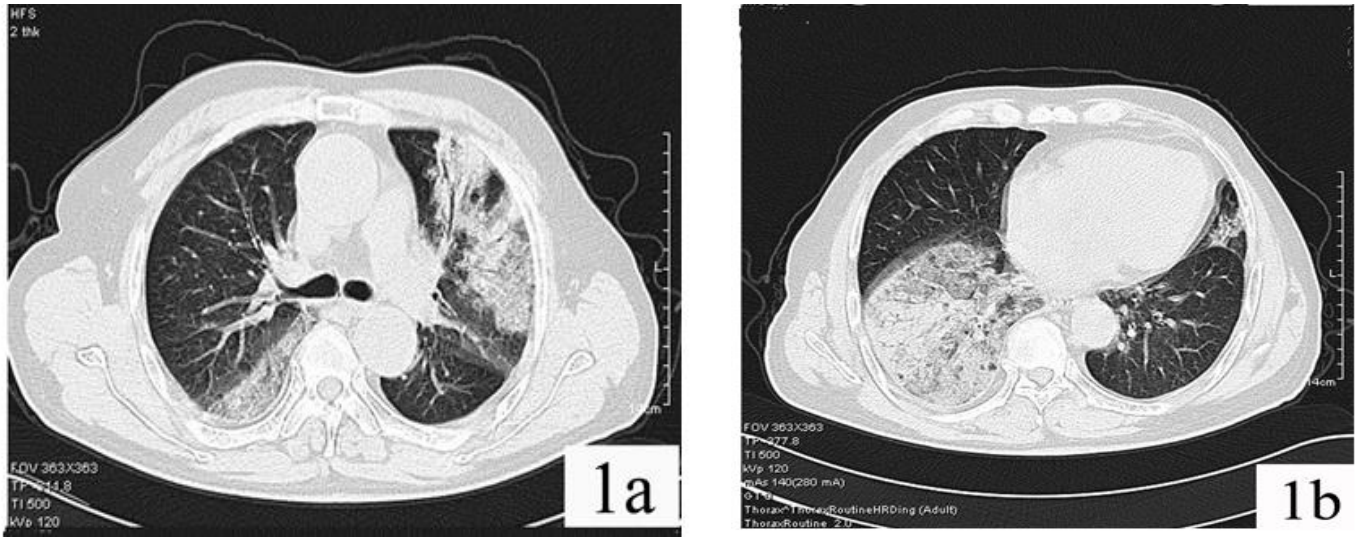

Fig. 1: Images of the 1st case: HRCT showed ground-glass attenuation in (a) the left upper lobe and (b) the right lower lobe

Table 1: Patients' main characteristics

	Patient 1	Patient 2		Patient 3		Normal range
Age	65	84		58		
Sex	Male	Male		Male		
Exposure history to birds in the past 7 days	Yes	No		Yes		
Underlying condition	Cholecystitis and Chaelithiasis	Chronic Obstructive Pulmonary Disease		No		
Symptom						
Temperature(℃)	38.5	38.9		39.3		
Sore throat	-	-		-		
Body pain	-	+		-		
Cough	+	+		-		
Sputum	+	-		-		
Dyspnea	-	+		-		
Abdominal pain	+	-		-		
Lab test		Initial	3 days later	Initial	2 days later	
WBC ($\times10^9$/L)	3.0	6.3	5.6	4.2	1.4	4-10
Neutrophils ($\times10^9$/L)	2.2	4.8	4.3	2.95	1.1	2-7
Lymphocytes ($\times10^9$/L)	0.56	0.9	0.8	0.8	0.3	0.8-4
CRP (mg/L)	140.5	25	53.4	/	87.3	<10
ALT (U/L)	65	/	21	/	40	<45
AST (U/L)	99	/	43	/	48	<35
LDH (U/L)	918	/	471	/	/	140-271
CK (U/L)	979	/	116	/	/	<171

†WBC= white blood cell; CRP= C Reactive Protein; ALT= alanine aminotransferase; AST= aspartate aminotransferase; LDH= lactate dehydrogenase; CK=creatine kinase

Case 2

This case involved an 84-year-old man who lived in a nursing home and had no known history of exposure to live birds during the 2 weeks before the onset of symptoms. He came to our hospital presenting with fever, dry cough, and dyspnea. He had a history of chronic obstructive pulmonary disease for 40 years. Chest auscultation revealed decreased breath sounds in both lungs. Initial routine blood tests showed a normal white blood cell (WBC) count (Table 1). The initial HRCT results (Fig. 2a) showed multiple bilateral ground-glass opacification. He was treated with moxifloxacin and the Chinese patented drug Lianhuaqingwen capsule for 3 days. However, his symptoms persisted and dyspnea worsened. A chest X-ray was performed and showed extensive bilateral ground-glass opacification (Fig. 2b). The patient was admitted to the respiratory ward and subsequently transferred to the intensive care unit because of respiratory failure and unconsciousness. He was intubated and given meropenem for antibiotic treatment. Another chest X-ray was performed on the next day, which revealed diffuse bilateral air-space consolidation (Fig. 2c). As a result of rapidly progressive unexplained pneumonia, viral pneumonia was suspected. Therefore, a nasopharyngeal swab sample was collected and analyzed by reverse transcription-polymerase chain reaction (RT-PCR) by our microbiology laboratory. A positive result for H7N9 virus was detected. This result was confirmed by the Zhejiang Center for Disease Control and Prevention.

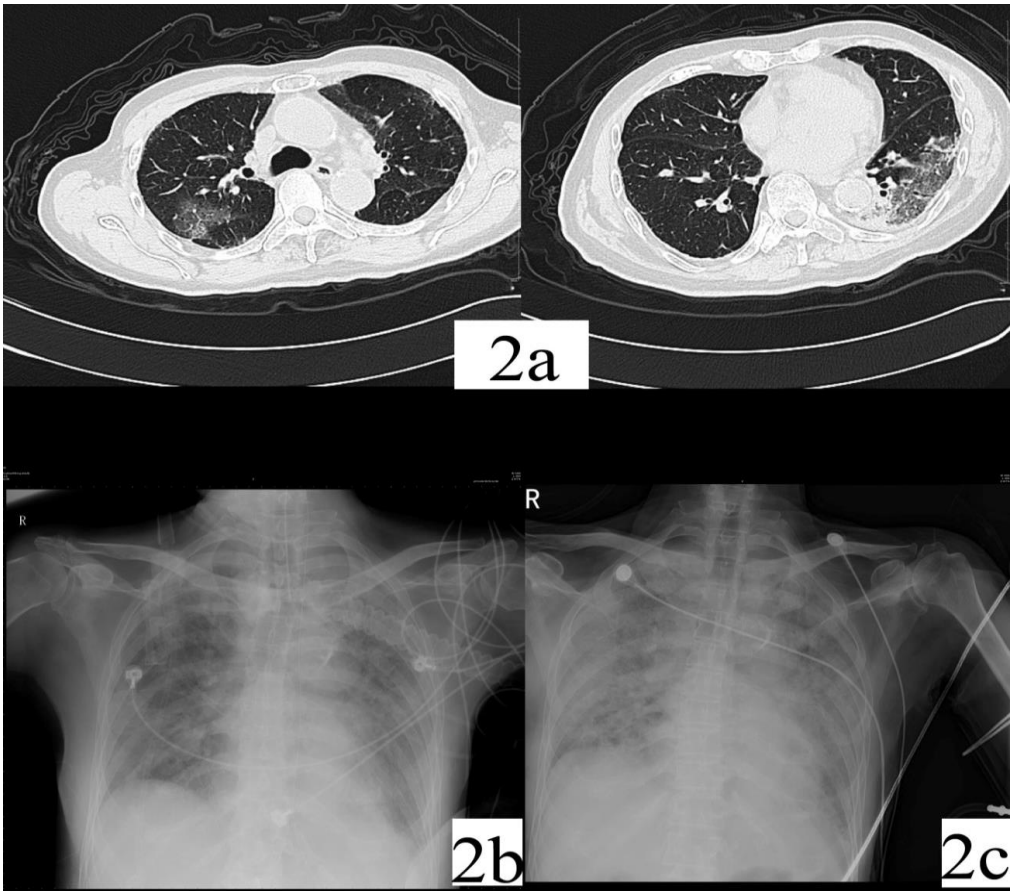

Fig. 2: Images of the 2nd case: (a) HRCT showed multiple bilateral ground-glass opacification. (b) Chest X-ray showed extensive bilateral ground-glass opacification. (c) Chest X-ray revealed diffuse bilateral air-space consolidation

Case 3

A 58-year-old man presenting with a 3-day history of fever, chills, and fatigue, without cough, chest pain, or dyspnea was admitted to our hospital. Epidemiological investigation found that he had bought a hen 13 days previously. He had been diagnosed with upper respiratory infection and treated with paracetamol, Qingkailing Capsule (a Chinese patented drug), and latamoxef for 2 days in a community health service center. Rechecking of routine blood tests showed leukopenia and lymphopenia (Table 1). Thus, he came to our hospital. Physical examination revealed a fever of 39.3°C and oxygen saturation on room air of 98%. No crackling sounds were heard. A chest X-ray showed infiltration in the left lung and subpleural consolidation (Fig. 3a). On the next day, a chest X-ray was performed again and revealed a large area of consolidation in the left lung (Fig. 3b). As the pneumonia was unexplained, RT-PCR of the nasopharyngeal swab samples was done by our microbiology laboratory and confirmed by the Zhejiang Center for Disease Control and Prevention to be positive for the H7N9 virus.

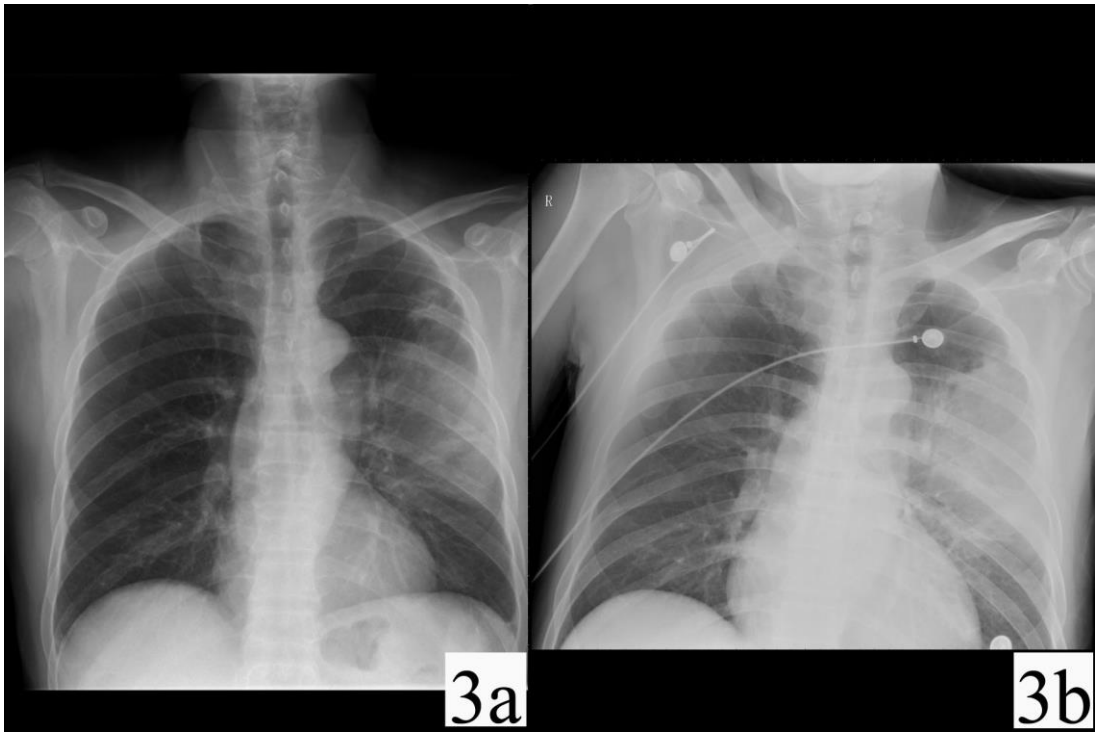

Fig. 3: Images of the 3rd case: (a) Chest X-ray showed infiltration in the left lung and subpleural consolidation. (b) Chest X-ray revealed a large area of consolidation in the left lung

Discussion

A novel reassortant H7N9 virus has emerged in China (3). The symptomatic case fatality risk is between 160 (63–460) and 2800 (1000–9400) per 100,000 symptomatic cases (4). Most cases are epidemiologically unrelated (5), but limited non-sustained human-to-human transmission cannot be ruled out and may have occurred among close-related family members (6).

In a clinical study (7), Gao and colleagues found that fever and cough were the most common presenting symptoms. Almost all patients had clinically apparent pneumonia. Multiorgan involvement could be seen during the disease process. Postmortem biopsies of three patients showed acute diffuse alveolar damage (8). Hematological abnormalities commonly seen were leukopenia, lymphopenia, thrombocytopenia, raised hepatic transaminase and creatine kinase levels, and im-

paired coagulation (9). Rapid virological diagnosis was established by RT-PCR for the M, H7, and N9 genes and confirmed by viral culture in cell lines. Serological testing was carried out for epidemiological investigation and screening.

Wang et al. found that rapidly progressive ground-glass opacification and consolidation with air bronchograms and interlobular septal thickening, with right lower lobe predominance, were the main imaging findings in patients with H7N9 pneumonia. The severity of these findings was associated with the severity of the clinical presentation (10). The initial radiological manifestations in our study also presented as bilateral ground-glass opacification or reticular opacification with or without associated focal or multifocal areas of consolidation. Researchers have found that characterization of ground-glass opacification and consolidation is generally pathologically attributable to the partial displacement of air from partial filling of air spaces, thickening of interstitial tissues from fluid or cells, partial alveolar collapse, increased capillary blood volume, or pleural retraction (11). The chest radiographic findings in all of our cases showed bilateral patchy or confluent areas of air-space consolidation or ground-glass opacification. In the second case, it rapidly progressed to diffuse bilateral ground-glass attenuation and air-space consolidation, which suggested progression to ARDS.

In addition to empirical treatment with broad-spectrum antibiotics, antiviral agents, alone or with corticosteroids, have been used in most patients. Extracorporeal membrane oxygenation and artificial liver support systems play an important role in improving oxygenation and maintaining homeostasis.

Implementing control measures, such as prompt isolation of the patient, active monitoring of close contacts, and implementation of standard, contact, and droplet precautions by health care personnel in hospitals are recommended (5). In addition, temporary closure of live bird markets and possible vaccination programs seem necessary and helpful to halt evolution of the virus into a pandemic agent (9). The influenza H7N9 A/Anhui/1/2013 strain has been proposed as a candidate vaccine (3), and research has demonstrated good protection against this strain in mice (12).

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

The authors declare that there is no conflict of interests.

References

1. Centers for Disease Control and Prevention (CDC) (2013). Emergence of Avian Influenza A (H7N9) Virus Causing Severe Human Illness - China, February-April 2013. *MMWR Morb Mortal Wkly Rep*, 62(18):366-71.
2. World health organization (2013). Human infection with avian influenza A (H7N9) virus – update. Available from: http://www.who.int/csr/don/2013_08_11/en/index.html
3. Gao R, Cao B, Hu Y, Feng Z, Wang D, Hu W, et al. (2013). Human Infection with a Novel Avian-Origin Influenza A (H7N9) Virus. *N Engl J Med*, 368(20):1888-97.
4. 4.Yu H, Cowling BJ, Feng L, Lau EH, Liao Q, Tsang TK, et al. (2013). Human infection with avian influenza A H7N9 virus: an assessment of clinical severity. *Lancet*, 382(9887):138-45.
5. Li Q, Zhou L, Zhou M, Chen Z, Li F, Wu H, et al. (2013). Preliminary Report: Epidemiology of the Avian Influenza A (H7N9) Outbreak in China. *N Engl J Med* doi: 10.1056/NEJMoa1304617.
6. Qi X, Qian YH, Bao CJ, Guo XL, Cui LB, Tang FY, et al. (2013). Probable person to person transmission of novel avian influenza A (H7N9) virus in Eastern China, 2013: epidemiological investigation. *BMJ*, 347:f4752.
7. Gao HN, Lu HZ, Cao B, Du B, Shang H, Gan JH, et al. (2013). Clinical findings in 111 cases

of influenza A (H7N9) virus infection. *N Engl J Med*, 368(24):2277-85.

8. Yu L, Wang Z, Chen Y, Ding W, Jia H, Chan JF, et al. (2013). Clinical, virological, and histopathological manifestations of fatal human infections by avian influenza A (H7N9) virus. *Clin Infect Dis* doi: 10.1093/cid/cit541.
9. Chen Y, Liang W, Yang S, Wu N, Gao H, Sheng J, et al. (2013). Human infections with the emerging avian influenza A H7N9 virus from wet market poultry: clinical analysis and characterization of viral genome. *Lancet*, 381(9881):1916-25.
10. Wang Q, Zhang Z, Shi Y, Jiang Y (2013). Emerging H7N9 Influenza A (Novel Reassortant Avian-Origin) Pneumonia: Radiologic Findings. *Radiology*, 268(3):882-9.
11. Mollura DJ, Asnis DS, Crupi RS, Conetta R, Feigin DS, Bray M, et al. (2009). Imaging findings in a fatal case of pandemic swine-Origin influenza A (H1N1). *AJR Am J Roentgenol*, 193(6):1500–3.
12. Smith GE, Flyer DC, Raghunandan R, Liu Y, Wei Z, Wu Y, et al. (2013). Development of influenza H7N9 virus like particle (VLP) vaccine: Homologous A/Anhui/1/2013 (H7N9) protection and heterologous A/chicken/ Jalisco/CPA1/2012 (H7N3) cross-protection in vaccinated mice challenged with H7N9 virus. *Vaccine*, 31(40):4305-13.