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## 12.1 Introduction

Human infected H5N6 avian influenza is an acute respiratory infectious disease caused by H5N6 subtype of avian influenza virus.

On May 6, 2014, throat swab of 1 patient with severe pneumonia showed positive to nucleic acid of H5N6 avian influenza virus in Nanchong, Sichuan, China. Further examination and test by CDC of China proved that the virus is H5N6 subtype of avian influenza virus. The patient reported a history of contact to dead poultry and was clinically diagnosed with acute severe pneumonia. And after emergency rescuing procedures, death still occurred in this patient and this is the first case of human infected H5N6 avian influenza worldwide.

On Dec. 23, 2014, the second case of human infected H5N6 avian influenza worldwide, also the first case in Guangdong province of China, was reported by the Provincial Health and Family Planning Commission in Guangdong. The patient, a 58-year-old man, bought a living chicken in a market and got caught in the rain all the way home on Dec. 22, 2014, and then the symptoms occurred. On the same day, further examination and test by CDC of China proved nucleic acid of H5N6 avian influenza virus positive. On the following day, consultation and analysis by experts group organized by the National Health and Family Planning Commission of China, in combination to the clinical manifestations, laboratory tests and epidemiological history, the diagnosis was

defined to be human infected H5N6 avian influenza. After active therapies in designated hospital of Guangzhou for more than 1 month, the patient was exempted from quarantine and expected to be discharged in recent days.

The symptoms of human infected H5N6 avian influenza resemble to human infected H5N1 and H7N9 avian influenza. After onset, the condition rapidly develops into severe pneumonia, with early respiratory symptoms of fever (with a body temperature of above 38 °C) and cough. In the following 5–7 days after onset, severe pneumonia occurs, with symptoms like dyspnea, which progressively aggravates. Anti-viral medications, such as oseltamivir, are effective for human infected H5N6 avian influenza.

The subtype H5N6 of avian influenza virus is categorized into the family of Orthomyxoviridae and is segmental negative-stranded RNA virus. Other subtypes of avian influenza virus include H5N1 and H7N9 avian influenza viruses. On Aug. 28, 2014, geese in the district of Shuangcheng (in Harbin, Heilongjiang province of China) showed symptoms like avian influenza, with 20550 sick geese including 17790 deaths. By tests in the National Reference Laboratory of Avian Influenza, the disease was defined as highly pathogenic H5N6 avian influenza. By Dec. 31, 2014, 25 outbreaks of H5N6 avian influenza occurred in poultries nationwide, including Heilongjiang, Zhejiang, Hubei, Guangxi, Anhui, Guizhou, Tibet, Guangdong, Hunan, Hebei, Fujian and Yunnan provinces and Chongqing city. Some of the tested samples were from farms, and some from living poultries markets or their environment.

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## 12.2 Typical Cases

### Case 1

#### [Brief Case History]

A 50-year-old man was hospitalized on Apr. 21, 2014 due to chief complaints of fever and cough for 8 days, dyspnea and bloody sputum for 1 day. At d 8 prior to his hospitalization (Apr. 13, 2014), he began to experience aversion to cold, fever (body temperature not reported), systemic soreness and runny nose. He then paid a visit in a local clinic and received oral intake of Chinese patent medicine for cold. However, his condition showed no obvious improvement. On Apr. 18, 2014, his symptoms obviously aggravated, with cough, aversion to cold, fever, systemic soreness, headache and accompanying poor appetite and malaise. After treatment by Compound Amionpyrine Antipyrene Injection and dexamethasone, his condition still showed no improvement. On Apr. 19, 2014, he began to experience abdominal upset, dyspnea, shortness of breath after physical activities, and expectoration of a little bloody sputum. On the following day, chest X-ray showed large consolidation in the left lung and nodular patches of opacity in the right upper lung. By the test of CDC in Nanyun, Sichuan province on Apr. 21, 2014, the nucleic acid of H5N6 avian influenza was shown positive. And death finally occurred on Apr. 22, 2014 after emergency rescuing procedures. By physical examination on admission, the body temperature was 37.3 °C, heart rate 96/min, breathing rate 30/min and blood pressure 106/74 mmHg. He showed complexion of acute disease, good consciousness, and poor spirits. By percussion, dull sound of the left lung and a little sporadic fine moist rales; while clear breathing sound of the right lung and no dry or moist rales. No other positive signs found. The patient was a farmer who had raised and saled poultries (including chickens and ducks) for a long time. He reported recent deaths of his poultries and a history of cooking and eating them. By routine blood test, WBC count  $1.48 \times 10^9/L$ , GR% 82.4%, and LY% 12.8%. By arterial blood glass analysis, PO<sub>2</sub> 55.0 mmHg, PCO<sub>2</sub> 34.0 mmHg, SaO<sub>2</sub> 91.0%; CRP 252.00 mg/L, PCT 3.600 ng/ml. By blood biochemistry, AST 84.4U/L, and Cr 70.8 μmol/L. On May 6, 2014, the tests by the National CDC of China further proved the diagnosis of human infected H5N6 avian influenza.

[Radiological demonstration] Fig. 12.1

[Diagnosis] Pneumonia induced by human infected H5N6 avian influenza

#### [Discussion]

In this case, the patient was the first case of human infected H5N6 avian influenza worldwide, with acute onset and rapid progression. His clinical manifestations were characterized by:

1. Definitive epidemiological history of contact.

The patient was a farmer who had raised and saled poultries (including chickens and ducks) for a long time. He reported recent deaths of poultries and a history of cooking and eating them.

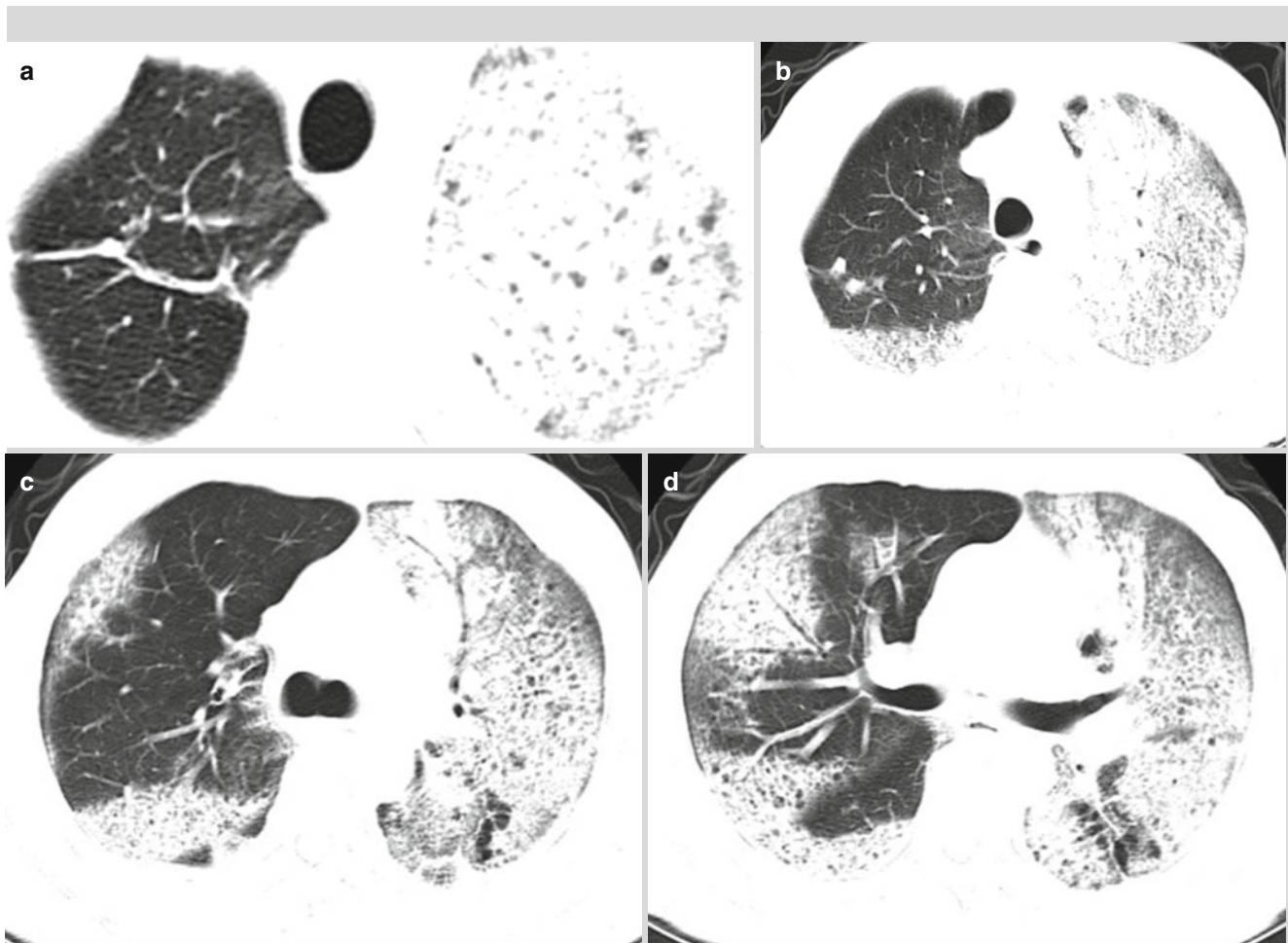
2. He experienced influenza like symptoms, including fever, cough, dyspnea and accompanying expectoration of bloody sputum.
3. Acute onset and rapid progression.

On d 7 after onset, the patient began to experience dyspnea and other symptoms of severe pneumonia, which progressively aggravated and finally developed into ARDS and death.

The radiological demonstrations are characterized by:

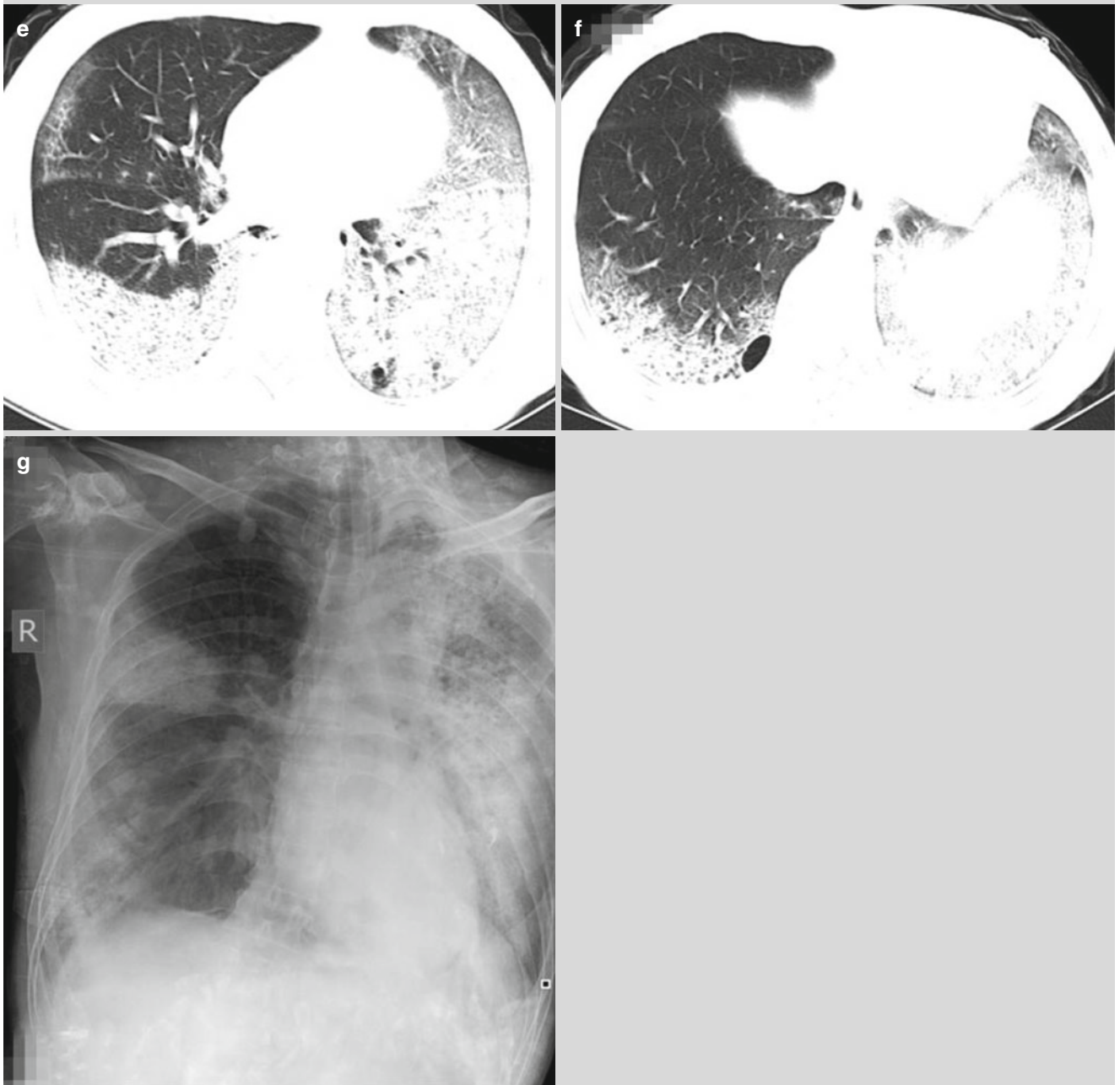
1. On d 8 after onset, chest CT scan showed that the lung lesions predominantly as consolidation and GGO, with multiple lobes and segments involved; obvious lesions in the lateral part of cortex.
2. On d 9 after onset, bedside chest X-ray demonstrated progression of lesions in the right lung, with enlarged areas of consolidation and GGO as well as lesions of ARDS. Meanwhile, pleural effusion in a small quantity in the left pleural cavity indicated progression of the disease.

Rapid progression and extensive lesions are the commonalities of pneumonia induced by type A influenza virus. In this first case of pneumonia induced by H5N6 avian influenza virus worldwide, due to our limited knowledge about radiological signs of the disease, its differential diagnosis from pneumonia induced by H7N9, H5N1, H5N6 avian influenza viruses and other type A influenza viruses is challenging. And the diagnosis was defined based mainly on the epidemiological history and etiological examination.



**Fig. 12.1** On d 8 after onset, chest CT scan demonstrated large flakes of increased density opacity in the left upper lung; cords like opacity in the right upper lung (a). The left upper lung was revealed with large flakes of increased density opacity, with flakes of increased density opacity in the apical posterior segment (b). The layer of bronchial bifurcation was revealed with large opacity of increased density in the left upper lung; with strips of increased density opacity in the subpleural area of the right upper lung lobe (c). The subcarinal layer was shown with consolidation in the left lung; with flakes of consolidation opacity in the middle and lateral areas of the right upper and middle lung lobes as well as the posterior

basilar segment of right lower lung lobe (d). The layer of right inferior pulmonary vein was shown with large consolidation in the left lung and the left lower lung; with GGO in the subpleural area of right middle lung lobe and the right lingual lung lobe (e). The layer of diaphragmatic dome was revealed with consolidation in the subpleural area of posterior basilar segment of right lower lung lobe and the left lower lung lobe; with lung bullae of 1.5 cm in diameter in the subpleural area of posterior segment of right lower lung lobe (f). On d 9 after onset, bedside chest X-ray showed large consolidation in the left lung and the right upper lung field; large GGO in the right middle and lower lung fields (g)



**Fig. 12.1** (continued)



## Case 2

### [Brief Medical History]

A 59-year-old man was hospitalized due to fever for 14 days and shortness of breath for 9 days. Fourteen days prior to his hospitalization, he began to experience fever with his body temperatures fluctuating between 39 and 40 °C and aversion to cold. After oral intake of Compound Pseudoephedrine Hydrochloride tablets by himself, his condition failed to be improved. He experienced no cough, expectoration, hemoptysis, chest distress and pain. Eight days prior to his hospitalization (d 6 after onset), his condition aggravated and he paid his clinic visit in a local hospital. He was preliminarily diagnosed with bacterial infection and given anti-infection therapy (details not known), with poor therapeutic efficacy. Chest X-ray in the local hospital showed multiple infections in both lungs. Routine blood test showed WBC count  $6.6 \times 10^9/L$ , GR% 91.6% and LY% 15.6%; PCT 1.21 ng/ml. Tablets of Ceftriaxone and Moxifloxacin Hydrochloride were prescribed to fight against infections, and non-invasive mechanical ventilation was ordered. Six days prior to his hospitalization (d 8 after onset), the patient showed aggravation of shortness of breath, with  $SpO_2$  level of 50–70%. Assisted ventilation via tracheal intubation was then ordered. Meanwhile, throat swab showed nucleic acid of H5 subtype of avian influenza virus positive, fungi positive (++++) in feces, and fungi positive in phlegm, which indicated highly pathogenic human infected avian influenza and severe pneumonia. Medications of Imipenem, Oseltamivir and Ethylprednisolone Sodium Succinate were prescribed, but showing poor therapeutic efficacy. The patient had a medical history of colon cancer 1 year ago, which was treated by sigmoidectomy in another hospital with following 4 sessions of chemotherapy. Reexamination 2 months ago in that hospital indicated no relapse of cancer. More than 30 years ago, the patient had a medical history of pulmonary tuberculosis, which was cured. By physical examination, the body temperature 36.6 °C and  $SpO_2$  95%; assisted ventilation via tracheal

intubation; weakened fremitus vocalis by palpation; dullness of both lungs by percussion; weak breathing sounds of both lungs and moist rales of both lower lungs by auscultation. He reported a history of buying a living poultry in a market that provided slaughtering service.

[Radiological demonstration] Fig. 12.2

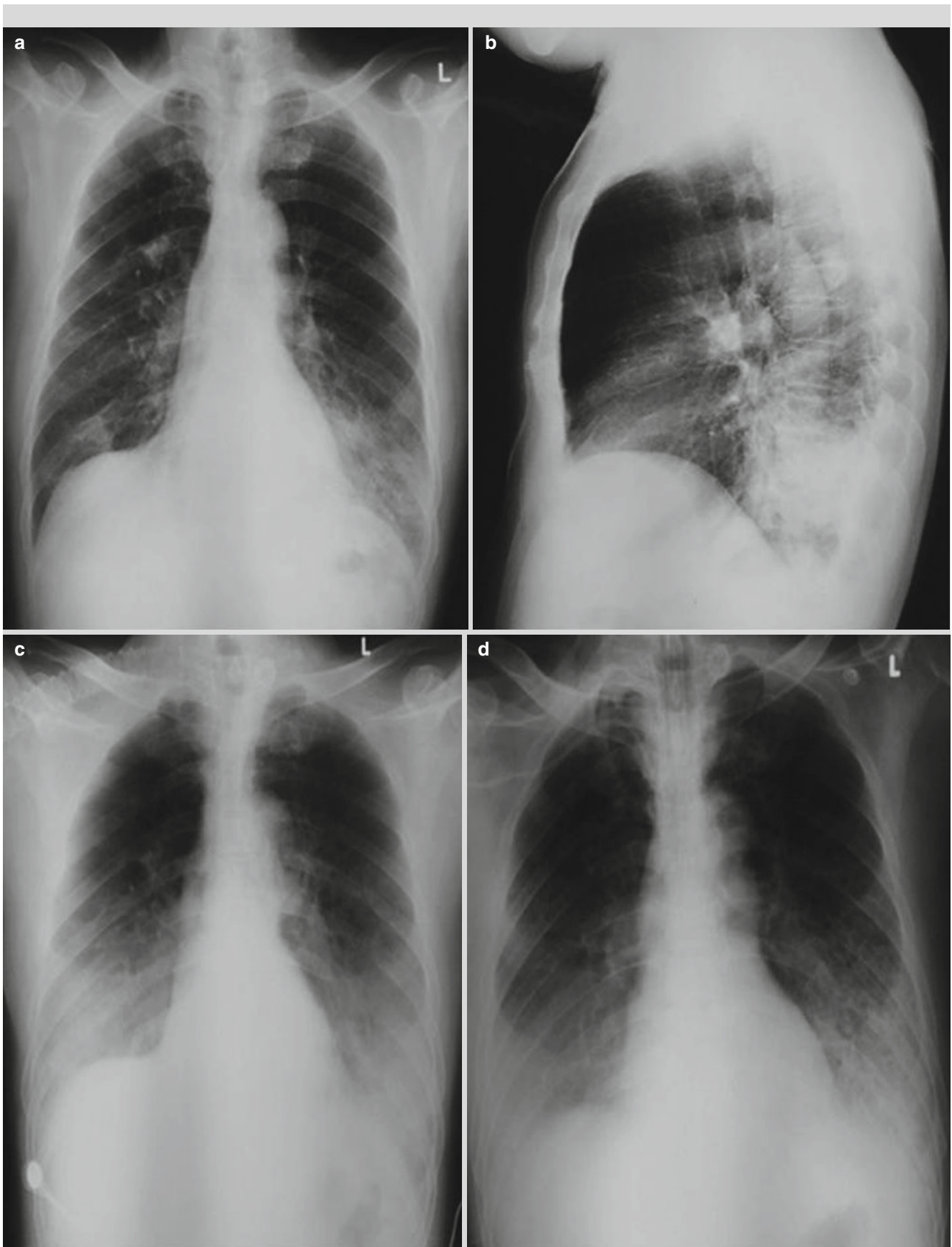
### [Discussion]

In this case of human infected H5N6 avian influenza, poorly defined patches of opacity and consolidation were radiologically revealed, multiple and sporadic, which were exudative lesions. These lesions mainly distributed in the middle and lower lung fields, with both lungs involved, and progressed rapidly, with fusion and extension within a short period of time. And the area with consolidation enlarged to involve multiple lobes and segments of both lungs. These radiological findings are in consistency with literature reports about pneumonia induced by avian influenza virus. On d 14 after onset, CT scan showed pleural effusion in a small quantity, which rarely occurs in the cases of SARS and other avian influenza virus pneumonia. Meanwhile, by deep phlegm culture, acinetobacter baumannii was positive, which may be the reason for pleural effusion. After that, anti-inflammatory treatment was strengthened, and the lesions were gradually controlled and improved.

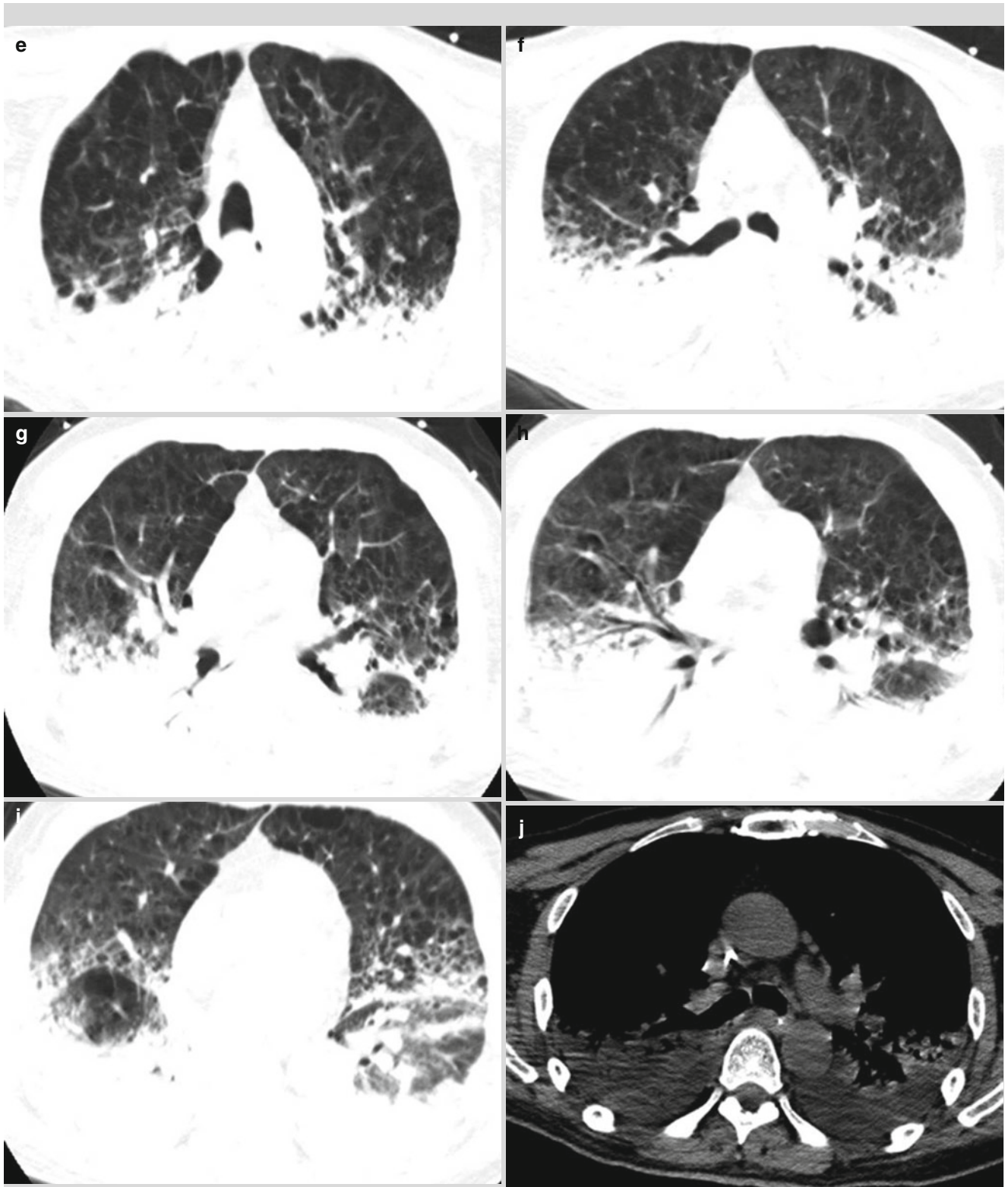
Radiologically, the disease should be differentiated from bacterial pneumonia, mycoplasma pneumonia and SARS. In the cases of human infected H5N6 avian influenza, the poorly defined patches of opacities distribute in both lungs, with multiple lesions and rapid progression. However, bacterial pneumonia is characterized by limited segmental consolidation and increased WBC count in peripheral blood. Prevalence of mycoplasma pneumonia is seasonal and is more common in children, with lesions in one lung and possibly in both lungs. By radiological follow-ups, the lung lesions in the cases of mycoplasma pneumonia hardly change within a short period of time. And its differential diagnosis from other infectious viral pneumonia is mainly based on epidemiological history and etiological examination.

**Fig. 12.2** On d 6 after onset, anterior-posterior and lateral chest X-rays demonstrated multiple poorly defined patches of opacity in both lower lung fields, predominantly in the left lower lung; partial consolidation in the posterior basilar segment of left lower lung; consolidated nodules in the right upper lung (tuberculomas defined by CT scan) (a, b). On d 8 after onset, reexamination by chest X-ray showed multiple poorly defined patches of opacity and consolidation in the middle and lower lung fields of both lungs, predominantly in both lower lungs; obviously increased lesions (c). On d 10 after onset, reexamination by chest X-ray demonstrated multiple poorly defined patches of opacity and consolidation in the middle and lower lung fields of both lungs; poorly defined patches of opacity in the left upper lung field (d). On d 14 after onset, chest CT scan

showed multiple poorly defined opacity and consolidation in both lungs, predominantly ground glass opacity in the anterior lungs and consolidation in the dorsal lungs; air bronchogram in the consolidation opacity. The lesions predominantly distributed in the dorsal parts of both lower lungs. The lesion of tuberculomas in the posterior segment of right upper lung calcified. Bilateral pleural effusion was shown in a small quantity, more in the left pleural cavity. Partial atelectasis was shown in the posterior basilar segment of both lower lungs due to compression (e–k). On d 23 after onset, chest CT scan demonstrated obviously decreased lesions in both lungs, relatively decreased pleural effusion and improved atelectasis of dorsal lungs (l–o). On d 50 after onset, chest CT scan showed absorption of most lesions and sporadic cords like opacity in both lungs (p–s)

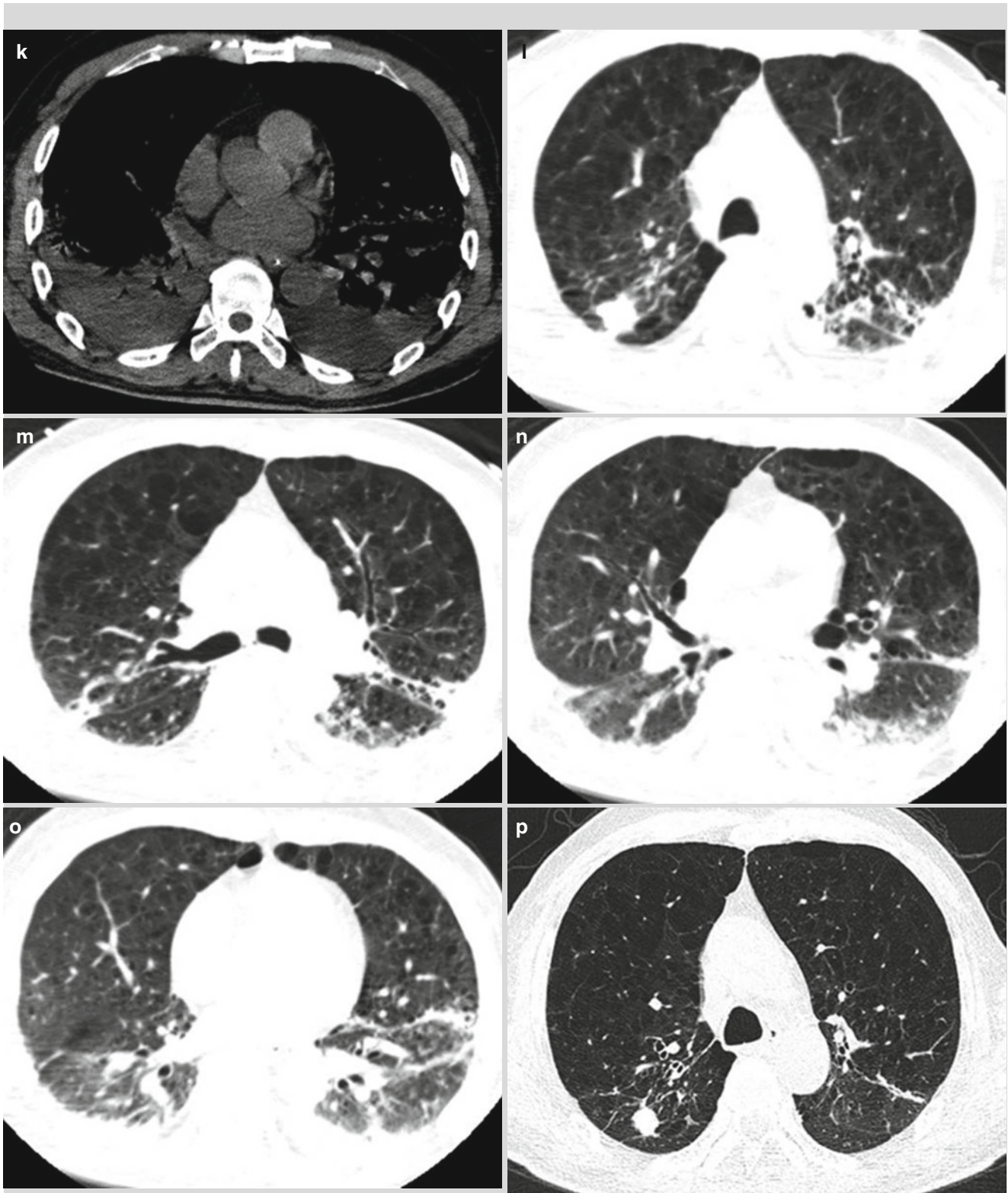


**Fig. 12.2** (continued)



**Fig. 12.2** (continued)





**Fig. 12.2** (continued)





**Fig. 12.2** (continued)

## References

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