Original article

Bedside chest radiography of novel influenza A (H7N9) virus infections and follow-up findings after short-time treatment

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Background Influenza A (H7N9) virus infections were first observed in China in March 2013. This type virus can cause severe illness and deaths, the situation raises many urgent questions and global public health concerns. Our purpose was to investigate bedside chest radiography findings for patients with novel influenza A (H7N9) virus infections and the follow-up appearances after short-time treatment.

Methods Eight hospitalized patients infected with the novel influenza A (H7N9) virus were included in our study. All of the patients underwent bedside chest radiography after admission, and all had follow-up bedside chest radiography during their first ten days, using AXIOM Aristos MX and/or AMX-IV portable X-ray units. The exposure dose was generally 90 kV and 5 mAs, and was slightly adjusted according to the weight of the patients. The initial radiography data were evaluated for radiological patterns (ground glass opacity, consolidation, and reticulation), distribution type (focal, multifocal, and diffuse), lung zones involved, and appearance at follow-up while the patients underwent therapy.

Results All patients presented with bilateral multiple lung involvement. Two patients had bilateral diffuse lesions, three patients had unilateral diffuse lesions of the right lobe with multifocal lesions of the left lobe, and the remaining three had bilateral multifocal lung lesions. The lesions were present throughout bilateral lung zones in three patients, the whole right lung zone in three patients with additional involvement in the left middle and/or lower lung zone(s), both lower and middle lung zones in one patient, and the right middle and lower in combination with the left lower lung zones in one patient. The most common abnormal radiographic patterns were ground glass opacity (8/8), and consolidation (8/8). In three cases examined by CT we also found the pattern of reticulation in combination with CT images. Four patients had bilateral and four had unilateral pleural effusion. After a short period of treatment the pneumonia in one patient had significantly improved and three cases demonstrated disease progression. In four cases the severity of the pneumonia fluctuated.

Conclusions In patients with influenza A (H7N9) virus infection, the distribution of the lung lesions are extensive, and the disease usually involves both lung zones. The most common imaging findings are a mixture of ground glass opacity and consolidation. Pleural effusion is common. Most cases have a poor short-time treatment response, and seem to have either rapid progressive radiographic deterioration or fluctuating radiographic changes. Chest radiography is helpful for evaluating patients with severe clinical symptoms and for follow-up evaluation.

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Influenza A (H7N9) virus infections were first observed in China in March 2013. Six cities have reported laboratory-confirmed cases of H7N9, mainly in coastal cities such as Shanghai (33 cases), Jiangsu (23 cases) and Zhejiang (33 cases). Influenza A viruses belong to the family Orthomyxovirus, with 16 varieties of hemagglutinin and 9 varieties of neuraminidase proteins used for sub-typing;[1] the influenza A (H7N9) virus is one subtype. Because the introduction of this subtype into humans in Asia has not been observed previously[1,2] and because this subtype can cause severe illness and deaths, the situation raises many urgent questions and global public health concerns.[3] The bedside chest X-ray (CXR) is an indispensable diagnostic tool for monitoring seriously ill patients.[4] Because most patients with H7N9 are severely ill, bedside chest radiography is a necessity. We now report the bedside chest radiography for influenza A (H7N9) virus infections patients at initial diagnosis and at follow-up after treatment.

METHODS

Of the twelve hospitalized patients with influenza A H7N9 infections in the Shanghai Public Health Clinical Center, eight underwent bedside chest radiography (three also had a CT scan) within 24 hours after admission, and they all had follow-up chest X-rays (CXRs) every day or every other day, using AXIOM Aristos MX (Siemens Medical Solutions Forchheim, Germany) and/or AMX-IV (GE Medical Systems, Waukesha, WS) portable X-ray units. The exposure dose was generally 90 kV and 5 mAs,

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Table 1. Summary of the clinical presentation

Cases	Age (years)	Sex	Time of admission (days after onset)	Symptoms				Co-existing medical condition	Epidemic history
				BT (°C)	Cough	Hyper-ponea	Expectoration		
1	81	F	5	39.0	Yes	No	No	No	Unknown
2	78	M	10	39.0	Yes	No	Yes (white phlegm)	Hypertension for 10 years	Unknown
3	75	F	10	39.0	Yes	Yes	Yes	Hypertension for 28 years, coronary heart disease for 7 years, post-mastectomy 2 years	Yes
4	74	M	7	39.3	Yes	Yes	No	Coronary heart disease for 5 years	Yes
5	65	M	5	39.0	Yes	No	Yes (blood in white phlegm)	Hypertension for 5 years, gout for 3 years	Unknown
6	62	M	10	39.0	Yes	Yes	Yes (white phlegm)	Hypertension for 10 years	Unknown
7	58	M	15	39.7	Yes	Yes	Yes	Hypertension for 5 years	Denied
8	56	M	3	39.0	Yes	No	No	No	Wife died of H7N9

F: female. M: male. BT: body temperature.

and was slightly adjusted according to the weight of the patients. Our subjects included the eight patients who underwent bedside chest radiography (six males and two females). The age of the patients ranged from 56 to 81 years (mean±SD: (68.6±8.9) years) (Table 1). Oropharyngeal and/or nasopharyngeal specimens for all patients were evaluated by real-time polymerase chain reaction (RT-PCR) and were positive for H7N9. Some patients underwent an additional microbiological evaluation for bacterial and fungal infections.

The initial CXR were evaluated for radiological patterns (ground glass opacity, consolidation, and reticulation), distribution types (focal, multifocal, and diffuse), lung zones involved, extent of the disease and appearances at follow-up. Two experienced radiologists reviewed all the images. Whenever a previous radiograph was available, the new CXR was compared to the previous one.

Ground glass opacity is defined as an area of hazy increased lung opacity within which the definition of lung structures is usually preserved; this pattern is less opaque than consolidation.[1,5,6] Consolidation is defined as a homogeneous increase in the pulmonary parenchymal attenuation, which obscures the margins of vessel and airways.[1,5,6] Reticular opacities are defined as linear opacities forming a web pattern.[1,7,8] The distribution of abnormalities is categorized as focal, multifocal or diffuse. A focal distribution is defined as a single focus of abnormality. A multifocal distribution describes more than one focus with further classified as unilateral or bilateral. A diffuse distribution is defined as an abnormality that involves an equivalent volume of one or both lung(s).[1,5,9] The location of each abnormality on the CXR is divided into the upper, middle or lower zone; based on dividing the vertical distance between the apices and the hemidiaphragmatic domes into thirds.[1,5,9]

RESULTS

Our study included eight patients with a confirmed diagnosis of H7N9 influenza virus infection who had undergone bedside chest radiography. Their ages ranged from 56 to 81 years; mean±SD was (68.6±8.9) years. Six were males and two were females. The date of admission ranged from 3 to 15 days after onset, and the average was (8.1±3.6) days. Six had co-existing medical conditions, such as hypertension or coronary heart disease. All the cases had a fever above 39ºC and a cough, four had hyperpnoea and five had expectoration, including one with blood in white phlegm. One case had a concurrent gram-positive cocci infection, while one had a concurrent yeast infection. With respect to epidemiological history, exposure to poultry was reported in two cases and denied in one case, the wife of one case died of H7N9, and the other four cases had no specific exposure history (Table 1).

Table 2. Radiologic findings of patients with influenza A (H7N9) virus infections

Cases	Distribution	Pattern	Lung zones	Pleural effusion	Follow-up
1	Multifocal (bilateral)	Ground glass opacity Consolidation	Both middle and lower	Right	Progression every day for five days
2	Diffuse (right) Multifocal (left)	Ground glass opacity Consolidation	The whole right and left lower	Right	Improvement on day 2, progression on day 4, then improvement on day 6
3	Diffuse (right) Multifocal (left)	Ground glass opacity Consolidation Reticulation	The whole right and left lower	Both	Progression on day 2, improvement after 3 days
4	Diffuse	Ground glass opacity Consolidation Reticulation	Both	Left	Progression on day 3, improvement after 5 days and rapid progression on day 7
5	Multifocal (bilateral)	Ground glass opacity Consolidation	Both	Both	Prominent improvement after one week (discharged, negative oropharyngeal specimen)
6	Diffuse (right) Multifocal (left)	Ground glass opacity Consolidation	The whole right, left middle and lower	Both	Progression of left lung lesions, improvement of right lung lesions on day 2, while progression on day 5
7	Diffuse	Ground glass opacity Consolidation	Both	Left	Progression on day 3, rapid progression on day 7 (gram positive cocci sputum smear positive on day 5)
8	Multifocal (bilateral)	Ground glass opacity Consolidation Reticulation	Right middle and lower, left lower	Both	Progression and rapid progression on day10 (yeast mycelium and spore sputum smear positive on day 8)

The CXR findings are summarized in Table 2. The total volume of the affected areas in any patient was more than one single lobe. Two patients had bilateral diffuse lesions, three patients had unilateral diffuse lesions of the right lobe with multifocal lesions of the left lobe, and the remaining three had bilateral multifocal lung lesions. The most common abnormal radiographic patterns were ground glass opacity (8/8) and consolidation (8/8) (Figure 1), which were present in the entirety of both lung zones in three, the entire right lung zone with the left middle and/or lower lung zone(s) in three, both middle and lower lung zones in one, and the right middle and lower lung zones with the left lower lung zone involved in one patient. Four patients had bilateral and four had unilateral pleural effusion. In three cases viewed by CT we can also find a pattern of reticulation in combination with CT images (Figure 2).

After steroids and antiviral drug treatment, we reevaluated the follow-up CXR images. One case (case 5) showed improvement of clinical symptoms (fever, cough and hyperpnoea) and prominent absorption of the pneumonia on the X-ray images (Figure 2). The patient was finally discharged with a negative oropharyngeal specimen after one-week of treatment. Three cases had pneumonia progression (Figure 3). In the remaining four cases, the severity of the pneumonia fluctuated (Table 2 and Figure 4). Two cases with concurrent infection of gram positive cocci or yeast showed significant rapid progression of the lung lesions.

DISCUSSION

In this study, the eight patients were in an older age category, ranging in age from 56 to 81 years with the average age of (68.6±8.9) years. Fever (8/8) and cough (8/8) were the most common symptoms, and sometimes occurred in combination with hyperpnoea (4/8) and expectoration (5/8). In general, the distribution of the disease was extensive. All eight cases had multifocal lesions that usually involved both lung zones, including bilateral or unilateral (right) diffuse lesions in five patients. The most common radiologic findings of the novel influenza A (H7N9) were ground glass opacity and consolidation. In three cases, we also found the pattern of reticulation in combination with CT images. Because of the limitations of bedside chest X-ray, CT was used to produce more imaging details of the lesions. All patients had pleural effusion. Two cases had superimposed infections, which may have made their conditions more serious.

In seven patients, pneumonia progressed or fluctuated on CXR images after treatment, suggesting most cases with severe pneumonia have a poor response to medical management. In the responding one, case 5, the affected lung areas were much smaller than the other seven cases. This case had a favorable prognosis and the patient was discharged after one-week of treatment. The early positive response to therapy in this case could be attributed to the early disease stage of the patient given that viral infection commonly produces extensive regions of either diffuse or localized diffuse alveolar damage in late stages.[10] Another possible explanation is that this patient had no concurrent infections and was admitted earlier.

The distribution, rapid progression of fluctuations of pneumonia, and consolidations may help differentiate H7N9 infection from other causes of pneumonia. For example, streptococcus pneumonia progresses more slowly than H7N9, and usually has a marked improvement after treatment. Diffuse parenchymal involvement is more often associated with viral pneumonia, but the radiologic findings are non-specific and may overlap with those of other thoracic viral pneumonias, such as H1N1 virus infection, sever acute respiratory syndrome (SARS),

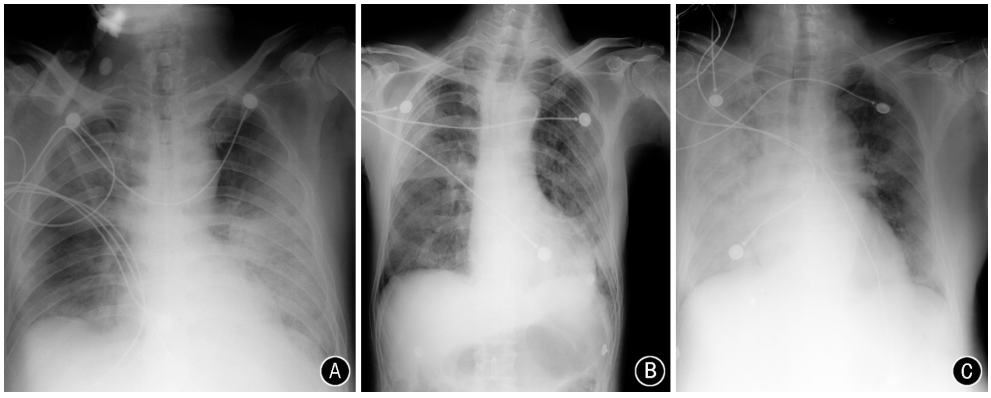

Figure 1. Chest X-ray of three patients shows the distribution of the disease: diffuse **(A)**, multifocal **(B)**, diffuse (right) and multifocal (left) **(C)**, and the pattern of the disease: ground glass opacities and consolidations.

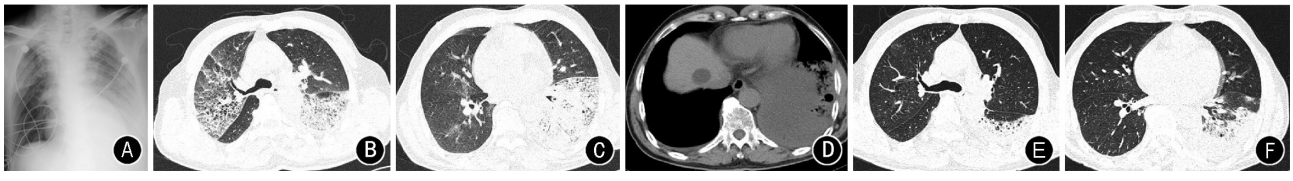

Figure 2. Chest X-ray and CT of a 65-year-old male diagnosed with H7N9 show bilateral, extensive, diffuse ground-glass opacities, consolidation, and reticulation (**A**–**C**), with bilateral pleural effusion (**D**). After treatment, the lung lesions disappeared (**E** and **F**) prominently.

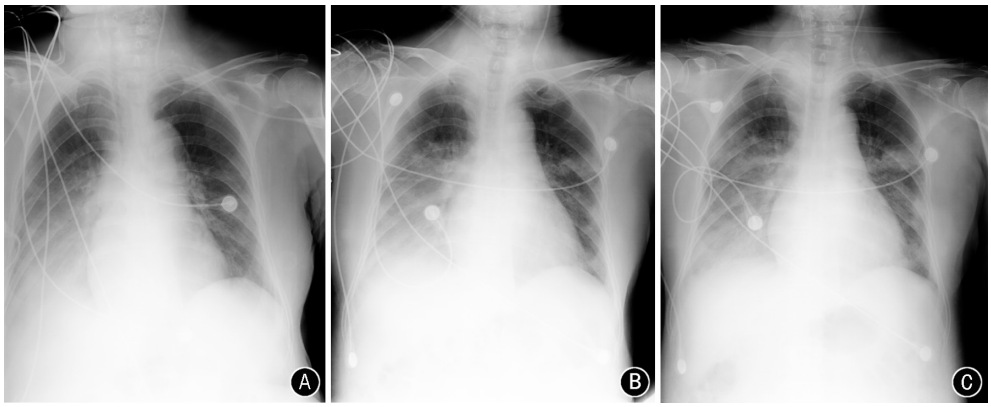

Figure 3. Three images of an 81-year-old female were obtained on days one (**A**), two (**B**), and three (**C**) after admission. Chest X-ray shows bilateral lung lesions that progressed extensively during treatment.

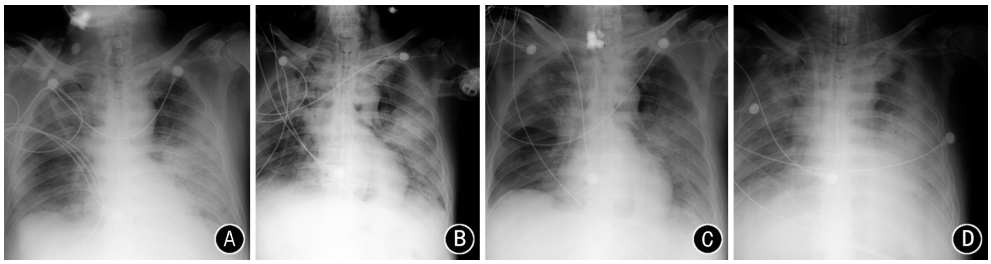

Figure 4. Four images of a 58-year-old male (the same patient of Figure 1A) were obtained on days one (**A**), three (**B**), five (**C**) and seven (**D**) after admission. Chest X-ray shows bilateral diffuse lung lesions that mildly progressed on day three, mildly absorbed on day five, and finally extensively progressed on day seven during treatment.

corona virus infection, and avian of influenza A (H5N1),[11] and the differential diagnosis is difficult by CXR. The final diagnosis cannot be made by the imaging features alone, and should be confirmed with laboratory tests.

CXR is usually the first imaging test performed for the assessment of acute respiratory symptoms, and sometimes the only way to evaluate the presence of pneumonia in follow-up, especially in those patients with severe pneumonia. We observed all patients after treatment in our study with CXR. As during the severe acute respiratory syndrome outbreak, patients with avian influenza A (H7N9) seemed to have either rapid progressive radiographic deterioration or fluctuating radiographic changes.

Our study has some limitations. First, our study had a small number of patients and few had CT scans performed. Therefore, we did not conduct statistical analysis of the patients. Second, all patients were from Shanghai. In the near future, a multicenter study comprising a larger group of patients is needed to explore imaging findings in more details.

In conclusion, the most common lung imaging findings of influenza A (H7N9) virus infections are a mixture of ground glass opacity and consolidation. On X-ray images, the distribution of the lesions is extensive, and the disease usually involves both lung zones. Pleural thickening or effusion is common. Most cases have a poor short-time treatment response, and seem to have either rapid progressive radiographic deterioration or fluctuating radiographic changes. Chest radiography is helpful for identifying patients with severe clinical symptoms and for follow-up evaluation.

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