Original Article

Severe adenovirus community-acquired pneumonia in immunocompetent adults: chest radiographic and CT findings

Dingyu Tan[1*], Yangyang Fu[1*], Jun Xu[1*], Zhiwei Wang[2], Jian Cao[2], Joseph Walline[3], Huadong Zhu[1], Xuezhong Yu[1]

[1]Department of Emergency, [2]Department of Radiology, Peking Union Medical College Hospital, Chinese Academy of Medical sciences, Beijing 100730, China; [3]Division of Emergency Medicine, Department of Surgery, Saint Louis University Hospital, Saint Louis, Missouri, USA

Contributions: (I) Conception and design: J Xu, X Yu, D Tan, Y Fu; (II) Administrative support: H Zhu, X Yu; (III) Provision of study materials or patients: J Xu, H Zhu, X Yu; (IV) Collection and assembly of data: D Tan, Y Fu, J Walline; (V) Data analysis and interpretation: D Tan, Y Fu, Z Wang, J Cao; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*These authors contributed equally to this work.

Correspondence to: Jun Xu, MD. Department of Emergency, Peking Union Medical College Hospital, Chinese Academy of Medical sciences, Beijing 100730, China. Email: xujunfree@126.com; Xuezhong Yu, MD. Department of Emergency, Peking Union Medical College Hospital, Chinese Academy of Medical sciences, Beijing 100730, China. Email: yxzpumch@126.com.

Background: Severe adenovirus pneumonia and its associated imaging features are well-described in immunocompromised patients but are rare and poorly understood in immunocompetent adults. We sought to describe the radiographic and CT findings of severe adenovirus community-acquired pneumonia (CAP) in eight immunocompetent adults.

Methods: We reviewed systematically chest imaging manifestations of laboratory-confirmed severe adenovirus pneumonia in eight immunocompetent adults from April 2012 to April 2014.

Results: All patients showed abnormal results on initial chest radiograph and CT, with the exception of one normal initial chest radiograph. The abnormalities of the initial chest radiographs were unilateral (n=4) or bilateral (n=3), including consolidation (n=4), dense patchy opacity (n=3), ground glass opacity (GGO) (n=1), and pleural effusion (n=1). The initial CT findings consisted of unilateral (n=5) and bilateral (n=3) abnormalities, including consolidation (n=8), GGO (n=2), pleural effusion (n=3) and small nodules (n=1). Focal consolidation was the predominant finding in six patients whose initial CT scans were examined within one week after illness onset. Follow-up radiologic findings showed rapid development of bilateral consolidation within ten days after illness onset, usually accompanied by adjacent ground-glass opacity and pleural effusion. The parenchymal abnormalities began to absorb around two weeks after illness onset, with no appearances of fibrosis.

Conclusions: Severe adenovirus CAP in immunocompetent adults mainly appears as focal consolidation followed by rapid progression to bilateral consolidation, usually accompanied by adjacent GGO and pleural effusion, which may resemble bacterial pneumonia. Adenovirus should be considered in severe pneumonia cases with negative cultures and failure to respond to antibiotics.

Keywords: Adenovirus; CT; infectious diseases; pneumonia; radiography

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Introduction

Adenovirus pneumonia typically is limited to newborns, immunodeficient hosts, and school or military camp populations (1). Severe adenovirus pneumonia has been frequently described in immunocompromised patients. However, with the advances and widespread use of viral screening, adenovirus has been increasingly found to be involved in sporadic cases and outbreaks of severe community-acquired pneumonia (CAP) in healthy adults (2,3).

Bilateral interstitial infiltrates were previously reported as the principal imaging findings in adults with adenovirus pneumonia, regardless of immune status (2,4,5). However, cytolysis, hemorrhagic necrosis, and grossly congested, consolidated lungs are the typical pathological changes seen in adenovirus pneumonia (1). More and more research supports consolidation rather than interstitial infiltrates as the main imaging characteristic of adenovirus pneumonia in immunocompetent adults (3,6-9), though only a few reports have included supporting CT findings (10,11). The purpose of this study was to describe the radiographic and CT findings of severe adenovirus CAP in eight immunocompetent adults.

Methods

Patients and clinical materials

From April 2012 to April 2014, viral screening was carried out for the etiological study of adult severe unexplained CAP at the Emergency Intensive Care Unit of Peking Union Medical College Hospital. Lower respiratory tract specimens of 128 patients were sent to the Institute of Medical Biology of Chinese Academy of Medical Sciences, to test for respiratory viruses. Eight sporadic cases were confirmed as adenovirus infection through sputum (n=2), tracheal aspirates (n=4) and bronchoalveolar lavage fluids (n=2) by means of real-time polymerase chain reaction (PCR) testing. Adenovirus serotyping were also performed (*Table 1*). HIV serology and microbiological tests including bacterial, fungal or viral cultures for rhinovirus, cytomegalovirus, influenza virus, metapneumovirus, parainfluenza virus, coronavirus, or respiratory syncytial virus were negative at admission in all eight patients. Three cases infected *Acinetobacter baumannii* during mechanical ventilation in the later phase of hospitalization. Bacterial tests included: (I) sputum specimens for staining and microbiological cultures; (II) urine specimens for *Legionella pneumophila* and *S. pneumonia* antigen detection; (III) blood culture; (IV) acute and convalescent serum samples for *Chlamydia Pneumoniae*, *Mycoplasma pneumoniae* and *Legionella pneumophila* antibody titer determination. We reviewed retrospectively the chest imaging manifestations of these patients. The institutional ethics review board approved this retrospective study.

There were eight patients (male-female ratio, 3:1) with an age range from 22 to 52 years (mean age, 35.9 years) (*Table 1*). Six patients had no significant underlying disease, while one patient had a history of cerebral infarction and hypertension, and another patient had hypertension, type 2 diabetes and asthma. None of the patients were severely immunocompromised. The major symptoms at presentation were high fever(>39 ℃) (n=8), dyspnea (n=8), cough (n=8), ARDS (n=8), septic shock (n=4), hemoptysis (n=4), chest pain (n=3), diarrhea (n=2), myalgias (n=1), and sore throat (n=1). The time interval from illness onset to admission was 1–15 days with a median of 6 days. Acute Physiology and Chronic Health Evaluation 2 (APACHE II) score at admission ranged from 4 to 17 [mean, 12.5±4.8 (SD)]. Empirical broad-spectrum intravenous antibiotics were given to all the patients, while one was prescribed oseltamivir prior to the confirmation of viral pneumonia in our study. Four patients received adjuvant intravenous immunoglobulin for 3–5 days, while five received corticosteroids for 3–7 days, including hydrocortisone or methylprednisolone. Six patients required invasive mechanical ventilation with a duration range from 8 to 23 days and a median of 11.5 days. The sole death was a 52-year-old man with three comorbidities, who died after 23 days of mechanical ventilation.

Imaging techniques

Chest radiographs were performed using computed radiography or portable computed radiography at bedside, both of which were performed in the anteroposterior projection. Some of the initial CT scans were performed in different institutions, where different types of scanners and protocols were used. The technical parameters included 0.625, 0.75 or 1 mm collimation at 2–7 mm section thicknesses. All CT scans were performed at the end of a deep inhalation with the patient in the supine position, without contrast administration with the exception of one patient. Images were photographed on both lung (window width 1,200–1,600 HU; level −500 to −700 HU) and mediastinal (window width 350–450 HU; level 20–40 HU) settings.

Table 1 Adenovirus serotype and radiological findings in patients identified with severe adenovirus community-acquired pneumonia

Patient No.	Patients' age/sex	Adenovirus serotype	Initial chest radiograph		Initial CT scan	
			Time (day)*	Main findings	Time (day)*	Main findings
1	29/F	7	9	Bilateral diffuse consolidation	5	LUL consolidation
2	38/M	55	2	LLL dense infiltration	2	LLL consolidation
3	52/M	3	6	RUL dense infiltration	13	Bilateral diffuse consolidation and right pleural effusion
4	52/M	55	4	LLL dense infiltration	5	LLL consolidation
5	33/M	55	7	Bilateral GGO, accompanied by partial consolidation and left pleural effusion	9	Bilateral GGO, accompanied by partial consolidation and bilateral pleural effusion
6	22/M	7	3	None	3	RLL focal consolidation
7	23/M	55	1	RLL consolidation	4	RLL consolidation and right pleural effusion
8	38/F	11	6	Bilateral lower lobe consolidation	7	Bilateral multifocal consolidation with slight patchy GGO and small nodules

*, time interval from illness onset to imaging. Note: LUL, left upper lobe; LLL, left lower lobe; RUL, right upper lobe; RLL, right lower lung; GGO, ground-glass opacity.

Image analysis

Two chest radiologists (with 15 and 8 years of experience in thoracic imaging, respectively) interpreted the images obtained before and after admission independently, with the decisions made by consensus in case of disagreement. They were blinded to the clinical information of the patients. Each lung was divided into upper and lower zones on radiographs for purposes of analysis. Abnormalities were considered to be distributed to the upper lung zone when they were located above the hilum, to the lower lung zone when they were located under the hilum, or random when both zones were involved. Criteria for chest radiographic and CT findings findings were preferentially defined according to the "Fleischner Society's Glossary of Terms" (12).

Results

Chest radiographic findings

Seven of the eight initial chest radiographs, which were obtained at 1–9 days [mean, 4.8±2.5 (SD) days] after the onset of illness, showed abnormal findings. The abnormal findings were unilateral (n=4) or bilateral (n=3), including consolidation (n=4), dense patchy infiltration (n=3) (*Figure 1A*), ground-glass opacity (GGO) (n=1) and pleural effusion (n=1) (*Table 1*). No reticular opacities were found on chest radiography. The areas of parenchymal abnormalities involved mainly the lower lung zones in four patients, the upper lung zones in one patient, and random in two patients. One patient had a normal initial chest radiograph, though corresponding CT images showed an obvious right lower lung focal consolidation.

Seven patients had follow-up chest radiographs, the time interval between initial chest radiographs and the first follow-up chest radiographs ranged from 1–5 days with a median of 3 days [mean, 3.2±1.6 (SD) days]. The first follow-up radiographs in five of seven patients showed a remarkable increase in both opacity and size of the abnormalities with more extensive bilateral consolidation compared with the initial chest radiographs (*Figure 1B*). Most follow-up chest radiographs showed a rapid progression of lesions within ten days of illness onset (*Figure 1C*), and then consolidation began to dissipate at about two weeks after illness onset (*Figure 1D*,*E*).

CT findings

The initial CT scans of all eight patients showed abnormalities. The initial CT scans were performed at 2–13 days [mean, 6.0±3.4 (SD) days] after illness onset. The abnormal findings of initial CT scans were unilateral (n=5) or bilateral (n=3), including consolidation (n=8), GGO (n=2) (*Figure 2*) and small nodules (n=1) (*Table 1*). Pleural effusion was found in three patients, being bilateral in one

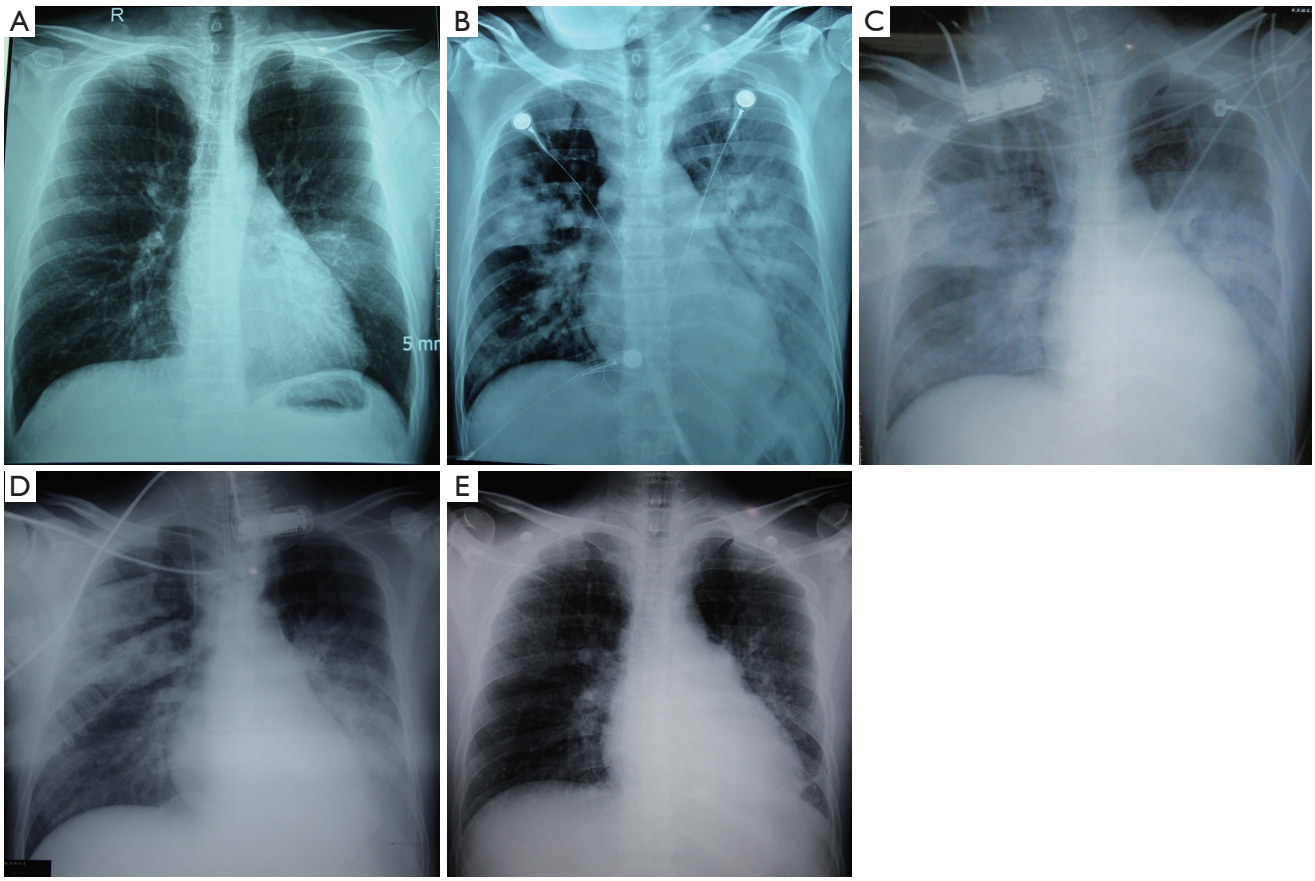

Figure 1 Patient 2: a 38-year-old man with adenovirus type 55 pneumonia. (A) Initial chest radiograph (day 2 after the onset of illness) shows dense patchy infiltration in the left lower lobe; (B) chest radiograph (day 7 after the onset of illness) reveals rapid progression, widespread consolidation in the left lung, with emerging irregular consolidation in the right lung; (C) follow-up chest radiograph on day 10 after onset (the day the patient was intubated) shows a continuous progression to widespread consolidation in both lung zones; (D) consolidation in both lungs has begun to decrease by day 15 after onset; (E) consolidation in both lungs has further decreased by day 18 after onset (the day the patient was extubated).

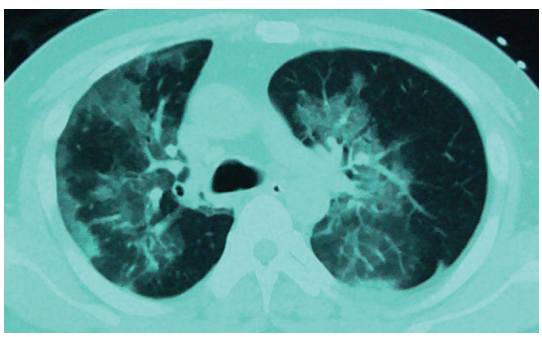

Figure 2 Baseline CT scan (day 9 after the onset of illness) in a 33-year-old man with adenovirus pneumonia shows bilateral ground-glass opacity, accompanied by partial consolidation and bilateral pleural effusion.

out of three. On the initial CT scans, focal consolidation (*Figures 3A*) were the main findings in six patients whose initial CT scans were examined within one week after illness onset. Predominant bilateral consolidation with adjacent GGO were seen in one patient's initial CT which was performed seven days after illness onset. Predominant GGO with adjacent consolidation were observed in one patient whose initial CT was examined nine days after illness onset (*Figure 2*).

All eight patients had follow-up chest CT images. The time interval between initial CT and the first follow-up CT ranged from 2 to 7 days with a median of 6 days [mean, 5.4±1.6 (SD) days]. The first follow-up CT scans which were performed within ten days of illness onset

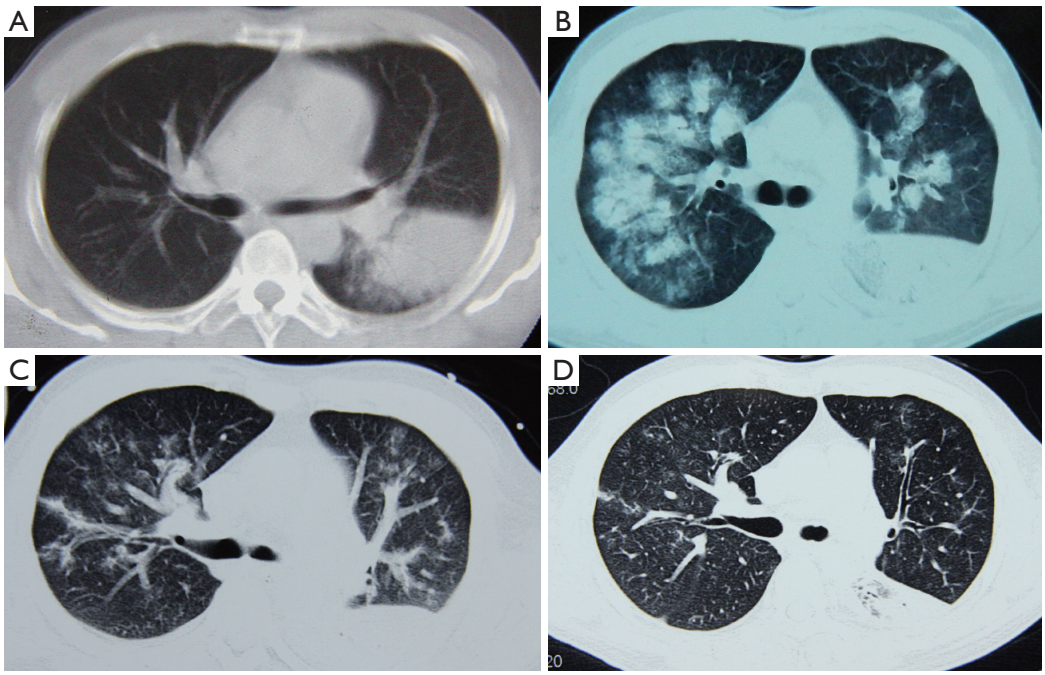

Figure 3 CT scans in a 52-year-old man with laboratory-confirmed adenovirus pneumonia. (A) Initial CT scan obtained at the level of tracheal bifurcation on day 2 after the onset of illness shows focal consolidation in the left lower lung; (B) rapid progression of consolidation in both lung zones with emerging patchy ground-glass opacities by day 8 after onset; (C) consolidation in both lungs has obviously decreased on day 16 after onset, with residual patchy ground-glass opacities; (D) parenchymal abnormalities have further decreased in both lungs by day 21 after onset with residual consolidation in the left lower lobe.

showed rapid progression of the abnormalities (*Figure 3B*); including, more extensive unilateral (1 of 6) or bilateral (5 of 6) areas of consolidation, and unilateral (2 of 6) or bilateral (4 of 6) pleural effusion. Follow-up CT scans of most patients had mixed patterns showing predominant consolidation with adjacent GGO. Numbers of lung lobe involved by consolidation in all eight patients were significantly more at the time of maximum severity (2 to 5, mean 4 lobes) than at the presentation (1 to 4, mean 1.7 lobes). In accordance with chest radiographs, CT parenchymal abnormalities began to absorb at about two weeks of illness onset (*Figure 3C,D*). The serial CT findings showed no appearances of fibrosis such as reticular opacities, cystic lesions, or traction bronchiectasis.

Discussion

Adenovirus, which is the cause of up to 3% of CAP, may be an under recognized cause of fatal pneumonia (13). More than 60% of adenovirus pneumonia patients need intubation and mechanical ventilation (2). Chest imaging has an important role in determining a presumptive etiology and severity assessment of CAP for clinical decision making. The most common initial radiological findings of our study population were focal consolidation, which are also commonly seen with bacterial pneumonia.

In accordance with the reputation of respiratory viruses for causing diffuse interstitial infiltrates, Clark reported widespread bilateral interstitial shadowing as the most common abnormality in 22 immunocompetent adults of adenovirus pneumonia (2). Patchy GGO with or without consolidation on CT were found most frequently both in immunocompromised and immunocompetent patients (4). Histopathologically, GGO reflects acute diffuse alveolar damage including hyaline membrane formation, interstitial lymphocyte infiltration, type II cell hyperplasia, and intraalveolar hemorrhage, edema and fibrin deposits (14). In our study, GGO as a subsidiary manifestation were also frequently observed in the progressive stages of severe adenovirus pneumonia, with only one in eight patients showed predominant GGO with adjacent consolidation.

To date, adenovirus is the only virus known to cause focal or lobar consolidation (the typical manifestation of

bacterial pneumonia) as its main imaging abnormality (15-17). Besides grossly congested and consolidated lungs, pathologic data revealed nuclear inclusions and smudge cells, typical histologic evidence of adenovirus pneumonia associated with necrotizing bronchiolitis and bronchopneumonia (6). However, similar to our study, bilateral infiltrates or consolidation were also reported frequently in adenovirus pneumonia (3,7,10,18). As Gu concluded, single lobar or segmental consolidation was more common in patients without ARDS, while patients with ARDS had bilateral and multilobar lung consolidation (11). In our study, focal consolidation were the primary findings within one week after illness onset, which indicates that multilobar involvement rapidly derived from single lobe infiltrates in severe adenovirus pneumonia with ARDS. Consistent with Sun's findings (10), delay from onset to a single lobar consolidation, then to bilateral multilobar lung infiltrates were about one week in our study, when significant deterioration was observed.

Parenchymal abnormalities of adenovirus pneumonia began to absorb at about two weeks after illness onset, which is about one week sooner than other viral pneumonia such as avian influenza virus infection (19). Focal consolidation on the initial CT scans in our study did not show any preference for specific segments of lung, though Hwang *et al*. (9) summarized that the right lower lobe was the specific zone of lung infiltration in adenovirus pneumonia. Pleural effusion was thought to be less commonly noted in adenovirus pneumonia (2,3). However 75% of patients in our study and 66.7% of ARDS patients in Gu's research (11) had pleural effusion, which might be related to more serious illness (8). Appearances of fibrosis which are common in other viral pneumonia were not observed in the present study, which may be another imaging characteristic that resembles bacterial pneumonia.

Our study has several limitations. First, it is retrospective and the scanning intervals for patients were dissimilar. Second, there were a relatively small number of cases owing to the absence of viral screening in non-serious cases combined with the relatively low incidence of adenovirus pneumonia. All the patients in our study had ARDS and no patients with mild clinical disease were included. Third, the relationship between CT and histopathology could not be evaluated since no lung tissue biopsies were available. Finally, technical parameters in image acquisition were not identical, since some initial chest radiographs and CT scans were performed at other institutions prior to a patient being transferred.

In conclusion, severe adenovirus CAP in immunocompetent adults manifests usually as focal consolidation followed by a rapid progression to bilateral consolidation, usually accompanied by adjacent GGO and pleural effusion. The initial image findings and clinical presentation of adenovirus pneumonia may resemble bacterial pneumonia. Screening of adenovirus should be considered in cases of severe pneumonia.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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