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Clinical characteristics and factors predicting respiratory failure in adenovirus pneumonia

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ABSTRACT

Background and objective: **Limited data exist regarding factors predicting respiratory failure (RF) in non-immunocompromised patients with adenovirus (AdV) pneumonia.**

Methods: **We described characteristics of AdV pneumonia ($n = 91$) versus non-AdV pneumonia ($n = 55$) and compared clinico-laboratory and radiological characteristics in patient groups categorized by RF.**

Results: **All 91 AdV pneumonia patients presented with acute respiratory symptoms and radiological infiltrations and had significantly lower levels of white blood cell counts and platelet counts compared with non-AdV pneumonia. Of them, 67 patients had mild pneumonia without RF (non-RF), 14 patients had no RF at admission but progressed to RF during hospitalization (progressed to RF) and 10 patients had RF at admission (initial RF). Initial monocyte percentage and absolute monocyte counts in RF patient groups (progressed to RF and initial RF) were significantly lower than those of non-RF patients (both $P < 0.001$), and the differences among progressed to RF and initial RF patients were not significant. Chest computed tomography findings such as dominant pattern or distribution, clinical symptoms, and bacterial or viral co-infections other than AdV were not discriminable between patients who had RF and those who did not. On univariate analysis, initial monocytopenia, multilobar infiltrations and pleural effusion were associated with RF. However, on multivariable analysis, only initial monocytopenia remained significant ($P = 0.004$) for predicting RF.**

Conclusion: **Our data suggest that initial monocytopenia may help to predict RF during the course of AdV pneumonia in non-immunocompromised patients.**

Key words: adenovirus, monocyte, pneumonia, predict, respiratory failure.

Abbreviations: AdV, adenovirus; CT, computed tomography; PCR, polymerase chain reaction; RF, respiratory failure.

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SUMMARY AT A GLANCE

We described the characteristics of adenovirus (AdV) pneumonia in non-immunocompromised adult patients and evaluated factors predicting the occurrence of respiratory failure (RF). Our data suggest that initial monocytopenia may help to predict RF during an AdV pneumonia in non-immunocompromised adult patients.

INTRODUCTION

Adenoviruses (AdV) are non-enveloped, double-stranded DNA viruses that cause diseases of various severity of the upper and lower respiratory tract.[1] It has been known that, in a non-immunocompromised host, AdV respiratory tract infection is usually mild, in contrast with immunocompromised hosts such as those with acquired immune deficiency syndrome or organ transplant recipients, in whom AdV infection is often fatal.[2–5] Interestingly, ever since a fatal case of AdV pneumonia in a healthy adult was reported in 1967,[6] sporadic cases of severe AdV pneumonia in non-immunocompromised patients have been reported,[7–10] and some studies have described distinct clinical characteristics of severe AdV pneumonia caused by particular serotypes.[11,12] In one recent study that evaluated outcomes in five severe AdV pneumonia cases caused by AdV-55, 80% of patients died, which highlights the need to focus on emerging highly virulent AdV pathogens even in non-immunocompromised patients.[13]

At present, no approved agents have proven beneficial in patients with AdV pneumonia, and there are limited data on the response to cidofovir.[3,11] One of the most concerning issues physicians face regarding the management of AdV pneumonia is difficulty predicting the progression to respiratory failure (RF) at the time of diagnosis, which could help to determine the appropriate medical interventions and may improve the overall clinical outcome.

However, there are no data regarding the predicting factors for RF in non-immunocompromised patients with AdV pneumonia. Therefore, in the present study,

we evaluated the clinical characteristics of AdV pneumonia patients compared with those of non-AdV pneumonia patients. We categorized the AdV pneumonia patients according to whether they had RF during hospitalization and attempted to identify risk factors predicting RF in AdV pneumonia in non-immunocompromised patients.

METHODS

Study subjects

We retrospectively reviewed the medical records of all consecutive adult patients who were admitted with community-acquired pneumonia between June 2014 and May 2015 at the Armed Forces Capital Hospital, South Korea. Because our hospital is the largest military referral centre and all soldiers are treated initially in military hospitals based on the unique characteristics of the Korean medical system, data from a relatively high number of patients were collected from a single centre, and approximately two-thirds of the pneumonia patients were from a military training facility. All patients were non-immunocompromised, as determined by a human immunodeficiency virus infection test. Of those, patients who did not undergo a respiratory virus polymerase chain reaction (PCR) test were excluded. Consequently, patients with negative PCR results for AdV (non-AdV pneumonia) and patients with positive PCR results for AdV (AdV pneumonia) were included in the analysis (Fig. 1).

The diagnosis of AdV pneumonia was confirmed when the following findings were present: (i) acute lower respiratory symptoms; (ii) lung infiltration on chest radiography or computed tomography (CT); and (iii) evidence of AdV infection identified by a respiratory virus PCR test from lower respiratory tract samples such as sputum or bronchoalveolar lavage fluid.[11,14] When samples obtained from the lower respiratory tract were considered inadequate, samples from the upper respiratory tract, including oropharyngeal or nasopharyngeal swabs, were obtained. The Institutional Review Board of the Armed Forces Capital Hospital and The Armed Forces Medical Command approved this study and permitted review and publication of patient records. The requirement for informed consent by individual patients was waived given the retrospective nature of the study.

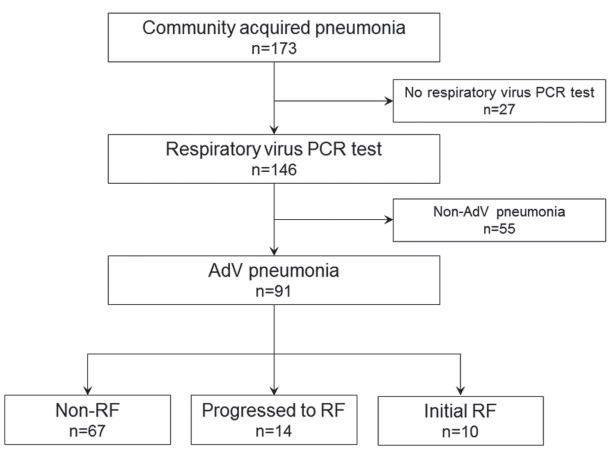

Figure 1 Patients included in the study analysis.

Patient management and data collection

Severe AdV pneumonia was diagnosed in several Korean military personnel from December 2012 to June 2014,[11,15] and physicians at the referral military hospital endeavoured to identify the causative respiratory viral agents using PCR tests, in addition to common bacterial agents. Thus, patients who presented with acute respiratory symptoms or who deteriorated despite antibiotic therapy for 2–3 days, and/or who had unusual haematological findings including leukopenia or thrombocytopenia, were suspected of having atypical causative agents and underwent aetiological investigations. Infectious aetiologies were evaluated in peripheral blood, sputum, oropharyngeal or nasopharyngeal secretions, and bronchoalveolar lavage fluid using techniques such as microbiological culture for bacteria and *Mycobacterium tuberculosis*; a multiplex real-time PCR test for bacterial agents including *Streptococcus pneumoniae*, *Haemophilus influenza* and *Mycoplasma pneumoniae*; and a multiplex real-time PCR test for respiratory viruses. Based on our previous study on the outcomes of administering cidofovir in patients with AdV pneumonia,[11] antiviral therapy with cidofovir was initiated in some patients.

Patients with AdV pneumonia were further categorized into three groups according to the occurrence of RF (Fig. 1): (i) patients who had no RF during hospitalization (non-RF group); (ii) patients who initially had no RF at admission but progressed to RF during hospitalization (progressed to RF group); and (iii) patients who had RF at admission (initial RF group). RF was defined as partial pressure of arterial oxygen/fraction of inspired oxygen ratio $\leq$300 with or without tachypnea (respiration rate $>$30 breaths per minute).[11,16] Some patients who had oxygen saturation $>$90% without oxygen requirement during hospitalization did not undergo arterial blood gas analysis, and they were considered non-RF group. All collected data and clinical outcomes were analysed.

Multiplex real-time PCR assay for respiratory viruses

Multiplex real-time PCR was performed to screen for 15 common respiratory virus pathogens, including AdV, rhinovirus, influenza virus A/B, respiratory syncytial virus A/B, bocavirus, coronavirus 229E/OC43/NL63/HKU1, parainfluenza virus 1/2/3 and metaneumovirus, using a Real-Q RV Detection kit (BioSewoom, Seoul, Korea) on a Roche Light Cycler 480 II instrument (Roche Diagnostics, Mannheim, Germany) according to the manufacturer's instructions. The serotype of human-AdV-positive samples was investigated by sequencing the partial hexon genomic region.[11]

Statistical analysis

Data are presented as medians and interquartile ranges for continuous variables and as numbers and

percentages for categorical variables. Data were compared using the Mann–Whitney *U*-test or Kruskal–Wallis test for continuous variables and the χ^2 or Fisher's exact test for categorical variables. To assess the predictive factors for the occurrence of RF in AdV pneumonia, univariate and multivariable analyses with a backwards logistic regression model were performed using variables with a *P*-value <0.20 on a univariate analysis. *P*-values were corrected using Bonferroni's method to counteract the problem of multiple comparisons, and a two-sided *P*-value <0.05 was considered to indicate statistical significance. Statistical analyses were performed using the PASW software program (ver. 18.0; SPSS Inc., Chicago, IL, USA).

RESULTS

Study patients

In total, 173 patients with community-acquired pneumonia were identified. Of these, 27 patients who did not undergo a respiratory virus PCR test were excluded. Fifty-five patients with non-AdV pneumonia and 91 patients with AdV pneumonia were identified (Fig. 1). Of the 91 AdV pneumonia patients, 67 had mild pneumonia without RF during hospitalization, 14 had no RF at admission but progressed to RF during hospitalization and 10 had RF at admission.

Comparative characteristics of AdV pneumonia against non-AdV pneumonia

We evaluated the clinical characteristics of AdV pneumonia patients compared with non-AdV pneumonia patients (Table 1). All patients were previously healthy men with a median age of 21 years. All patients presented with clinical symptoms of pneumonia, and AdV pneumonia patients had significantly higher rates of sore throat ($P < 0.001$), dyspnea ($P = 0.036$) and diarrhoea ($P = 0.017$) versus non-AdV pneumonia patients. The white blood cell counts ($P < 0.001$) and platelet counts ($P < 0.001$) in AdV pneumonia patients were significantly lower than those of non-AdV pneumonia patients. Overall, 24 (27%) of 91 AdV pneumonia patients progressed to RF during hospitalization, which was a greater incidence than in the non-AdV pneumonia patient group ($P = 0.005$).

Table 1 Clinical characteristics of AdV pneumonia patients compared with non-AdV pneumonia patients

Characteristics	AdV	Non-AdV	*P*-value
Patients	91 (100)	55 (100)	
Age (year)	21 (20–22)	21 (20–21)	0.568
Sex (male)	91 (100)	55 (100)	NA
Underlying condition			
Bronchiectasis	1 (1)	1 (2)	0.999
Pulmonary tuberculosis	2 (2)	0 (0)	0.527
Asthma	1 (1)	0 (0)	0.377
Clinical symptoms or signs			
Fever	89 (98)	50 (91)	0.104
Cough	81 (89)	51 (93)	0.569
Purulent sputum	51 (56)	39 (71)	0.112
Sore throat	40 (44)	7 (13)	<0.001
Myalgia	42 (46)	16 (29)	0.054
Dyspnea (>MMRC scale II)	41 (45)	15 (27)	0.036
Diarrhoea	13 (14)	1 (2)	0.017
Initial laboratory findings			
White blood cell count (/μL)	4900 (3420–6620)	8550 (5700–11 840)	<0.001
Platelet count (×10^3/μL)	139 (109–170)	198 (166–224)	<0.001
C-reactive protein (mg/dL)	7.75 (5.16–12.07)	8.05 (4.67–11.33)	0.777
Positive results of respiratory virus PCR test	91 (100)	8 (15)	<0.001
AdV	91/91	0/55	
Rhinovirus	7/91	5/55	
Influenza A	0/91	2/55	
Respiratory syncytial virus	0/91	1/55	
Enterovirus	1/91	0/55	
Positive results of microbiological test	30 (33)	29 (53)	0.024
Streptococcus pneumoniae	19/91	19/55	
Haemophilus influenzae	21/91	10/55	
Mycoplasma pneumoniae	2/91	13/55	
Chlamydia pneumoniae	0/91	1/55	
Klebsiella pneumoniae	0/91	1/55	
Presence of RF during hospitalization	24 (27)	4 (7)	0.005

Data are shown as medians (interquartile range) or number (%).
AdV, adenovirus; MMRC, modified medical research council; NA, not applicable; PCR, polymerase chain reaction; RF, respiratory failure.

Aetiology of pneumonia and therapeutic agents

As shown in Table 1, co-infections with respiratory viruses other than AdV were identified in the AdV and non-AdV patient groups, such as rhinovirus, influenza A, respiratory syncytial virus and enterovirus. Bacterial aetiologies were more commonly identified in the non-AdV pneumonia group ($P = 0.024$), in whom *S. pneumoniae* and *Haemophilus influenzae* were the most frequently isolated pathogens. Among the 91 AdV pneumonia patients, 30 had a bacterial infection, and 12 of the 30 had co-infections of *S. pneumoniae* and *H. influenzae*.

All 146 pneumonia patients received initial empirical antibiotics, including ceftriaxone + azithromycin ($n = 61$), moxifloxacin ($n = 34$), levofloxacin ($n = 24$), amoxicillin and clavulanate ($n = 17$) and piperacillin/tazobactam ($n = 10$). Cidofovir was applied in 21 (23%) of the 91 AdV pneumonia patients (in seven patients with initial RF, 11 patients who progressed to RF and 3 with no RF).

Clinico-laboratory findings in AdV pneumonia according to RF

We compared clinico-laboratory findings among AdV pneumonia patients, who were categorized into three groups consisting of non-RF, progressed to RF and initial RF groups (Table 2). Age, body mass index, smoking status and clinical symptoms or signs did not differ among the AdV patient groups, except for a lower rate of initial dyspnea in the non-RF group ($P < 0.001$).

Regarding initial laboratory findings, interestingly, monocyte percentage and absolute monocyte counts in RF patients were significantly lower than those of non-RF patients (both, $P < 0.001$). However, the differences in monocyte percentage and absolute monocyte count between patients who progressed to RF and those who had initial RF were not significant (Figures S1 and S2 in Supplementary Information). In addition, monocytopenia ($<150/\mu L$)[17,18] was more common in RF patients than in non-RF patients ($P < 0.001$).

The most commonly isolated AdV serotype was human AdV-55, and bacterial co-infections did not differ among the patient groups. Of the 24 patients with AdV pneumonia who had RF, six required mechanical ventilation, one required extracorporeal membrane oxygenation support and one died of RF and massive hemorrhagic infarction.

Initial chest CT findings in AdV pneumonia according to RF

Of 91 AdV pneumonia patients, initial chest CT images were available in 83 patients (Table 3). All patients who progressed to RF and had initial RF showed predominantly consolidation with a ground glass opacity (Fig. 2a and b), and more than 70% of them had lobar distributions, while only 62% of non-RF patients had predominantly consolidation with a ground glass opacity (Fig. 2c and d); approximately half of them had lobar distributions. Bilateral involvement ($P = 0.006$), multilobar infiltrations (≥ 3 lobes) ($P = 0.003$) and pleural effusion ($P = 0.003$) were significantly more common in the RF patients.

Evaluation of predictive factors for RF in AdV pneumonia

To assess the predictive factors for the occurrence of RF, univariate and multivariable analyses with a logistic regression model were performed among patients who had no RF and patients who progressed to RF during hospitalization (Table 4). On univariate analysis, monocytopenia ($P = 0.001$), multilobar infiltrations ($P = 0.043$) and pleural effusion ($P = 0.019$) were significantly associated with RF. However, on multivariable analysis, only monocytopenia remained significant ($P = 0.004$) for predicting RF.

DISCUSSION

In the present study, we described characteristics of AdV pneumonia in non-immunocompromised adult patients and evaluated predicting factors for the occurrence of RF. The most important finding was that initial monocytopenia may help to predict RF during the course of disease in AdV pneumonia patients. Moreover, given that clinico-laboratory parameters routinely investigated at admission, such as partial pressure of arterial oxygen, oxygen saturation and serum C-reactive protein levels, reflect only the present condition, predicting the risk of RF at the time of diagnosis of AdV pneumonia may help to stratify further medical interventions and determine whether to start early antiviral therapy.[11]

To date, there are no accurate data on which modalities could help to predict clinical deterioration in non-immunocompromised patients with AdV pneumonia. Regarding the abnormal haematological findings associated with the severity of AdV infection, Chen *et al.* recently indicated that patients with pneumonia, upper respiratory infection and asymptomatic infections had higher neutrophil percentages, lower lymphocyte percentages and lower platelet counts compared with healthy controls.[19] However, they reported that patients with relatively severe infections, such as pneumonia or upper respiratory infection, tended to have higher monocyte percentages than those with asymptomatic infection or healthy controls during acute phases of infection. This partial contradiction between studies regarding the monocyte percentage in AdV infections could be explained by the fact that we only included pneumonia patients and compared characteristics according to the presence of RF, reflecting disease progression. Of our 67 patients who had mild pneumonia without RF, similar to the aforementioned study, more than half ($n = 35$, 52%) had elevated monocyte percentages (>10% of the differential cell count), and only one patient had monocytopenia.

Adenovirus infection initially leads to neutrophilic interstitial inflammation with alveolitis and subsequent monocyte infiltration into the lungs. In later stages of the illness, the neutrophilic/monocytic inflammation may convert to lymphocytic inflammation.[20–22] Regarding

Table 2 Comparisons of clinico-laboratory findings among AdV pneumonia patient groups

Characteristics	Non-RF	RF		*P*-value
		Progressed to RF	Initial RF	
Patients	67 (100)	14 (100)	10 (100)	NA
Age (year)	21 (20–22)	21 (20–22)	21 (20–21)	0.622
Body mass index (kg/m^2)	22.9 (21.2–25.4)	23.9 (22.1–28.2)	21 (20–21)	0.627
Current or ex-smoker	15 (22)	5 (36)	3 (3)	0.245
Clinical symptoms or signs				
Fever	65 (97)	14 (100)	10 (10)	0.999
Cough	59 (88)	14 (100)	8 (80)	0.228
Purulent sputum	36 (54)	10 (71)	5 (50)	0.479
Sore throat	35 (52)	4 (29)	1 (10)	0.060
Myalgia	27 (40)	9 (64)	6 (60)	0.199
Dyspnea (>MMRC scale II)	19 (28)	13 (93)	10 (100)	<0.001
Diarrhoea	6 (9)	4 (29)	3 (30)	0.099
PaO_2/FiO_2 ratio	380 (352–450)	337 (314–383)	208 (152–248)	<0.001
SpO_2 on room air (%)	97 (96–98)	95 (93–97)	90 (86–91)	<0.001
Initial laboratory findings				
White blood cell count (/μL)	5300 (3800–6670)	3710 (3013–5343)	4095 (3003–4885)	0.096
Leukopenia (<4000/μL)	17 (25)	7 (50)	4 (40)	0.148
Lymphocyte (%)	21.8 (15.4–29.3)	19.7 (10.9–30.9)	21.3 (18.1–28.9)	0.582
Absolute lymphocyte count (/μL)	1121 (809–1442)	775 (528–847)	866 (641–1051)	0.003
Lymphocytopenia (<1500/μL)	48 (72)	13 (93)	9 (90)	0.191
Monocyte (%)	10.2 (7.7–13.8)	5.1 (2.8–7.1)	3.5 (2.1–5.3)	<0.001
Absolute monocyte count (/μL)	541 (339–709)	202 (97–322)	110 (74–254)	<0.001
Monocytopenia (<150/μL)	1 (2)	6 (43)	6 (60)	<0.001
Platelet count ($\times 10^3$/μL)	145 (118–172)	126 (99–174)	127 (86–152)	0.142
Thrombocytopenia (<150 000/μL)	35 (52)	10 (71)	7 (70)	0.324
C-reactive protein (mg/dL)	6.59 (4.20–11.81)	9.04 (6.66–14.6)	12.2 (9.05–15.11)	0.027
Results of respiratory virus PCR test				
AdV	67 (100)	14 (100)	10 (100)	NA
AdV-55	42/44	10/10	6/7	
AdV-4	2/44	0/10	1/7	
Non-AdV	7 (10)	0 (0)	1 (10)	0.751
Rhinovirus	6/67	0/14	1/10	
Enterovirus	1/67	0/14	0/10	
Positive results of microbiological test	24 (36)	3 (21)	3 (30)	0.623
Streptococcus pneumoniae	17/67	1/14	1/10	
Haemophilus influenzae	18/67	3/14	1/10	
Mycoplasma pneumoniae	1/67	0/14	1/10	
Chlamydia pneumoniae	0/67	0/14	0/10	
Klebsiella pneumoniae	0/67	0/14	0/10	
Death	0 (0)	0 (0)	1 (10)	0.330

Data are shown as medians (interquartile range) or number (%).

*Data were missing in 30 cases in non-RF group.

AdV, adenovirus; FiO_2, fraction of inspired oxygen ratio; MMRC, modified medical research council; NA, not applicable; PaO_2, partial pressure of arterial oxygen; PCR, polymerase chain reaction; RF, respiratory failure.

these inflammatory processes, Wenxin *et al.* recently demonstrated that AdV infection initially induces cytokines such as interleukin-6 and interleukin-8, which mediate the neutrophil recruitment; subsequently, chemokines such as macrophage inflammatory proteins and γ-interferon-inducible protein-10 may contribute to monocyte infiltration during the disease process.[23] Several studies have additionally indicated that severe AdV infection is associated with a marked imbalance of inflammatory cells and cytokine responses, including interleukin-1ra, interleukin-6, interleukin-8, tumour necrosis-α and γ-interferon.[21,24,25] Based on these data, our results imply that as AdV pneumonia becomes more severe, the inflammatory process including monocyte chemotaxis or inflammatory cell production can become uncontrolled or aberrant, which may contribute to the abnormal haematological findings. In this context, our results highlight important clinical implications of abnormal findings in peripheral blood, especially progressive monocytopenia, when treating patients with AdV pneumonia.

When evaluating the severity of pneumonia, radiological findings of multilobar infiltration or pleural effusion generally indicate greater severity status,[26,27]

Table 3 Comparisons of initial chest CT findings among AdV pneumonia patient groups

Characteristics	Non-RF	RF		*P*-value
		Progressed to RF	Initial RF	
Chest CT (n = 83)	59 (100)	14 (100)	10 (100)	
Dominant pattern				0.117
Consolidation + ground glass opacity	37 (62)	14 (100)	10 (100)	
Consolidation	16 (27)	0 (0)	0 (0)	
Ground glass opacity	5 (9)	0 (0)	0 (0)	
Nodules ± micronodules	1 (2)	0 (0)	0 (0)	
Distribution				0.357
Lobar	32 (54)	11 (79)	7 (70)	
Peribronchovascular	13 (22)	0 (0)	0 (0)	
Multifocal	8 (14)	1 (7)	2 (20)	
Focal	4 (7)	0 (0)	0 (0)	
Diffuse	2 (3)	2 (14)	1 (10)	
Laterality				0.006
Unilateral	44 (75)	5 (36)	3 (30)	
Bilateral	15 (25)	9 (64)	7 (70)	
Multilobar infiltrations (≥3 lobes)	20 (34)	9 (64)	9 (90)	0.003
Location of mainly involved lobe				0.458
Left lower lobe	25 (42)	8 (58)	3 (30)	
Left upper lobe	9 (15)	0 (0)	1 (10)	
Right lower lobe	11 (18)	1 (7)	2 (20)	
Right middle lobe	1 (2)	0 (0)	0 (0)	
Right upper lobe	5 (9)	1 (7)	0 (0)	
Both lower lobe	4 (7)	2 (14)	1 (10)	
Both upper lobes	1 (2)	0 (0)	0 (0)	
Whole lung	3 (5)	2 (14)	3 (30)	
Pleural effusion	11 (19)	7 (50)	7 (70)	0.003

Data are shown as number (%).
AdV, adenovirus; CT, computed tomography; RF, respiratory failure.

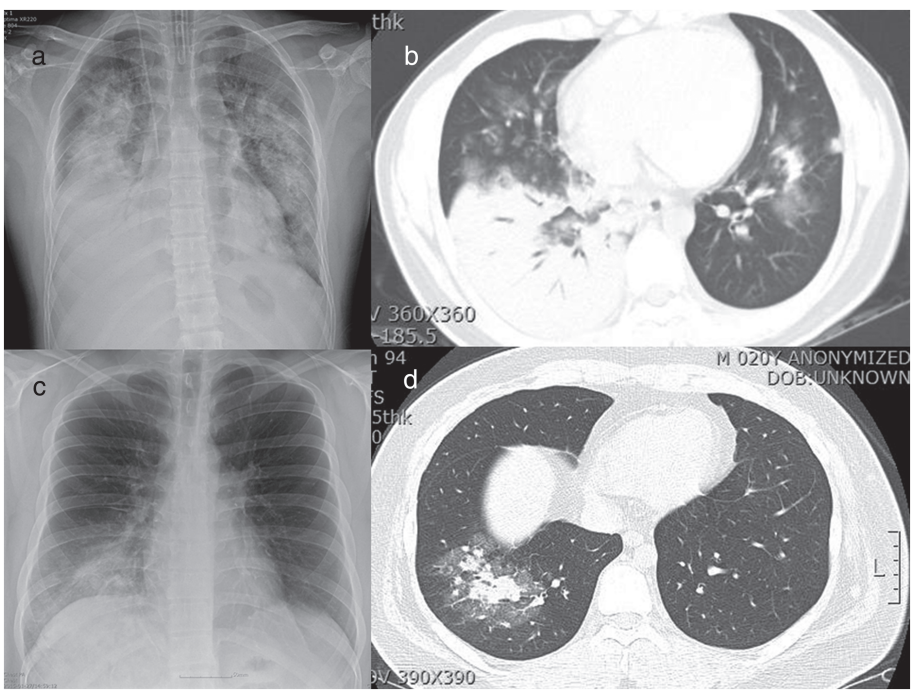

Figure 2 Chest radiography and computed tomography findings in adenovirus pneumonia patients. Initial chest radiography (a) in a patient who had respiratory failure initially showed prominent consolidation in the right lower lobe and diffuse infiltrates in both upper and lower lobes. The patient was intubated and received mechanical ventilation and vasopressors via a central venous catheter. Chest computed tomography (b) showed prominent consolidation in the right lower lobe with an air bronchogram and bilateral patchy ground glass opacities. Initial chest radiography (c) in a patient who had mild pneumonia without respiratory failure showed focal consolidation in the right lower lobe. Chest computed tomography (d) showed focal consolidation surrounded by ground glass opacities.

Table 4 Univariate and multivariable analysis with logistic regression model for predicting of RF in AdV pneumonia

Variable	Univariate analysis		Multivariable analysis	
	OR (95% CI)	*P*-value	Adjusted OR (95% CI)	*P*-value
Clinical symptoms or signs				
Sore throat	0.37 (0.15–1.28)	0.116	—	—
Diarrhoea	4.00 (0.96–16.74)	0.058	—	—
Initial laboratory findings				
Leukopenia (<4000/μL)	2.88 (0.88–9.42)	0.080	—	—
Lymphocytopenia (<1500/μL)	5.15 (0.63–42.11)	0.127	—	—
Monocytopenia (<150/μL)	49.50 (5.27–465.23)	0.001	26.25 (2.76–249.6)	0.004
Thrombocytopenia (<150 000/μL)	2.29 (0.65–8.02)	0.197	—	—
Initial chest CT findings				
Consolidation + ground glass opacity	6.05 (NA)	0.998	—	—
Multilobar involvement (≥3 lobes)	3.51 (1.04–11.88)	0.043	—	—
Pleural effusion	4.36 (1.27–15.01)	0.019	—	—

AdV, adenovirus; CI, confidence interval; CT, computed tomography; NA, not applicable; OR, odds ratio; RF, respiratory failure.

and radiological parameters alone may not accurately predict the prognosis without serial follow-up. As expected, in our study, a dominant pattern or distribution in CT images was not discriminable between patients who had RF and those who did not. Moreover, although several parameters that indicate increased severity, such as multilobar or pleural effusions, tended to be more frequently observed in RF patients, there was no statistical significance on multivariable analysis for predicting RF in AdV pneumonia.

Interestingly, in our study, most of the isolates typed were AdV-55, which was similar to our previous study that reported seven cases of severe AdV pneumonia.[11] One previous study evaluated serotypes among Korean military recruits and showed that type 7 was the most common isolate, but the patients included only had mild acute respiratory disease.[5] In one study that evaluated 48 cases of AdV pneumonia,[28] patients with AdV-55 had more severe disease compared with those infected with other serotypes. Thus, AdV-55 could be an emerging major pathogen; however, limited data exist, so further surveillance is needed.

The present study had several limitations. First, because our study was conducted at a military hospital, our population was not representative of the general population in terms of age, gender, living conditions and mode of infection. Second, because our study was retrospective, the possible effects of bacterial or other viral co-infections on the clinical course of pneumonia cannot be excluded. Third, the most common AdV serotype in our study patients was AdV-55, so inflammatory responses to different AdV serotypes should be evaluated.

In conclusion, our data suggest that initial monocytopenia may help to predict RF during the course of AdV pneumonia in non-immunocompromised adult patients.

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Supplementary Information

Additional Supplementary Information can be accessed via the *html* version of this article at the publisher's website:

Figure S1 Comparisons of initial monocyte percentages among adenovirus pneumonia patients categorized according to the respiratory failure.

Figure S2 Comparisons of initial lymphocyte counts among adenovirus pneumonia patients categorized according to the respiratory failure.

