Successful Treatment in Fatal Adenovirus Pneumonia with the Use of Extracorporeal Membrane Oxygenation

Su Ji Kim, Yang Bin Jeon, Yiel-Hea Seo, Sung Hwan Jeong, Jeong-Woong Park, JiYoung Shin, Yu Jin Kim

1Division of Pulmonology, Department of Internal Medicine, 2Thoracic and Cardiovascular Surgery, and 3Laboratory Medicine, Gachon University Gil Medical Center, Gachon University, Incheon, Korea

Severe adenovirus pneumonia that causes acute respiratory failure can occur in infants, children, and immunocompromised patients. However, severe adenovirus pneumonia is rare in adults with a normal immune system. Adenovirus pneumonia may progress to acute respiratory failure in a few hours or a few days, and its clinical course cannot be predicted. In addition, the mortality rate is very high (range, 50% to 66%). However, the optimal treatment of adenovirus pneumonia has not been established. Herein, we report the successful treatment of acute respiratory failure due to adenovirus pneumonia with extracorporeal membrane oxygenation.

Keywords: Aenovirus pneumonia; Extracorporeal membrane oxygenation; Acute respiratory distress syndrome

INTRODUCTION

Adenovirus infections occur mainly in infants and children; in fact, >80% of adenovirus infections occur before the age of 4 years. While the clinical course can vary, the majority of cases have naturally improved outcomes. The majority of severe adenovirus infections have been reported in infants, children, and immunocompromised patients [1-3]. However, there are rare reports of severe adenovirus infection in adults with a normal immune system in both domestic and international military camps and medical institutions [2-6]. To date, a total of nine cases of severe adenovirus pneumonia have been reported in Korea [2,4,7]. Two of these cases were reported in immunosuppressed patients, six in the military, and one in a healthy patient [2,4,7]. Three of the nine cases were accompanied by acute respiratory failure and all died with the exception of the one healthy patient [2,4,7]. Reports of severe adenovirus pneumonia are extremely rare and sporadic. Despite the high mortality rate, there is no established treatment for severe adenovirus pneumonia. Herein, we report the successful treatment of acute respiratory failure due to adenovirus pneumonia with extracorporeal membrane oxygenation (ECMO).

CASE REPORT

A 24-year-old healthy male with no significant past medical history was admitted to the emergency room with a high fever. Seven days prior to admission, the patient developed a high fever and dry cough. During conservative treatment, the patient’s status deteriorated. He developed dyspnea and a cough with blood-tinged sputum and was admitted to the emergency room of this hospital. There were no abnormal findings in the patient’s past medical or family histories. One month prior to admission, he began military boot camp. The patient had a 5-pack-year smoking history and drank a bottle of soju alcohol two or three times per month. On admission the patient’s blood pressure was 122/70 mm Hg, pulse 114 beats/min, respiratory rate 22/min, and body temperature 38.8°C. The patient was alert, but he appeared acutely ill. His heart rate was regular without murmurs. There were no specific findings on neck examination; however, rales were present in the left lower lung during chest examination. No other abnormalities were
noted on physical examination, including abdominal and neurological examinations. An arterial blood gas analysis on room air revealed a pH of 7.42, PCO$_2$ of 28 mm Hg, PO$_2$ of 48 mm Hg, and a HCO$_3^-$ of 18.2 mEq/L. Complete blood count demonstrated a white blood cell count of 4,140/mm$^3$ (89.1% neutrophil and 9.2% lymphocyte), a hemoglobin of 14.2 g/dL, and a platelet count of 300,000/mm$^3$. The C-reactive protein was 15.09 mg/dL, and the erythrocyte sedimentation rate was 3 mm/hr. The procalcitonin level was 1.15 ng/mL. Liver function tests revealed the following values: total protein 6.0 g/dL, albumin 3.7 mg/dL, total bilirubin 0.5 mg/dL, aspartate aminotransferase 130 IU/L, alanine aminotransferase 44 IU/L, and alkaline phosphatase 52 IU/L. Other analyses showed blood urea nitrogen of 9.2 mg/dL, creatinine of 0.7 mg/dL, sodium of 135 mEq/L, potassium of 3.7 mEq/L, and a lactate dehydrogenase of 896 IU/L. The patient’s lab work revealed no evidence of human immunodeficiency virus, syphilis, or hepatitis. On the multiplex real-time reverse transcription polymerase chain reaction (Anyplex II RV 16 Detection kit; Seegen, Seoul, Korea) conducted at admission by throat swap specimen for virus study. At the time of admission a chest radiograph showed patchy consolidations in both lungs. Chest computed tomography (CT) on admission revealed diffuse consolidations and ground glass opacities in both lung fields. The chest CT also revealed dense patchy consolidations predominantly in the left lower lobe with a small effusion (Fig. 1). Gram stain and culture of sputum, blood, and urine did not show any evidence of a bacterial pathogen. Tuberculosis was also ruled out. A rapid influenza A and B antigen test by nasal swab and a malarial smear test were also negative. The patient was treated empirically with ceftriaxone and roxithromycin, but his dyspnea worsened, high fever persisted, and chest radiograph findings deteriorated. On day three of the patient’s hospitalization, his antibiotics were changed to piperacillin/tazobactam and levofloxacin. The patient’s dyspnea continued to worsen and the pulmonary infiltrates noted on earlier chest radiographs progressed rapidly. The patient was transferred to the intensive care unit (ICU) for mechanical ventilation. On hospitalization day 4, echocardiography showed a 38% ejection fraction, moderate global hypokinesis, no pericardial effusion, and a pleural effusion. Despite mechanical ventilation, the patient’s PaO$_2$ level had decreased to 50 mm Hg and his PaO$_2$/FiO$_2$ ratio was less than 50. To recover heart and lung function, 17- and 21-F cannulas were inserted into the right femoral artery and vein. Venoarterial (VA) ECMO was performed using a centrifugal pump (Rotaflow; MAQUET Cardiovascular, Hirlinger, Germany). For VA ECMO, blood flow from the right atrium via the right femoral vein was oxidized using a polymethylpentene oxidizer (Quadrox PLS; MAQUET Cardiovascular) and then reinjected into the femoral artery via the arterial cannula. On hospitalization day 6, ribavirin 300 mg and oseltami-
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Fig. 2. High-resolution computed tomography 6 months after admission demonstrates improved diffuse ground glass opacities and consolidation. (A-D) However, probable post-infectious fibrosis, mild bronchiectasis and a bulla in the basal segment of the left lower lobe were noted.

Adenovirus-positive results were also obtained on hospitalization day 7. Thereafter, chest radiograph findings improved gradually, and on hospitalization day 16 the patient was taken off ECMO. On hospitalization day 19, both mechanical ventilation and CRRT were discontinued. The patient was transferred to the general ward, and on day 46 of hospitalization the patient was discharged. At the 6-month follow-up, the patient’s pulmonary and renal functions were improved. Follow-up high-resolution CT findings showed improvement in ground glass opacities and patchy consolidation (Fig. 2).

DISCUSSION

There are rare reports of severe adenovirus pneumonia in patients with normal immune systems in the military or medical institutions [1-3,6]. More than 50 adenovirus serotypes are known. Of these 50 serotypes, 3, 4, and 7 are known to cause pneumonia, and adenovirus type 7 is the most virulent [1-3]. In a study of adenoviruses isolated from Korean military trainees, all adenoviruses isolated from patients with acute respiratory disease were type 7 [8]. To date, a total of nine cases of severe adenovirus pneumonias have been reported in Korea, two of which occurred in immunocompromised patients [7]. Heo et al. [2] reported six cases of adenovirus pneumonia in military hospitals with a fatality rate of 50%. Of these patients, the two whose diseases proceeded to acute respiratory failure died. The fatality rate for severe adenovirus
pneumonia overseas is 50% to 66%, similar to the rate reported in Korea [2,3,7]. The progression from adenovirus pneumonia to acute respiratory failure varies in duration and ranges from hours to a few days. The clinical course of adenovirus pneumonia cannot currently be predicted [1,9]. Early chest radiographs in adenovirus pneumonia show lobar consolidation, which is rare in other viral pneumonias and differs from the normal reticulonodular pattern [9,10]. Adenovirus pneumonia is often mistaken for bacterial pneumonia, and difficulties in identifying adenovirus pneumonia can delay appropriate treatment. Conservative treatment is still standard in severely immunocompromised patients with an adenovirus infection. No antibiotic treatment has changed the disease outcome. Gu et al. [10] treated adenovirus pneumonia with acyclovir, but this treatment was ineffective. Drugs such as ribavirin, intravenous immunoglobulin, and ganciclovir have also been used; however, a standardized and effective treatment for adenovirus pneumonia has not been established [1,2,7,10,11]. One recent study reported a low mortality rate in patients treated with ECMO and shed new light on its role in the treatment of patients with acute respiratory distress syndrome [12]. A worldwide H1N1 influenza pandemic occurred during the 2009-2010 influenza season. In the United States, approximately 25% of hospitalized H1N1 patients were treated in the ICU, 36% of whom developed acute respiratory failure. During this period, a large number of patients with respiratory failure underwent ECMO treatment [12-14]. Bonastre et al. [13] proposed the use of ECMO to treat refractory respiratory failure caused by H1N1 infection. Low et al. [3] used ECMO to treat severe adenovirus pneumonia and suggested the use of ECMO if mechanical ventilation alone was insufficient.

In conclusion, antiviral drug therapy for severe adenovirus pneumonia has not been established. We report a case of acute respiratory failure due to severe adenovirus pneumonia successfully treated with ECMO, and suggest the use of ECMO and viral diagnostic studies in cases of acute respiratory failure in addition to mechanical ventilation.

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REFERENCES