Acute Respiratory Distress Syndrome Induced by Adenovirus in an Otherwise Healthy Woman

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Acute respiratory distress syndrome (ARDS) caused by adenovirus is a rare event in healthy adults, especially in non-military settings. Although treatment with intravenous ribavirin has been reported, supportive care, including mechanical ventilation, is known to be the mainstay in the treatment of ARDS caused by adenovirus, with high-dose steroid treatment having rarely been reported. We report our experience with a 41-year-old, otherwise healthy, woman with ARDS, treated with high-dose steroid and mechanical ventilatory support.

Key Words: Adenovirus, acute respiratory distress syndrome

INTRODUCTION

It is well known that adenoviruses are a group of DNA viruses, which cause a wide range of respiratory diseases from bronchitis to acute respiratory distress syndrome (ARDS). Most adenoviral respiratory infections have been reported in children, immunocompromised patients, and those in a military clinical setting.¹,² Adenoviral pneumonia occurs rarely in healthy adults in non-military settings. To our knowledge, only 13 adult cases of fatal adenoviral pneumonia have been reported among non-military subjects.³ Steroid therapy for patients in the fibroproliferative phase of ARDS caused by various causative agents including various bacteria may be benefi-­cial.⁴ Treatment with high-dose steroid in the case of ARDS caused by adenovirus has been rarely reported.⁵ We present a case of ARDS caused by adenovirus.

CASE REPORT

On Dec. 14, 2000, a 41-year-old nonsmoking woman was admitted to hospital because of progressively worsening dyspnea and a fever of 2 days duration after 7 days of myalgia. She had no history of underlying diseases and was not taking any medication. On admission, her blood pressure was 160/100 mmHg, pulse rate 120 beats/min, respiratory rate 24/min, and body temperature 38.6°C. On physical examination, coarse crackling sounds were heard over the whole lung field in auscultation. Laboratory study showed whole blood cells 12,000/mm³ (neutrophil 90.4%, lymphocyte 6.5%, monocyte 2.7%, eosinophil 0.2%, basophil 0.2%), hemoglobin 9.9 g/dl, platelet count 250,000/mm³, total bilirubin 2.6 mg/dl, aspartate aminotransferase (AST) 52 IU/L, alanine aminotransferase (ALT) 34 IU/L, lactate dehydrogenase (LDH) 1344 IU/L, creatinine phosphokinase (CPK) 201 IU/L, albumin 2.9 g/dl and aPTT 46.1 sec. (normal range 29-44 sec.) An arterial blood gas study on room air revealed a pH of 7.46, PaCO₂ 37 mmHg, PaO₂ 69 mmHg, HCO₃⁻ 26 mEq/L and SaO₂ 91%. Sputum gram stain and culture for bacteria revealed few polymorphonuclear neutrophil leukocytes (PMNs) and no organisms. Direct examinations of sputum were negative for acid-
fast organism and fungus. Diffuse interstitial infiltrates were noted on chest radiography. Homogenous, diffuse ground glass opacities in the whole lung field were noted on chest CT scan. (Fig. 1) During the 6 days following admission, her dyspnea worsened with a respiratory rate of 50/min. on the 7th day, when her temperature had also increased to 39.5°C. Her PaO₂ level had decreased to 50 mmHg in spite of breathing 10 L/min of 100% oxygen via a mask. The gross appearance of the sputum was whitish and not purulent. No pathogens were evident on sputum culture. Antibody studies for rickettsia, leptospira, Haemophilus influenzae, Mycoplasma pneumoniae, human immunodeficiency virus, rheumatoid factor and ds DNA were all negative, as was an antigen study for Streptococcus pneumoniae. Gram stains and cultures in blood and urine for bacteria and fungus were negative. On the 8th day, she was intubated and mechanically ventilated with FiO₂ 100% and a positive end expiratory pressure (PEEP) of 5 mmHg. In spite of the intensive mechanical ventilator setting, her PaO₂/FiO₂ (Ed-I suggest you insert ‘ratio’ here) of 51 met the diagnostic criteria of ARDS of the American-European Consensus Conference.³ Broad spectrum intravenous antibiotics with cefotaxime and levofloxacin were administered empirically. On the 9th day, we performed video-assisted thoracoscopic surgery (VATS) for pathologic diagnosis, and fiberoptic bronchoscopy for identification of the possible causative pathogen. Because there was no evidence suggesting the presence of bacterial infection and because the possibility of acute interstitial pneumonitis had been indicated by chest CT scan, 1 gr. of methylprednisolone sodium succinate was administered daily for the following 2 days and consequently this treatment was tapered off over the following 7 days. After 12 hours of methylprednisolone pulse therapy, her gas-exchange parameters improved significantly. (Fig. 2) The PaO₂/FiO₂ ratio dramatically increased to 141 and the FiO₂ level could be maintained below the level of oxygen toxicity. The patient became afebrile and diffuse interstitial infiltrates were lessened on serial chest radiographs. Histologic findings of the thoracoscopic lung biopsy showed a mixture of acute and organizing diffuse alveolar damage with alveolar pneumocyte proliferation, and prominent hyaline membranes (H & E stain, × 200).
membranes were prominent and alveolar pneumocyte proliferation was also seen. Although extensive background interstitial fibrosis was observed, it consisted mainly of fibroblasts with little collagen deposition. The etiology of this case could not be determined histologically. The characteristic intranuclear inclusion of adenovirus was not identified. No bacterial or fungal organisms were identified on Gram staining or culture of a bronchial washing specimen. Cultures for influenza, parainfluenza, and respiratory syncytial viruses in the bronchial washing specimen were also negative. Adenovirus was identified in a specimen of bronchial washing inoculated into Hep-2 cell culture and was confirmed by immunofluorescence assay (IFA) on the 16th day. The patient became febrile with a progressively worsening oxygenation status from the 17th day. The results of sputum, blood and urine cultures were negative on the 19th day. Methylprednisolone at the same dosage was reintroduced and a similar response obtained. We changed the mode of the mechanical ventilator from assisted/control mode ventilation to synchronized intermittent mandatory ventilation on the 23rd day. The patient was weaned from the mechanical ventilation on the 25th day, and discharged with mild dyspnea on the 37th day. IFA results of her sputum from both the 9th and 18th days were positive for adenovirus, but not in sputum from the 30th day.

**DISCUSSION**

Although ribavirin has been tried in the treatment of adenoviral pneumonia, including ARDS (Ed- this has already been defined in the introduction), its effectiveness remains controversial. Supportive treatment including mechanical ventilation is recognized as the main treatment option. Studies of high-dose steroid treatment in sepsis or ARDS patients in the early phase of the disease process have failed to show any benefit and have even demonstrated harmful effects. The beneficial effects of corticosteroids in the late phase of acute lung injury have been reported. The effect of steroid therapy in late ARDS patients is presently the focus of multicenter, prospective randomized clinical trials. Of the only two reported experiences of treating fatal adenovirus pneumonia in adults with intravenous steroid in a non-military setting, one patient received steroid therapy in the late phase of ARDS and the other received steroid therapy in the early phase of ARDS and showed a better clinical response. In our case of an otherwise healthy adult, we treated with high-dose steroid in the late phase of ARDS caused by adenovirus. The high-dose steroid therapy proved effective and immediately improved the patient's oxygenation parameters. It is not known whether this steroid has an effect on adenovirus infection. Recently it was found that adenovirus could massively release many cytokines, thereby inducing severe early inflammatory reactions that may cause ARDS. These cytokines, including interleukin-6 (IL-6), IL-12 and tumor necrosis factor-alpha, were released as early as 6 hours after adenovirus administration in animal model studies. Therefore, we believed that the high-dose steroid treatment during the late stage of ARDS might have suppressed the massive cytokine release induced by the adenovirus, and therefore decreased the related inflammatory reactions of the lung. This may be the reason that our case showed good response to steroid treatment.

We report upon a case of ARDS caused by adenovirus that was successfully treated with high-dose steroid.

**REFERENCES**

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