Acute Respiratory Failure Associated with Miliary Tuberculosis Successfully Treated with Sivelestat Sodium Hydrate

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The hematogenous spread of Mycobacterium tuberculosis causes miliary tuberculosis which is a life-threatening disease that is a recognized cause of acute respiratory distress syndrome (ARDS) (1). The neutrophil elastase inhibitor sivelestat sodium hydrate can effectively treat lung injury associated with systemic inflammatory response syndrome (SIRS) (2). Here, we describe the first successful application of this drug to control ARDS associated with SIRS caused by miliary tuberculosis.

A 63-year-old man was admitted to the hospital because of fever and progressive dyspnea of 10 days duration. He had been administered daily prednisolone (10 mg) and azathioprine (50 mg) due to pemphigus erythematosus. He presented with the following signs: temperature 38.7°C, pulse rate 123 beats/min, blood pressure 124/72 mmHg and audible crackles over the bilateral lower lungs. The patient had an elevated white cell count (10,600 /mm³, 92.8% neutrophils), an erythrocyte sedimentation rate of 60 mm/h and a C-reactive protein value of 12.7 mg/dl. Blood gases at room atmosphere showed compensating respiratory alkalosis with hypoxemia: pH 7.470, PaCO₂ 30.0 mmHg, PaO₂ 53.7 mmHg and bicarbonate 21.6 mmol/l. A chest CT revealed numerous small bilateral nodules, diffuse ground-grass opacification and consolidation (Fig. 1A). The patient was treated for presumed community-acquired pneumonia in an immunocompromised host with pazofoxacin, sulfamethoxazole-trimethoprim, as well as high-dose methylprednisolone and immunoglobulin to address the possibility of infection with typical pathogens, atypical pathogens (Chlamydia, Mycoplasma), Pneumocystis jiroveci and Cytomegalovirus, but the patient’s symptoms gradually deteriorated. Twenty-four hours after admission, noninvasive positive pressure ventilation (NIPPV) was applied due to worsening blood gases. We established a diagnosis of ARDS based on the ratio of PaO₂/FiO₂ being <200 mmHg (93 mmHg) and no evidence of left atrial hypertension determined by ultrasonic cardiography and therefore administered sivelestat sodium hydrate (0.2 mg/kg/hour). By the following day, the PaO₂/FiO₂ ratio had improved to 193 mmHg and antituberculosis therapy (isoniazid, rifampicin, ethambtold and pyrazinamide) was applied because acid-fast bacilli were detected in the sputum and polymerase chain reaction test for Mycobacterium tuberculosis was positive. Infection with pathogens except Mycobacterium tuberculosis was denied, therefore pazufloxacin and sulfamethoxazole-trimethoprim treatment were discontinued and methylprednisolone was tapered. Cultures from sputum and blood samples later established these organisms as Mycobacterium tuberculosis, thus confirming a diagnosis of miliary tuberculosis. The NIPPV was terminated with a PaO₂/FiO₂ ratio of 300 mmHg on day 4 of sivelestat administration. The sivelestat was continued for 14 days, after which a chest CT showed that although miliary nodules remained, the ground-grass opacification and consolidation had almost totally disappeared (Fig. 1B). Therefore, antituberculosis therapy was continued to address the miliary tuberculosis.

Tuberculosis is uncommon but definite cause of ARDS, which is associated with a high fatality rate (1, 3). Although antituberculosis therapy is the first choice of the treatment for ARDS due to tuberculosis, delays in the diagnosis of tuberculosis and initiation of antituberculosis therapy have been recognized as the main cause of death (3). In the present case, sivelestat could have initiated fast improvement of the PaO₂/FiO₂ ratio after initiation of antituberculosis therapy, which enhanced the positive outcome of ARDS. On the other hand, we applied NIPPV due to worsening the PaO₂/FiO₂ ratio. A recent review showed that the addition of NIPPV to standard care in the setting of acute hypoxemic respiratory failure reduces the rate of endotracheal intubation, length of intensive care unit (ICU) stay, and ICU mortality (4). According to a report of the use of NIPPV in tuberculosis ARDS (5), however, improvement of the PaO₂/FiO₂ ratio after initiation of NIPPV was not remarkable, therefore the authors suggested that NIPPV is an option for ventilatory support until of the antituberculosis therapy takes effect. Additionally, high-dose methylprednisolone applied due to suspected Pneumocystis jiroveci infection does not affect the outcome of early ARDS (6). Sivelestat improves lung function and thus there is a higher incidence of both ICU discharge and weaning from mechanical ventilation.

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among patients with lung injury associated with SIRS (2). Therefore, we believe that sivelestat sodium hydrate combined with antituberculosis therapy presents a novel therapeutic option in the treatment of ARDS due to tuberculosis.

References


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