CASE REPORT

Corticosteroid Therapy for Hemolytic Anemia and Respiratory Failure Due to Mycoplasma pneumoniae Pneumonia

Ryosuke Tsuruta, Yoshikatsu Kawamura, Takeshi Inoue, Shunji Kasaoka, Daikai Sadamitsu and Tsuyoshi Maekawa

Abstract

This is a report of hemolytic anemia and respiratory failure due to Mycoplasma pneumoniae pneumonia. His chest CT scans showed bilateral diffuse thickened bronchovascular bundles and emphysematous changes. The pulmonary function test supported the diagnosis of chronic obstructive pulmonary disease (COPD). He was diagnosed as cold-agglutinin-associated hemolytic anemia and M. pneumoniae pneumonia in inapparent COPD. Corticosteroid administration was remarkably effective for hemolytic anemia and beneficial for acute exacerbation of COPD.

Key words: cold-agglutinin, hematuria, emphysema, steroid pulse therapy

Introduction

Extrapulmonary manifestations such as hemolytic anemia, myocarditis, pericarditis, meningoencephalitis, and a variety of skin lesions, are not common in Mycoplasma pneumoniae infection. Involvement of the extrapulmonary manifestations may explain the pathogenesis of immune-complex disease (1), produced by circulating complexes of antibody and complement bound to mycoplasma. Once diagnosed as extrapulmonary manifestations of Mycoplasma pneumoniae infection, corticosteroid therapy seems reasonable in addition to specific antimicrobial therapy. Furthermore, corticosteroid should be administered to patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) (2). Herein is an unique case of simultaneous occurrence of hemolytic anemia and respiratory failure due to M. pneumoniae pneumonia in inapparent COPD.

Case Report

A 49-year-old man was transferred to our ICU, because of respiratory failure and jaundice on December 15, 2000. He had no significant pleuropulmonary history other than smoking (2 packs of cigarettes daily for 29 years). He had medication for hypertension and diabetes mellitus. He was well until ten days previously, when flu-like symptoms developed. The symptoms continued until two days before admission. He was admitted to a hospital because of dyspnea with wheeze and nonproductive cough. A physician diagnosed bacterial pneumonia and treated him with flomoxef. On the day of admission to our ICU, he began to have jaundice and dark urine.

On admission, he appeared dyspneic and mildly jaundiced. His heart rate was 115 beats/min, respiratory rate was 32 breaths/min, blood pressure was 175/100 mmHg, and body temperature was 37.6°C. Auscultation of the lungs revealed wheezes. There were no abnormal findings of his heart, abdomen, extremities, or nervous system. Laboratory examinations on admission showed the following results; hemoglobin (Hb) 8.5 g/dl, hematocrit 23.8%, red blood cell (RBC) 259x10^6/μl, white blood cell 38,200/μl, neutrophils 90.5%, lymphocytes 4.0%, monocytes 4.0%, eosinophils 0.5%, and atypical lymphocytes 1.0%, platelet count 58.8x10^4/μl, C-reactive protein 27.6 mg/dl, urea nitrogen 21 mg/dl, glucose 278 mg/dl, total bilirubin 5.1 mg/dl, direct conjugated bilirubin 1.0 mg/dl, haptoglobin 8.0 mg/dl, lactate dehydrogenase 1,889 IU/l, creatine kinase 807 IU/l, aspartate aminotransferase 72 IU/l, alanine aminotransferase 26 IU/l, prothrombin time 13.3 seconds (control 12.3 seconds), partial thromboplastin time 36.7 seconds (control 31.7 seconds). The urine was red and gave a markedly positive test for occult blood, glucose and protein. The arterial blood gas (ABG) analysis under 9 l/min oxygen revealed; PaO₂ 41.6 mmHg, PaCO₂ 47.4 mmHg, pH 7.37. His chest radiograph showed bilateral diffuse infiltrates involving bilateral lower lobes (Fig. 1). The chest CT scans revealed diffuse thickened bronchovascular bundles, emphysematous changes and mucoid impactions (Fig. 2A and 2B). The tuberculin skin test reaction was negative.

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He was intubated and mechanically ventilated. The ventilator setting was pressure controlled, fraction of inhaled oxygen 0.7, and positive endexpiratory pressure 3 cm H₂O. The ABG analysis revealed; PaO₂ 133.8 mmHg, PaCO₂ 54.8 mmHg, pH 7.35, and Hb 6.5 g/dl. The decrease of Hb was due to intravascular hemolysis and hematuria. A test for cold agglutinins was positive in a titer of 1:1,024, and a Coombs test was positive only for complement. He was treated with 4,000 units of haptoglobin, 2 units of warmed packed RBCs, 500 mg of erythromycin (EM), and 500 mg of meropenem. His extremities were kept warm. At 21 hours after admission, the steroid pulse therapy (methylprednisolone 1 g daily for 3 days) was added because the former treatments did not improve anemia and hematuria. The color of urine turned amber 2 hours later and normal yellow 15 hours later, after the intravenous steroid. However, he needed 4 more units of RBC transfusion to maintain Hb at more than 6.0 g/dl for 2 days.

Finally, he was diagnosed as 1) *Mycoplasma pneumoniae* pneumonia with cold-agglutinin-associated hemolytic anemia, when his antmycoplasma antibody titer by complement fixation was high as >1:1,024 on the 4th and on the 12th hospital days, 2) COPD, 3) diabetes mellitus. He had been treated with EM or clarithromycin for 2 weeks, prednisolone tapering therapy following the steroid pulse therapy (Fig. 3), inhalation of oxitropium bromide, and intravenous insulin. He was extubated on the 8th hospital day. His pulmonary function test on the 11th hospital day revealed; forced vital capacity 3,530 ml, forced expiratory volume in 1 second (FEV₁₀) 2,420 ml, FEV₁₀% 68.5%, %FEV₁₀ 69.7%, peak flow rate 6.63 l/second.

Discussion

*Mycoplasma pneumoniae* infection has been well recognized as one of the causes for acute exacerbation of asthma. Likewise, in patients with COPD, *M. pneumoniae* infection might be associated with acute exacerbation of COPD (3). In the present patient, COPD had not been detected until the chest CT showed bilateral emphysematous changes. However, he had been a current smoker and having symptoms of dyspnea and wheezes. Furthermore, his pulmonary function test revealed obstructive pattern and no effect of beta2-agonists on FEV₁₀.
Mycoplasma-induced Hemolysis & Hypoxemia

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>EM</td>
<td>1.5 g/day</td>
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<tr>
<td>CAM</td>
<td>0.4 g/day</td>
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<tr>
<td>MEPM</td>
<td>1.0 g/day</td>
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<tr>
<td>mPSL</td>
<td>1,000 mg/day</td>
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<td>PSL</td>
<td>60, 40, 20, 10, 5</td>
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**Intubation**  
**Extubation**

**SIMV**  
**PSV**  
**NPPV**

Figure 3. Clinical course after admission. EM: erythromycin, CAM: clarithromycin, MEPM: meropenem, mPSL: methylprednisolone, PSL: prednisolone, SIMV: synchronized intermittent mandatory ventilation, PSV: pressure-support ventilation, NPPV: noninvasive positive pressure ventilation, CRP: C-reactive protein, WBC: white blood cell.

Figure 4. Chest CT scan shows no thickened bronchovascular bundles.

Hemolytic anemia due to *M. pneumoniae* infection is less common than acute respiratory failure due to this organism. This hemolytic anemia is related to cold agglutination. Cold-agglutinin-associated hemolytic anemia is seen in three clinical situations; 1) during the course of certain infections such as mycoplasma pneumonia, 2) in association with lymphoproliferative disease such as lymphoma, and 3) in idiopathic cold-agglutinin disease (4). *M. pneumoniae* infection stimulates the production of autoantibodies not only to lung but also to brain, smooth muscle and RBCs. The interaction of I antigen on the surface of RBCs with *M. pneumoniae* is speculated (5). However, the pathogenesis of autoimmune phenomena is not clear. Interestingly, remarkable leukocytosis was seen in this case. A leukocyte count less than 10,000/μl is common in *M. pneumoniae* pneumonia. However, previous reports on *M. pneumoniae* pneumonia with hemolytic anemia showed leu-
kocytosis (5, 6). The difference is unknown but leukocytosis in *M. pneumoniae* pneumonia might be a clue to suspect the existence of hemolytic anemia.

The therapy for hemolytic anemia associated with *M. pneumoniae* pneumonia depends on the severity of anemia. In addition to treating the patient with the specific antimicrobials, keeping their extremities warm is important and the packed RBCs should be warmed before transfusion. To administer steroids in such a patient seems reasonable. The response appears to be quick and dramatic (6, 7), as seen in the present case. However, no formal treatment studies on hemolytic anemia have been carried out.

In conclusion, the simultaneous occurrence of hemolytic anemia and respiratory failure due to *M. pneumoniae* pneumonia is a unique case. Severe anemia and hematuria respond well to high-dose corticosteroid therapy. The steroid tapering therapy following the pulse therapy may be beneficial for respiratory failure in inapparent COPD.

References