

Acute respiratory distress syndrome caused by *Mycoplasma pneumoniae* in a child: the role of methylprednisolone and clarythromycin

Síndrome do desconforto respiratório agudo causada por *Mycoplasma pneumoniae* em uma criança: o papel da metilprednisolona e claritromicina

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ABSTRACT

Mycoplasma pneumoniae is recognized as an important agent of pneumonia in pediatric population. In rare situations, severe pulmonary injury can develop. The use of corticoids in these cases remains controversial. A case of a girl with acute respiratory distress syndrome and bilateral pleural effusion secondary to pneumonia due to *Mycoplasma pneumoniae* is described, with good recovery after appropriate use of methylprednisolone and clarythromycin.

Keywords: *Mycoplasma pneumoniae*; Steroids; Child; Acute Respiratory Distress Syndrome; Clarythromycin; Case reports

RESUMO

Mycoplasma pneumoniae é reconhecido como um importante agente causador de pneumonia em crianças. Raramente pode evoluir para lesão pulmonar grave. O uso de corticoide nesses casos ainda é controverso. Descrevemos aqui o caso de uma menina com síndrome do desconforto respiratório agudo e derrame pleural bilateral secundário à pneumonia por *Mycoplasma pneumoniae* com boa recuperação após utilização de metilprednisolona e claritromicina.

Descritores: *Mycoplasma pneumoniae*; Esteroides; Criança; Síndrome do Desconforto Respiratório Agudo; Claritromicina; Relatos de casos

INTRODUCTION

Mycoplasma pneumoniae is a common cause of pneumonia. It accounts for 10 to 20% of community-acquired pneumonia. The pulmonary infection is often classified as an atypical pneumonia. This can be justified by the clinical presentation that resembles a systemic

viral infection. The disease is highly transmissible and infection occurs throughout the year, with clear peaks during the autumn and early winter⁽¹⁾.

In children, *M. pneumoniae* is an agent responsible for upper and lower respiratory infections, often minor and self-limited. It includes cases of pharyngitis, tracheobronchitis, bronchiolitis and pneumonia. Twenty percent of these infections are asymptomatic and mortality is rare⁽¹⁾.

Severe pulmonary injury due to *M. pneumoniae* is extremely unusual and there are few descriptions in the literature of patients who develop pleural effusion or acute respiratory distress syndrome/acute lung injury (ARDS/ALI)⁽²⁻⁵⁾.

The case of a child with an atypical evolution of pneumonia due *M. pneumoniae* is described, emphasizing the therapeutic aspects of the disease, such as mechanical ventilation support, antibiotics and the use of corticosteroids for ARDS, with attention to specific indications for *M. pneumoniae*. The basic differences between classical ARDS and ARDS due to *M. pneumoniae* are also discussed.

CASE REPORT

A 14-year-old female was transferred to the Pediatric Intensive Care Unit (PICU) with a seven-day history of cough. She had fever and respiratory distress 1 day prior to admission. In her past medical history, only two episodes of pneumonia were diagnosed.

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On admission, she had a respiratory rate of 50 breaths/minute and heart rate of 140 beats/minute, with temperature of 37°C. Auscultation of the lungs revealed coarse crackles on the right. Laboratory exams showed: hemoglobin 11.5 g/dL, white blood cell 12,500/ μ L, neutrophils 55%, and C-reactive protein 445 mg/dL. Her chest radiography showed bilateral diffuse infiltrates (Figure 1A). Ceftriaxone and oxygen therapy were initiated.

After 24 hours, her clinical and respiratory status worsened. The chest radiograph and computerized tomography scan revealed bilateral pleural effusion

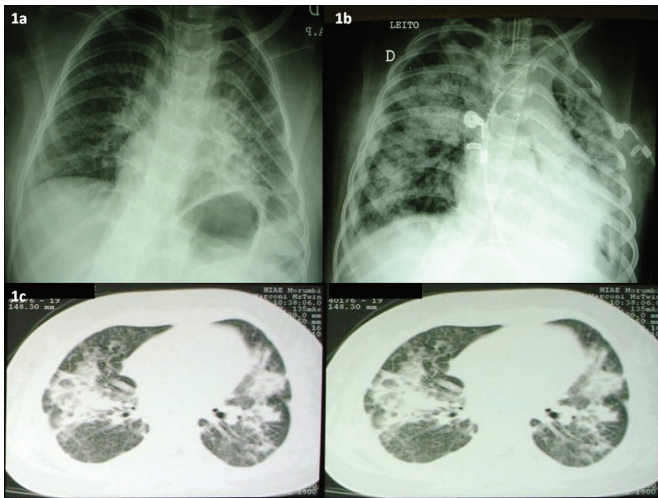


Figure 1. (A) Chest radiography upon admission showing bilateral infiltrate. (B) Radiography on day 2, showing worsening in bilateral infiltrate along with bilateral pleural effusion. (C) Chest computed tomography showing collapsed areas and diffuse pulmonary infiltrate

(greater extension on left side) and increased bilateral infiltrate (Figures 1B and 1C).

She was intubated and mechanically ventilated. The antibiotic scheme was changed to teicoplanin and imipenem. The treatment of pleural effusion was conservative.

Despite the use of higher ventilator settings, her $\text{PaO}_2/\text{FiO}_2$ was 65 mmHg. After combined analysis of the oxygenation status ($\text{PaO}_2/\text{FiO}_2 < 200$ mmHg), chest radiography (bilateral infiltrate), acute progression and no evidence of left atrial hypertension, the PICU staff diagnosed an ARDS.

Regarding the ventilator settings, the lung-protective strategy was applied with the use of high PEEP (positive end-expiratory pressure) and lower tidal volume (6 to 8 mL/kg). Despite the use of recruitment maneuvers and PEEP up to 20 cmH₂O, the $\text{PaO}_2/\text{FiO}_2$ ratio remained above 125 mmHg. After the increase in the PEEP settings, the patient developed hypotension (treated with fluids and dopamine up to 10 mcg/kg/min).

After 7 days of antibiotics, the patient remained febrile, with no improvement in the $\text{PaO}_2/\text{FiO}_2$ status. Blood culture, investigation for *Pneumocystis carinii* and tuberculosis were negative. Serology for *M. pneumoniae* (indirect microparticle agglutinin) and the test for cold agglutinins were positive. Clarithromycin was initiated.

Even after 48 hours of macrolide use, there was no increase in the oxygenation status.

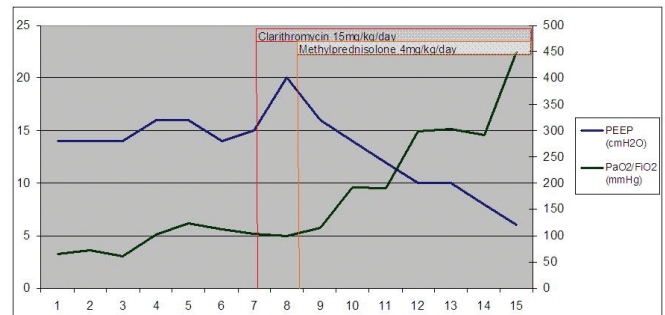


Figure 2. Correlation between PEEP (cmH₂O) and PaO₂/FiO₂ (mmHg). Red line: initiation of clarithromycin. Orange line: initiation of corticosteroids

After 9 days, corticosteroid therapy was added due to no improvement in $\text{PaO}_2/\text{FiO}_2$. After 2 days of methylprednisolone use (4 mg/kg/day), the $\text{PaO}_2/\text{FiO}_2$ increased above 200 mmHg (Figure 2).

The anti-inflammatory effect of corticosteroids permitted the reduction of PEEP. On the 14th day the patient was extubated and transferred to the pediatric ward. Clarithromycin was interrupted after 14 days and methylprednisolone after 7 days.

DISCUSSION

Pneumonia due to *M. pneumoniae* is usually a benign self-limited disease, but severe and fatal cases have been described. In these cases, mortality is higher due to decreased response to therapy⁽¹⁾.

The classical treatment for severe pulmonary infection caused by *M. pneumoniae* include the use of a macrolide, mechanical ventilation and Intensive Care Unit (ICU) support⁽⁵⁾.

The therapeutic strategy in mechanical ventilator settings in ARDS due to *M. pneumoniae*, as with any other agent, should target the use of higher PEEPs and lower tidal volumes. In children, the literature is scarce and the applicability of these strategies should be considered only in selected cases.

In our case, even with the use of higher PEEP (up to 20 cmH₂O), low tidal volume and lung recruitment maneuvers, the child was not able to restore a normal

PaO₂/FiO₂ after 1 week of these strategies (along with broad spectrum antibiotics).

Regarding the use of steroids for ARDS, a critical appraisal of the ARDS network trial and recent literature was conducted by Meduri et al.⁽⁶⁾ and the conclusion was that prolonged use of corticosteroids (≥ 7 days) improves patient-centered outcome variables, such as improvement in gas exchange, reduction in markers of inflammation and decreased duration of mechanical ventilation and ICU stay. If initiated before day 14 of ARDS, the use of steroids can have an additional survival benefit.

This potential benefit of steroids for ARDS seems to be more important in severe cases of pneumonia due to *M. pneumoniae*. Evidence points to the strong consideration of steroid use in ARDS/ALI due to *M. pneumoniae* or severe pneumonia⁽²⁻⁵⁾. Due to the delay in starting methylprednisolone treatment, the present case is very illustrative in this aspect, since it shows the amazing recovery after the steroid use.

The potential benefit of steroids in these cases is consistent with the hypothesis that cell-mediated immunity plays an important role in *M. pneumoniae* pneumonia. This was demonstrated by the presence of mononuclear periluminal infiltrates on lung tissue⁽⁷⁾. Also, there are studies that show low incidence of *M. pneumoniae* pneumonia in immunocompromised patients⁽⁸⁾.

On immunocompetent patients, the severe cases of pneumonia due to *M. pneumoniae* could be explained by the fact that stronger cellular-immunological responses may induce more severe pneumonic infiltrates, mainly in patients with repetitive community-acquired infections⁽⁹⁾. Unlike the histological pattern of classical ARDS, primary centered on neutrophil migration into the airways, this response in *M. pneumoniae* infection is deemed as a “lymphoid” ARDS, considering that the more vigorous the cytokine and the cell-mediated immune response, the more severe is the pulmonary injury⁽²⁾.

Summarizing, corticosteroids downregulate the cell-mediated response and therefore may play an important role in severe pneumonia due to *M. pneumoniae*. The question that has to be answered is which patients should receive steroids and how to identify them.

Narita et al. reported that higher concentrations of interleukin 18 (IL-18) and interleukin 8 (IL-8) in serum or pleural fluid samples of patients in acute phase of *M. pneumoniae* infection were closely associated with severity of the disease. The authors recommend that IL-8 and IL-18 should be measured (in serum or pleural fluid) and could be used as predictors for disease severity in *M. pneumoniae* pneumonia and help deciding whether to use or not corticosteroids⁽¹⁰⁾.

In conclusion, even though still controversial for all cases of ARDS, there is clear evidence in the literature of reliable use of corticosteroids in extremely severe cases of *M. pneumoniae* ARDS. Other patients with less severe cases could benefit from steroid use, but the application should be considered as an option, due to weak evidence. Hence, further studies are necessary to confirm the benefit and to address other important questions regarding which patients are candidates for use, the ideal dose and timing of methylprednisolone.

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