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CASE REPORT

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Necrotizing pneumonia due to *Mycoplasma* in children: an uncommon presentation of a common disease

The authors declare no conflict of interest

Abstract

Mycoplasma pneumoniae is a common respiratory pathogen, especially in children, responsible for community-acquired pneumonia. Although, in most cases, infections caused by this bacterium follow a benign self-limited clinical course, cases of severe respiratory infections have been reported.

We present two pediatric cases of necrotizing pneumonia due to *Mycoplasma pneumoniae.* Both patients initially presented with low-grade fever, cough and mild respiratory symptoms, however, imaging techniques showed necrotizing pneumonia. Initially, a typical bacterial pneumonia was suspected, so antibiotic empiric regimen did not included macrolides. When clinical evolution was not adequate, antibiotic treatment was modified in order to provide coverage to unusual pathogens. Both patients finally recovered once Mycoplasma was suspected, and oral macrolides were added to their treatment.

Although *M. pneumoniae* is a rare cause of necrotizing pneumonia, it must be considered, when usual antibiotic empiric therapy is not being successful. Before thinking of uncommon germs, we must remember that: 'The unusual presentation of a common disease is generally more likely than the usual presentation of an uncommon disease'.

Key words: children, *Mycoplasma pneumoniae*, necrotizing pneumonia, community-acquierd pneumonia

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Introduction

Mycoplasma pneumoniae (*M. pneumoniae)* is a pathogen of the *Mycoplasmataceae family,* characterized by its small size and the absence of cell wall, which determines its natural resistance to beta-lactam antibiotics [1].

M. pneumoniae is considered a significant pathogen of both upper and lower respiratory tract infections and it is responsible for more than 50% of community-acquired pneumonia (CAP) in children over 5 years of age, but a large number of microorganisms have been implicated as etiologic agents of pneumonia in children [2]. Pneumonia caused by *M. pneumoniae* is referred to as "atypical pneumonia", characterized by a benign slow clinical course, low-grade fever, malaise and cold-like symptoms. Atypical bacterial pathogens include *Chlamydia Trachomatis, Chlamydophila Pneumoniae and M. Pneumoniae* [3]. The initial treatment of children with pneumonia is generally empiric, and clinical and epidemiologic features can be used to determine the most likely pathogens to orientate this therapy [4]. In atypical pneumonia, laboratory analyses do not generally show substantial alterations, and chest radiographs usually have a reticulonodular pattern, without clear consolidations. The clinical course of pneumonia caused by *M. pneumoniae* is generally good, with very rare complications. Nevertheless, several cases with poor outcomes have been previously reported, such as necrotizing pneumonia, systemic failure, sepsis, and even death, have been attributed to this organism [5].

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We report two pediatric cases with necrotizing CAP due to *M. pneumoniae*, an uncommon presentation of a common disease.

Case presentation

Case 1

Healthy 7-year-old girl, with Down syndrome, who presented to the emergency room with low-grade fever and cough. Past medical history showed only recurrent episodes of obstructive bronchitis. On physical examination she was febrile (38.6°C), with a respiratory rate of 32 per minute (bpm), and normal oxygen saturation (96%), with good general condition, and without signs of respiratory distress. Chest auscultation identified hypoventilation and crackles in the left hemithorax. Chest radiography (Fig. 1) showed consolidation in the upper lobe of the left lung with a small air-fluid level image inside the consolidation and blunting of the costophrenic angle. Laboratory tests, showed moderate increase of acute phase reactants: complete blood count (CBC) 16,000 white cells/mm^3, with 91.8% neutrophils; C-reactive protein (CPR) 22 mg/dL (reference range, 0–1); and procalcitonin level, 0.5 ng/mL (reference range, 0–0.5). Patient was admitted to hospital, diagnosed as complicated CAP with parapneumonic effusion and necrotizing pneumonia, and parenteral antibiotics were started (cefotaxime 200 mg/kg/day and clindamycin 40 mg/kg/day). Lung ultrasonography confirmed the pleural effusion and heterogeneous parenchymal texture, sugestive of an underlying necrotizing pneumonia. Chest computed tomography (CT) scan (Fig. 2) showed extensive lobar consolidation in the left hemithorax with necrosis in the left upper lobe, left pleural effusion and initial involvement of the right upper lobe parenchyma. Repeated radiography showed disease progression, and fever and tachypnea persisted. A thoracentesis was performed, and pleural effusion analysis showed: cellular count, 120 erythrocytes/mm^3; 200 leucocytes/mm^3, glucose: 88 mg/dL; protein: 45.4 g/L;

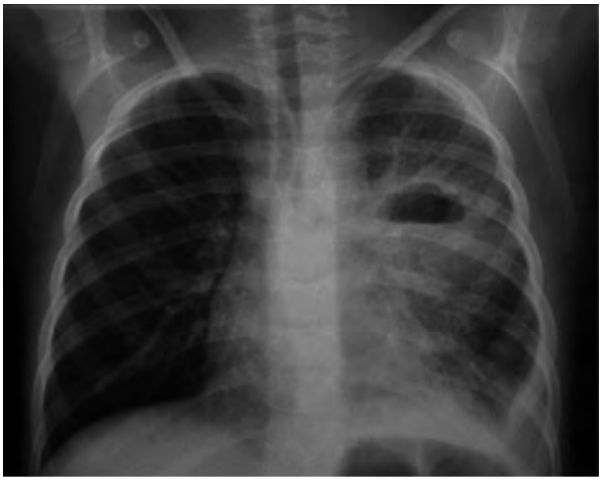

Figure 1. Chest radiography at diagnosis (Case 1), showing consolidation in the upper lobe of the left lung with an air-fluid level image inside the consolidation revealing cavitation and blunting of the costophrenic left angle. Pleural effusion and necrotizing pneumonia

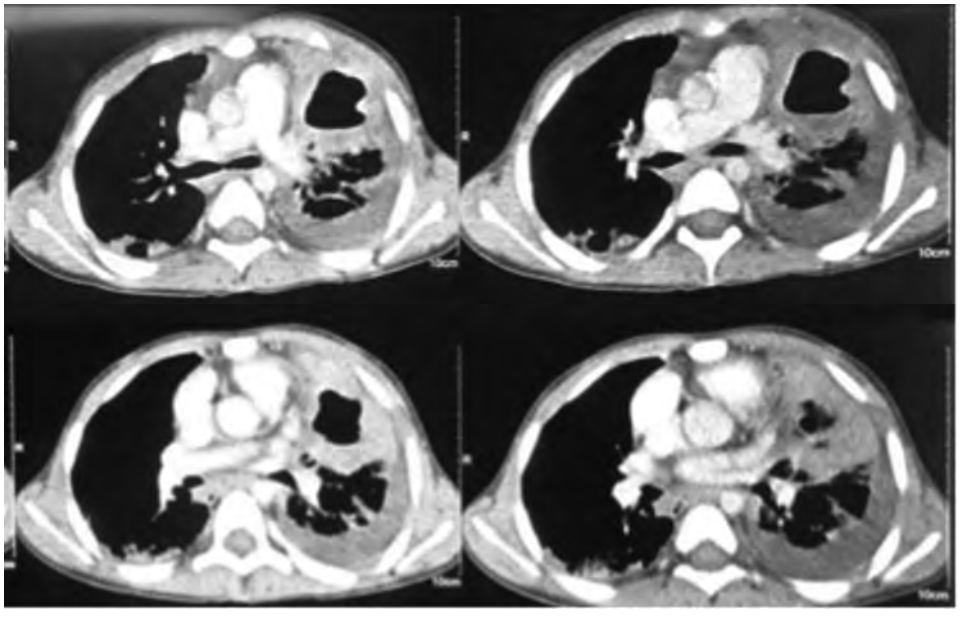

Figure 2. Computed tomography chest scan at diagnosis (Case 1), shows loss of normal pulmonary architecture, decreased parenchymal enhancement and multiple thin-walled cavities extensive lobar consolidation in the left hemithorax with necrosis and pleural effusion

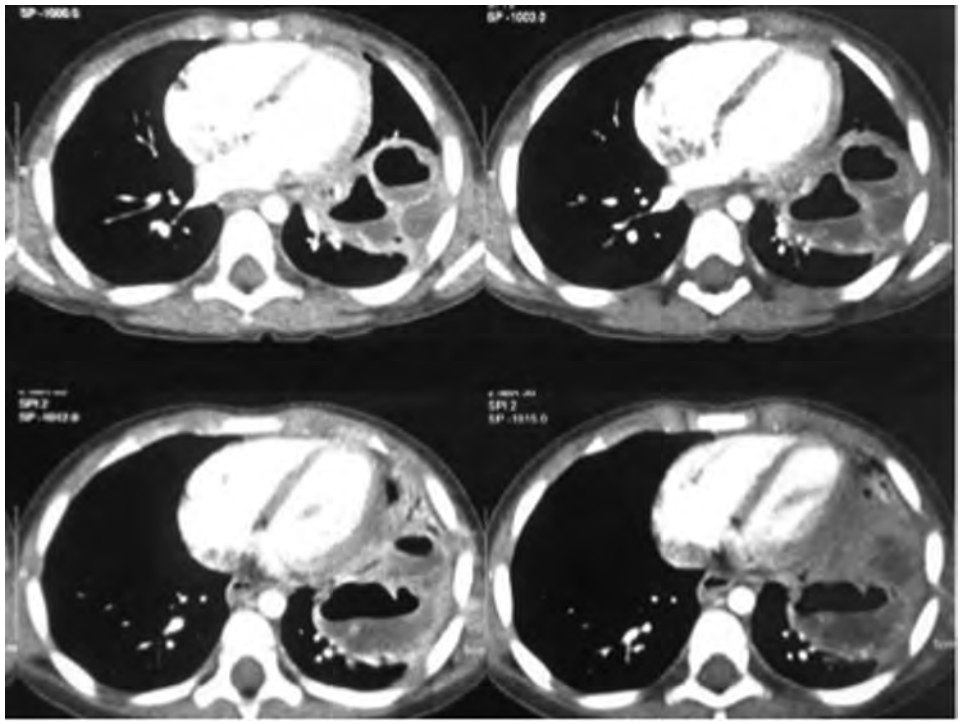

Figure 3. Computed tomography chest scan at diagnosis (Case 2) demonstrating a necrotic area with thin-walled cavities within the left lower lobe. Necrotizing pneumonia, with no evidence of pleural effusion

and lactate dehydrogenase: 211 U/L. After 4 days, fever, cough and tachypnea persisted and even though general condition was good, patient failed to improve as anticipated. Clinical history was re-evaluated and further complementary tests were done. Although patient had no history of previous important infectious diseases, humoral and cellular immunity studies were conducted to rull out an immunocompromised host, but they were both normal. Regarding the etiologic study, latex agglutination test of the pleural fluid for *Streptococcus pneumoniae,* and the polymerase chain reaction (PCR) analysis of respiratory viruses were all negative. Blood and pleural fluid cultures were also negative. Quantiferon-TB Gold Test (QFT) for mycobacteria and Mantoux test also were negative. Serology test for *M. pneumoniae:* MP-specific immunoglobulin M (IgM) were high, and as a possible atypical pneumonia was suspected, oral azithromycin, 10 mg/kg/day for 5 days, was added, with a clinical significant improvement the day after it was initiated. Acute infection was documented by antibody titer changes (serologic diagnosis increase of MP-specific immunoglobulin titer after initial measurement). The patient remained hospitalized for 19 days; her general condition was good at all times and she remained afebrile, once azithromycin was started. Consecutive blood tests showed a gradual decrease of infectious parameters, and control chest x-rays showed reduced consolidation and resolution of the pleural effusion after the treatment with macrolide. The patient was followed as an outpatient, in the pediatric respiratory clinic, and further laboratory tests showed gradual improvement of the infectious-inflammatory parameters, with negative IgM titers and an increase of IgG *M. pneumonia* titers. Chest X-ray obtained 2 months after was normal and without any sequelae.

Case 2

Second patient is a previously healthy 3-year-old boy, who was brought to the emergency room with a history of 6 days of fever, cough and myalgia. Oral amoxiciline had not improved the symptoms. Physical exam showed good general health without respiratory distress. On admission, patient was febrile, (38.1°C), pulse rate was 151 bpm, respiratory rate 32rpm, and oxygen saturation was 98%. Pulmonary auscultation showed hypoventilation and crackling, over the left lung base. Chest radiography showed left lower lobe consolidation with trapped air seen within this area. Laboratory test results included a partial increase of acute phase reactants: CBC 22,500 white cells/mm^3; 77% neutrophils; erythrocyte sedimentation rate, 63 mm/hour; CPR 8.8 mg/dL, and

procalcitonin level 0.3 ng/mL. The patient was admitted with diagnosis of CAP and intravenous antibiotics (cefotaxime 200 mg/kg/day and clindamycin 40 mg/kg/day) were administered. His respiratory symptoms and respiratory rate did not improve, during the first days of treatment, and fever persisted. The chest CT scan (Fig. 3) showed a necrotizing pneumonia of the left lower lobe, with no evidence of pleural effusion. Regarding the etiologic agent, no *S. pneumoniae* antigen was found in urine sample, and TBC test and blood cultures were all negative. Humoral and cellular immunity studies were performed with normal results. Viral PCR were negative. Positive serology titters of *M. pneumoniae* were found, suggestive of an acute infection (MP-specific-IgM increased antibody titers). Oral azithromycin was added to the previous treatment and administered for 5 days. Fever disappeared, patient was eupneic and blood analyses showed gradual improvement of the infectious-inflammatory parameters. Chest X-ray showed gradual decrease in lesion size. Chest CT scan showed a decrease in the consolidation size, but several images of air-liquid levels persisted, the largest of which was 4.7 cm in diameter at discharge. The boy was followed, as an outpatient, in the pediatric respiratory clinic. His follow-up radiograph and CT scan were normal 3 months after and he was negative for IgM and had decreased IgG *M.pneumonia* titers.

Discussion

Community-acquired pneumonia (CAP) is defined as an acute infection of the pulmonary parenchyma acquired in the community, as distinguished from hospital-acquired pneumonia. Childhood CAP is still an important cause of morbidity in the developed world [6]. A large number of different microorganisms have been implicated as etiologic agents of pneumonia in children, and the true prevalence of the etiologic agents in CAP is uncertain [7]. Generally in children, clinical finding, radiological features and commonly used laboratory tests can only provide indirect evidence of etiology. Necrotizing pneumonia is generally caused by gram-positive cocci (*Staphylococcus aureus*, *Streptococcus pyogenes*, or *S. pneumoniae*) or by anaerobic bacteria, such as *Klebsiella pneumoniae,* more frequently seen in children with risk factors for aspiration [8].

Complicated CAP requires a broader spectrum of antibiotic including beta-lactam-resistant and methicillin resistant staphylococcus aureus (MRSA) as well as other anaerobes and gram-negative organisms. Clinical response to empiric therapy and results of microbiologic and laboratory studies, will help to determine whether changes in antibiotics regimen are needed [9, 10].

In our patients, when diagnosis of necrotizing pneumonia was made, the empiric antibiotic therapy used for typical bacteria was indicated, to cover bacterial spectrum generally responsible for this entity, including cefotaxime, and clindamycin. When clinical symptoms persisted other possibilities were considered such as an underlying immunodeficiency condition, the development of complications, TB infection or an ineffective antibiotic coverage (travels or contact with birds or other animals were investigated and excluded). The immunodeficiency screening in both patients, including a complete blood count, cellular and humoral immunity evaluation and HIV testing, was normal. The use of a bronchoscopy, or other more invasive methods, in order to obtain a microbiologic diagnosis was evaluated but finally not necessary. When positive results of *M. pneumoniae* titers were obtained, and atypical pneumonia was clinically suspected, azithromycin was added to the treatment, with excellent results.

To assume that *M. pneumoniae* was the etiologic agent in the current cases was complicated; it is impossible to visualize the bacterium on Gram staining, and isolating the organism in culture is difficult and inefficient. Initially we could only rely on a single high antibody titer, and a single serologic test has limited values for diagnosis, but the subsequent seroconversion and the clinical response to macrolides treatment supported our findings [9].

The polymerase chain reaction (PCR) for *M. pneumoniae* was not available in our center, therefore, we had to rely only on the positive serology for *M. pneumoniae,* and the clinical findings. However, we also relied on the negativity of all the other complementary tests performed on both patients when searching for another etiologic agent (*S. pneumoniae´*s antigen was negative in urine samples and in pleural fluid; lack of bacterial growth in serial blood cultures and in pleural fluid; and Mantoux test negative, in both cases, also viral PCR were also negative, including test for influenza pneumonia, herpes virus, and most common respiratory viruses). These laboratory results can only support the diagnosis of necrotizing pneumonia caused by *M. pneumoniae*, but the clinical presentation of both patients, also supports this hypothesis. Neither of patients had high fever, toxic appearance,

respiratory distress or signs of severe systemic infection. Blood tests were only slightly affected with moderate increase in the inflammatory markers. We consider important to emphasize the good general condition of both patients, the rapid response to macrolide treatment, the lack of any other etiologic agent and the total recovery of both children in a short time. This led us to conclude, that the pneumonia, in both cases, might be caused by *M. pneumoniae* [5, 9, 10].

In conclusion, we would like to emphasize that it is rare, but not impossible, to find necrotizing pneumonias in children caused by this bacterium. Therefore, we think, it is important to memorize this possibility, and if clinically an atypical pneumonia is suspected, a macrolide should be added to the antibiotic regimen. Based on patient age, clinical and radiological factors, and coexisting illness empirical antibiotic treatment is decided. The first line antibiotic treatment in patients with clinical or radiological findings suggestive of pneumococcal pneumonia is not a macrolide. Oral amoxicillin is the recommended initial oral drug, and other antibiotics can be used depending of the suspected germ. Generally, in severe cases an intravenous third generation cephalosporin should be used, but in children aged 4 and older, affected by a community acquired pneumonia, a macrolide should be added if evolution is not clinically adequate or if a Mycoplasma infection is clinically suspected, regardless of the severity of the presentation [2, 7, 9].

Clinical and epidemiologic features can be used to determine the most likely pathogens and to initiate an empiric therapy in children. When usual antibiotic empiric regimen is not being successful, before thinking of uncommon germs, we must remember that: The unusual presentation of a common disease is generally more likely than the usual presentation of an uncommon disease [11, 12].

Conflict of interest

All authors declare the above mentioned were their current affiliations during the realization of this paper and that they have no competing interests. Dr Laura Moreno-Galarraga is a postdoctoral researcher supported by the FEP (Spanish Foundation of Pediatrics) in the Department of Pediatrics, Division of General Pediatrics in Mass General Hospital, Boston, MA 02114.

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