

Mycoplasma pneumoniae pneumonia – challenges related to diagnosis and treatment in children

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ABSTRACT

Introduction. Pneumonia is a common infectious disease among children, very familiar to pediatricians and a major cause of hospitalization worldwide. *Mycoplasma pneumoniae* (*M. pneumoniae*), an atypical pathogen, is estimated to be responsible for approximately 30-40% of community-acquired pneumonias.

The aim of the paper was to underline the diagnostic and treatment difficulties in a case of pneumonia with *M. pneumoniae* in a school-aged boy, with multiple presentations in the Emergency Service for respiratory difficulties.

Material and method. We present the case of a 7 years and 10-month-old male patient, admitted to our clinic for wheezing, cough and dyspnea.

Results. The clinical exam at admission pointed out influenced general status, wheezing, thoraco-abdominal swing, intercostal draft, sibilant and crackles, oxygen saturation 89%, tachycardia 134 beats/minute. The blood tests revealed mild leukocytosis, with neutrophilia, slightly increased inflammatory biomarkers. Considering the general status and the presence of functional respiratory syndrome, steroid and symptomatic anti-inflammatory treatment is initiated. However, the general condition remains stable, which required the widening of the spectrum of investigations with the performance of a chest CT noticing a pneumonic condensation with an air bronchogram located at the level of the right upper lobe. Considering the stationary respiratory functional syndrome and the radiological appearance of the pneumonia as well as the age, we performed serology for atypical germs and identified a positive titer of Ig M antibodies for *M. pneumoniae* by instituting Azithromycin po, but after 3 days, the evolution remains stationary, thus we changed the treatment with intravenous Levofloxacin, with a favorable subsequent evolution.

Conclusions. Pneumonia with atypical pathogens such as *M. pneumoniae* is a well-defined and well-known pathology in the literature, but it still remains a condition that imposes multiple difficulties related to the diagnosis and therapeutic management of pediatric cases.

Keywords: child, pneumonia, *M. pneumoniae*, imaging evaluation, treatment

INTRODUCTION

Pneumonia is a common infectious disease among children, very familiar to pediatricians and a major cause of hospitalization worldwide. Even more, given that most new infectious diseases that cause pandemics (including COVID-19) are caused by respiratory pathogens, the clinical significance is all the greater. Despite its importance, especially in the pediatric population, the diagnosis, treatment and prevention of pneumonia are mostly based on

studies conducted in adults. Thus, in recent years, a lot of studies have been carried out in developed and developing countries to improve the diagnosis and treatment of pneumonia in children [1].

Pneumonia is the main cause of death in young children under 5 years of age worldwide. Globally, pneumonia-related deaths were estimated to be 0.76 million, while the mortality rate was 5.5 cases per 1000 live births in 2015 [2]. In a recent large epidemiological study in the United States, the annual

incidence of community-acquired pneumonia requiring hospitalization was found to be 15.7 cases per 10,000 children, with the highest rate among children under 2 years of age [3]. In recent years, a decrease in the rate of illness and mortality has been observed in both developed and developing countries, this decrease being due to both the economic level, the improvement of the nutritional status, and to the specific interventions for pneumonia, from improving case management, including administration of empiric antibiotic treatment, until effective vaccines against the main causes of pneumonia in children are available [4].

M. pneumoniae, an atypical pathogen, is an important cause of respiratory tract infections, especially in children and young adults, estimated to be responsible for approximately 30-40% of community-acquired pneumonias [5-7]. The symptomatology is especially that of tracheobronchitis or pneumonia, accompanied by coughing, but desaturation or wheezing may also occur. School-aged children are more susceptible to this infection than small children [8,9]. Extrapulmonary symptoms such as arthritis, encephalitis or even Stevens-Johnson syndrome may also occur [10-12].

More studies have found an *M. pneumoniae* infection rate of 10-20% in hospitalized children and adolescents and 20-40% in pediatric patients from specialized outpatient clinics [13-15]. Clinically, pneumonia with *M. pneumoniae* cannot be differentiated from pneumonia of another cause, the specific diagnosis being very important because the treatment of pneumonia with *M. pneumoniae* must be based on macrolides, in the first phase, to significantly reduce the duration of the disease [16-17].

The aim of this paper was to underline the diagnostic and treatment difficulties in a case of pneumonia with *M. pneumoniae* in a school-aged boy, with multiple presentations in the Emergency Service for respiratory difficulties.

CASE REPORT

Reasons of admission

We report the case of a 7 years and 10-month-old male, known from his personal pathological history with multiple episodes of wheezing, who presents to the Emergency Service at the territorial level for wheezing, cough and dyspnea, where laboratory tests showed leukocytosis with neutrophilia, slightly elevated inflammatory markers (CRP 8.1 mg/l), and chest x-ray revealed a bilaterally accentuated interstitial pattern and a condensation area at the level of the right upper lobe. Considering all the aforementioned facts, the patient was initiated antibiotic treatment with iv Ampicillin and symptomatic, but without improvement, being referred to the Pediat-

ric Clinic I for monitoring, additional investigations and specialized treatment.

Diagnostic focus and assessment

The clinical exam on admission revealed influenced general status, wheezing, thoraco-abdominal balance, intercostal draft, sibilant and crackling rales, oxygen saturation 89% in ambient air, 98% with oxygen, tachycardia 134 beats/minute, having a weight of 35 kg. The laboratory tests on admission showed mild leukocytosis (12,470/ μ L) with neutrophilia (8,610/ μ L, 69%), slightly increased inflammatory markers (CRP 12 mg/l and ESR 34 mm/h). Considering the general stationary status, with the maintenance of the functional respiratory syndrome and oxygen saturations of 92-93% in the ambient air, anti-inflammatory steroid treatment and symptomatic treatment were initiated. However, the functional respiratory syndrome persisted, which necessitated the widening of the spectrum of investigations with the performance of a chest CT which highlighted the area of pulmonary condensation with an air bronchogram located at the level of the right upper lobe, mediastinal, prevascular and axillary lymph nodes of an inflammatory nature. We mention that other causes of viral respiratory infections, TB and allergic pathology were ruled out. Considering the persistent functional respiratory syndrome and the radiological appearance of pneumonia as well as the age, the presence of an atypical pathogen, such as *M. pneumoniae* or *C. pneumoniae*, was suspected, and the IgM antibodies for *M. pneumoniae* were found to be positive. Taking into account the previously mentioned result, we instituted treatment with Azithromycin po, in a dose of 10 mg/kg/day, but after 3 days, the patient's evolution showed no improvement, and therefore we changed the treatment with Levofloxacin in a dose of 350 mg intravenous. After approximately 3 days of treatment, the patient's evolution was favorable, with the remission of functional respiratory syndrome and stetic changes. Thus, the patient was discharged after 10 days of treatment, in good general condition, cardiac and respiratory balanced.

DISCUSSIONS

M. pneumoniae is one of the most important pathogens for community-acquired pneumonia in children. *M. pneumoniae* pneumonia is usually mild and even presents as a self-limiting disease [18,19]. However, in recent years, more and more severe episodes and refractory forms appear in pneumonia with *M. pneumoniae*, posing great challenges to pediatricians [20-23]. *M. pneumoniae* is classically referred to as an atypical pathogen, with both asymptomatic infections and infections of the upper

and lower respiratory tract being reported [24-27]. As we mentioned above, in most cases, the infection is self-limiting, but a percentage of 18-20% requires hospitalization, and some patients may even develop severe forms that associate problems with diagnosis and treatment as it was in the case of our patient considering that empirical treatment initiated initially corresponding to a typical community-acquired pneumonia given the rare incidence of atypical pneumonia cases in the pediatric age.

The diagnosis is established on both the clinical manifestations, which are non-specific, and on the abnormal laboratory tests - increased inflammatory markers, and radiological examinations ranging from an accentuated interstitial lung pattern to a condensation area with air bronchogram, most often appearing at the level of the right upper lobe [28], as in the case of our patient. The term RMPP-refractory *M. pneumoniae* pneumonia is often used to describe cases that are difficult to treat, the main points used in the definition of a refractory case being: prolonged or even exacerbated clinical or radiological manifestations and lack of adequate response to macrolide treatment [29]. In recent years, more and more cases of refractory *M. pneumoniae* pneumonia have been reported in China and all around the world, drawing attention to this pathology. Our case can be considered a refractory case because it fulfills the two main criteria: the progression or lack of improvement in respiratory symptoms, with the maintenance of the need for oxygen on the mask, under antibiotic treatment with macrolides and symptomatic.

M. pneumoniae pneumonia in pediatric population is a major cause of community-acquired pneumonia worldwide. In China, a 10-year study was carried out in Beijing at the Children's Hospital, which aimed to explore the epidemiological characteristics of *M. pneumoniae* pneumonia and the development of severe forms. A number of 27,498 children and adolescents were included in the study, of which 37.5% had pneumonia with *M. pneumoniae*, and it was observed that periodic epidemics occur in this area, every 2-3 years, with an increase in the positivity rate for *M. pneumoniae* in these periods, the age peak being between 6-10 years, 75.2%, more than in other age groups. Regarding seasonal incidence, most cases were recorded in September, October and November. In addition, 13% were severe forms of pneumonia with *M. pneumoniae*, but during the 10-year study period, the rate increased to 42.6%, the average age of these patients being 6.7+/-3 years, the small age being associated with milder forms [30,31]. Another study carried out in Suzhou province, also in South China, for 9 years, on a number of 20,021, reported an *M. pneumoniae* infection rate between 30.27-36.08% [32,33]. This study aimed to analyze the epidemiological characteristics and

ensure a scientific basis for correct diagnosis and treatment, as well as the implementation of control measures for the public health department [33].

The multiple studies that have been carried out both in Europe and in Asia regarding community-acquired pneumonia, which together with malnutrition still remains a main problem worldwide in the pediatric population, with the aim of developing a monitoring and limitation strategy of infections, as well as early diagnosis and correct treatment to prevent both severe forms or relapse to treatment, as we have seen occur in pneumonia with *M. pneumoniae*, as well as to prevent long-term complications (bronchiolitis obliterans, bronchiectasis) [34].

Regarding treatment, a change in initial treatment should be considered when symptoms are persistent despite macrolide treatment, especially when refractory *M. pneumoniae* pneumonia is suspected [35]. Different studies tested the treatment with minocycline and doxycycline, recommended in a dose of 4 mg/kg/day, showing fast efficacy and a relatively low incidence of adverse reactions, but taking into account the possible adverse reactions of tetracyclines, they present limited utility in children under 8 years old [36-38]. Another option are fluoroquinolones represented by tosufloxacin, moxifloxacin, ciprofloxacin and levofloxacin [39-43]. The main controversies regarding the treatment with fluoroquinolones in the pediatric population are related to the effects on the growth cartilages and on the musculoskeletal events which are, however, reversible [44]. For example, oral Tosufloxacin was authorized in Japan as a second-line treatment for children and adolescents with community-acquired pneumonia [45], at a dose of 12 mg/kg/day, with minimal adverse effects, joint symptoms being rarely reported [46,47]. However, the experience of administering fluoroquinolones in children diagnosed with *M. pneumoniae* pneumonia is limited [47].

CONCLUSIONS

Although pneumonia in the pediatric population is a very well-known pathology and multiple studies were performed to improve its management regarding both investigations and treatment, it still remains a major health problem that can pose multiple difficulties related to both management and long-term sequelae. Thus, by understanding the epidemiology and characteristics of pneumonia with *M. pneumoniae* in the pediatric population, we can contribute to the timely treatment and diagnosis of these cases, improving the prognosis of children with pneumonia with severe or refractory forms of *M. pneumoniae*.

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