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Different faces of Mycoplasma pneumoniae in children - cardiological and skin complications- case reports and literature review

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Abstract:
Mycoplasma pneumoniae is one of the main pathogens responsible for atypical pneumonia, especially in children over the age of 5, where it accounts for about 40% of cases of extramedullary pneumonia. In addition to respiratory-related symptoms, it can lead to a variety of extrapulmonary manifestations associated with involvement of other organs. In this article, we present case reports of two pediatric patients with detected M. pneumoniae infection with associated cardiac and skin complications. The first case report describes an 11.5-year-old boy who was admitted to the Department of Pediatrics because of chest pain, fever and moist cough for several days, who was diagnosed with myocarditis during M. pneumoniae infection. The second case report describes a 17-year-old girl with a recent respiratory infection who was admitted to the hospital for pain, swelling, blistering of the lips and oral mucosa. Mycoplasma pneumoniae infection can lead to extrapulmonary complications in children, which can produce nonspecific symptoms, so clinical vigilance and early recognition are important to minimize the risk of complications.

Keywords: Mycoplasma pneumoniae, children, myocarditis, mucocutaneous lesions

Introduction

Mycoplasma pneumonie is one of the most important pathogens responsible for the development of so-called atypical pneumonia. It is responsible for as many as 40% of cases of extramedullary pneumonia in children over the age of 5. The infection is transmitted by the droplet route, and the average incubation time is 1 to 3 weeks (20-23 days on average). [1] The infection is endemic and causes epidemics every 4-7 years or so, which can be explained by the disappearance of population immunity and the emergence of new serotypes. Symptoms include an unremitting fever, a persistent dry cough, sore throat, headache, muscle pain and deterioration of mood. In more severe cases, dyspnea may occur, and the nature of the cough resembles pertussis. [2] Diagnosis is based on the determination of serum antibodies and a PCR test. Treatment includes the use of an antibiotic from the macrolide group (azithromycin, clarithromycin, erythromycin). In addition to respiratory involvement, extrapulmonary manifestations may occur in 7-8% of cases, the most important of which are complications from the nervous system (meningitis, encephalitis, myelitis, Guillain-Barré syndrome), cardiovascular system (myocarditis, pericarditis, cardiac arrhythmias), renal (tubular necrosis, interstitial nephritis, glomerulonephritis), gastrointestinal (hepatitis), and dermal-mucosal complications (erythema nodosum, erythema multiforme, Stevens- Johnson syndrome). [3,4]

Case reports

An 11.5-year-old boy was admitted to the Department of Pediatrics because of chest pain, fever (38 degrees) and a moist cough for several days. In addition, the patient awoke during the night reporting stabbing, localized chest pain. He rated it a 6 on a 10-degree pain scale. On physical examination on admission, he was in fairly good general condition, with efficient cardiopulmonary function, and auscultation of crackles over the lung fields. Other than that, no other deviations. Laboratory tests performed showed elevated inflammatory exponents- CRP=20.5 mg/L [N:<10], high troponin- hsTnI=5847.21 pg/ml [N<45] and NTproBNP=571 pg/ml [N<125]. Chest X-ray showed inflammatory changes in the lower left lung field. A cardiology consultation was carried out, during which an ECG was performed which showed

irregular sinus rhythm and slight ST elevation in II, V5- V6 1.5-2 mm, and an ECHO was performed which showed features of myocarditis with good left ventricular systolic function. The diagnosis was expanded by performing a PCR respiratory panel, which confirmed Mycoplasma pneumoniae infection. Treatment included spironolactone, enalapril, mucolytic, parenteral hydration and clarithromycin. During the following days of hospitalization, improvement in the boy's clinical condition and normalization of cardiac parameters were observed. The patient was discharged home in good general condition.

A 17-year-old girl with hypothyroidism was admitted to the Department of Pediatrics for pain, swelling, blistering of the lips and oral mucosa. The day before, the patient had experienced oral discomfort and chapped lips. The overall picture gave suspicion of Stevens-Johnson syndrome. She had a history of upper respiratory tract infection 2 weeks earlier. The patient reported nausea and had an elevated body temperature (37.8 degrees). On physical examination on admission in moderately good general condition, reddened throat, chapped lips, blisters filled with serous contents on the lips and oral mucosa present. Oral mucous membranes desquamated; tongue coated with fibrin. Above the lung fields auscultatorically crackles and furls on the left side. A chest X-ray was performed, which showed sparse streaky shadowing on the left side consistent with inflammatory and atelectatic changes. Laboratory tests performed showed elevated inflammatory markers- CRP=32 mg/l [N<10]. Symptomatic treatment was instituted, and bacteriological and virological tests were taken. A positive result of IgM class antibodies against Mycoplasma pneumoniae- 133 U/ml (>25 positive) was obtained. Antibiotic therapy - clarithromycin was implemented, achieving clinical improvement. During hospitalization, an additional erythematous rash localized on the skin of the lower and upper extremities appeared, which subsided after treatment with an anti-allergic drug. The patient was consulted cardiologically, and a cardiac ECHO study was performed, which revealed mitral valve prolapse. The girl was also consulted endocrinologically, due to emerging abnormalities in thyroid hormone tests. In the ultrasound of the thyroid gland performed, the picture was normal. After the treatment, the symptoms almost completely disappeared, except for a slight swelling of the labial mucosa. Due to her good clinical condition, the patient was discharged home.

Discussion

Mycoplasma pneumoniae although usually benign and self-limiting in nature, in some cases it can give extrapulmonary complications. Although extrapulmonary symptoms are fairly well known, there are various theories regarding their etiology Cardiac complications associated with the infection, especially in children, are quite rare. Their incidence ranges from 1 to 8.5% and was much more common in adults than in the pediatric population. [5] Known cardiac complications include pericarditis, conduction abnormalities, as well as cardiac thrombosis, endocarditis and heart failure, and myocarditis, which was described in a clinical case. [6] Myocarditis caused by M.pneumoniae can lead to serious consequences. The exact mechanisms of action causing the inflammation are multifaceted and have not yet been fully elucidated. They may include activation of the host immune response, which leads to the release of pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor- α in cardiac tissues. [7,8] An autoimmune mechanism, involving cross-reactivity between components of M.pneumoniae cells and cardiac tissues, also plays an important role in cardiac damage. [8] Increased levels of circulating immune complexes and elevated titers of T-cell immunoglobulin and mucin domain 1 have been implicated in the development of myocarditis. [9] In addition, it has been suggested that M. pneumoniae may directly attack cardiac cells, causing damage and contributing to the inflammatory cascade. [10] It has been proven that children with severe atypical pneumonia have a high risk of thrombosis. [11] Liu et al. described a series of 43 cases of thrombosis in children caused by M. pneumoniae, characterized by various clinical manifestations. They found that lung consolidation (>2/3 lobe) and high levels of inflammatory markers (CRP >97.5 mg/L and LDH >735.1 IU/L) were risk factors strongly associated with thrombosis.[12] Often, young patients may not exhibit specific cardiac symptoms and may be difficult to distinguish from symptoms of primary lung disease. Young children may not be able to report their complaints accurately, so diagnosis in children is often delayed. Studies show that, on average, it takes about seven days from the onset of symptoms to diagnosis. Song S. et al. in their study showed that in children, pulmonary embolism associated with pneumonia caused by M. pneumoniae usually occurred about 2 weeks after the onset of the original illness, and embolic symptoms appeared only after the temperature stabilized and the cough subsided. In addition, the time of diagnosis of pulmonary embolism did not always coincide with the acute phase of the disease. [13] Therefore, children with abnormal laboratory indicators should be closely monitored for new symptoms and worsening of existing ones, due to possible developing cardiac complications.

Mucocutaneous lesions are probably the most common complication of M. pneumoniae infections in children. Their overall incidence is about 22.7-25%. [14,15] They can manifest as urticaria, papulopustular rashes, erythema nodosum, Kawasaki disease, erythema multiforme, Stevens- Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN).[16,17] The overlap of clinical manifestations of these conditions sometimes makes a definitive diagnosis difficult. In 2015. Canvan et al. proposed distinguishing a new disease entity-mucocutaneous disease caused by M. pneumoniae (MIRM). MIRM is characterized by a predominance of mucosal involvement compared to skin, a milder course compared to SJS and TEN, a different pathomechanism related to the presence of the pathogen in skin lesions, and different optimal treatment. The diagnostic criteria for this condition are shown in table 1.

Classification	**MIRM**
Detachment	<10% BSA
No. of mucosal sites involved*	≥2
Few vesiculobullous lesions, or scatteres atypical targets	Yes
Targetoid lesions	±
Evidence of atypical pneumonia	
1)Clinical	Fever, cough, positive ausculatory findings
2) Laboratory	Increase in M. pneumoniae antibodies, M. pneumoniae in oropharyngeal or bullae cultures or PCR, and/or serial cold agglutinins

*Rare cases have <2 musocal sites involved

Table 1. Diagnostic criteria for MIRM.

In addition, the authors distinguish between the MIRM sine rash and severe MIRM forms. Cutaneous lesions in the MIRM sine rash form may be absent or may include few and fleeting morbilliform lesions, or few vesicles. Severe MIRM is characterized by the presence of extensive widespread blisters or flat atypical targets.[18] Mucosal lesions are most commonly localized in the oral cavity, on the conjunctiva, and in the genital area. A small percentage of patients have multiple skin lesions. In terms of morphology, the lesions are vesicular or “shooting disc” in nature, usually diffuse and localized on the extremities. [19]

Some cases of skin lesions and mucous membranes may be accompanied by the aforementioned blisters, as in the case of the described patient, so differential diagnosis with HSV infection is important. The prognosis of MIRM is good, and management includes antibiotic therapy directed against M. pneumoniae, relief of discomfort and adequate hydration.[20] There are no current data on the efficacy of immunosuppressive treatment. Steroid therapy and intravenous supply of immunoglobulins are used only in patients with particularly severe disease. [21]

Conclusions

M. Pneumoniae infection, although commonly known for causing respiratory symptoms can lead to a variety of extrapulmonary complications in children. Often cardiac symptoms can be nonspecific, overlapping with pneumonia symptoms, and skin symptoms can be difficult to differentiate, so clinical vigilance and early recognition are important to minimize the risk of complications.

Disclosure

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Author's contribution

All authors contributes to the article.

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