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CASE REPORT

Erythema and mucositis induced by Mycoplasma pneumoniae as a differential diagnosis of herpes gingivostomatitis: a case report

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Abstract

The present case report describes and relate extrapulmonary manifestations of an infection caused *by Mycoplasma pneumoniae*. We present an eight years old patient, female, initially presenting with respiratory symptoms associated with fever, developed progressively worsening mucocutaneous scaling lesions, which were initially misdiagnosed as a case of herpetic gingivostomatitis. Upon hospitalization, pneumonia was diagnosed, and suspicion of *Mycoplasma pneumoniae* infection was raised, later confirmed through serological testing. Erythema and mucositis induced by *Mycoplasma* (MIRM) should be suspected in children with respiratory symptoms as cough, fever, non-well-being, approximately one week before mucocutaneous eruption. Laboratorial evidences of *M. pneumonie* (IgM antibody, pathogen detection in oropharynx or blister content culture) reinforces the diagnosis.

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INTRODUCTION:

Mycoplasma pneumoniae infection is common in pediatric patients, with a higher incidence in school-aged children, accounting for approximately 10% of community-acquired pneumonias. Extrapulmonary manifestations of the pathogen have been studied, such as hemolytic anemia, arthritis, cardiac abnormalities, and mucocutaneous manifestations, which are present in up to 25% of patients infected by the pathogen.[1]

Mucocutaneous manifestations represent a recent clinical entity, with the first reports dating from 2015. These manifestations present as mucosal lesions that are more intense than cutaneous lesions and may be confused with urticarial reactions, erythema nodosum, Stevens–Johnson syndrome, and drug reaction with eosinophilia and systemic symptoms (DRESS).[1,2] Compared with these diagnoses, Mycoplasma-induced rash and mucositis (MIRM) generally has a benign course and a better prognosis.[2]

The pathophysiology is not well defined; however, the involvement of immune complexes and the complement system is believed to play a role. At the histopathological level, cellular apoptosis and dermal perivascular infiltrate are observed.[1,3]

Cases can be subdivided into three categories: 1. Classic MIRM, whose lesions resemble those already described; 2. MIRM without rash, when the patient meets the classic criteria but does not present an evident rash; and 3. Severe MIRM, with involvement of more than two mucosal sites and extensive rash.[1]

Differential diagnoses that must be ruled out include Kawasaki disease, pemphigus vulgaris, herpetic gingivostomatitis, severe hand-foot-and-mouth disease, autoimmune diseases, and drug-induced epidermal necrolysis.[6,7]

Treatment of the condition is not well established. It is believed that patients benefit from therapy directed against the microorganism. Therefore, macrolides, tetracyclines, and quinolones may be used, with macrolides being the first-line option.

The prognosis is good, with more than 80% of patients achieving complete recovery and recurrence rates below 10%. The most common sequelae are mucosal synechiae and pigmentary changes. Systemic complications are extremely rare.[1,8] The case described below reports the clinical course of a patient with a confirmed diagnosis of *M. pneumoniae* infection with extrapulmonary manifestations. The article followed ethical guidelines and was approved by a local ethics committee under CAAE 81778624.8.0000.0121.

CASE DESCRIPTION:

Female, 8 years old, five days prior to admission with dry cough, fever, prostration, and an aphthous lesion on the lower lip three days before admission, progressing to lip desquamation and difficulty eating or drinking liquids. She sought medical care two days prior to admission and was prescribed macrolide antibiotic therapy and symptomatic treatment, which she used for less than 24 hours. Due to worsening of the lip lesions, she sought care at a referral hospital, where she was diagnosed with community-acquired bacterial pneumonia (CAP) evidenced on imaging and was referred to a tertiary hospital for treatment.

Upon arrival, she presented perioral lesions with hemorrhagic crusts and multiple ulcerated lesions, marked lip edema (3+/4+), difficulty opening the mouth, refusal of oral intake, bilateral coarse crackles on lung auscultation, and a prior diagnosis of pneumonia. Crystalline penicillin and symptomatic treatment for oral lesions were initiated, which were initially diagnosed as herpetic gingivostomatitis. A viral panel was collected by nasal swab, with bleeding during the procedure due to intranasal lesions. On the second day of hospitalization, due to the presence of extensive lesions without the typical vesiculobullous appearance of herpetic lesions (Figure 1), intravenous macrolide therapy was initiated and serology for *M. pneumoniae*, PCR for herpes simplex virus types 1 and 2, complete blood count, and C-reactive protein (CRP) were collected, all of which showed no significant abnormalities.



Figure 1. Perioral mucocutaneous lesions with hemorrhagic crusts and ulcerated lesions on hospital day 1, with lip edema 3+/4+.



Figure 2. Cicatricial mucocutaneous lesions two days after completion of treatment, with absence of lip edema.

On the third day of hospitalization, after antibiotic infusion, the patient developed a non-pruritic erythematous rash on the arm and forearm, with spontaneous resolution. The decision was made to maintain the medication. On the following day, a new erythematous rash appeared. Due to the possibility of an allergic reaction, the medication in use was discontinued, and penicillin was restarted. At that time, the patient showed clinical improvement of the lip lesion, with minimal edema (+/4+), desquamative lesions, improved acceptance of liquids, and improvement in lung auscultation and cough. After 72 hours of intravenous penicillin, positive results for *M. pneumoniae* (IgM and IgG) were obtained, and penicillin was replaced with oral macrolide therapy. The patient evolved without allergic reaction, with improvement of perioral lesions.

She returned to the service for reevaluation two days after completion of treatment, showing significant improvement of the lesions (Figure 2). At the time of follow-up, negative results were obtained for herpes simplex virus types 1 and 2.

DISCUSSION:

Mycoplasma is a Gram-positive bacterium first described in 1898.[9,10] In 1944, *M. pneumoniae* was isolated from a patient with pneumonia and, since then, it has been recognized as one of the main causative agents of pneumonia in pediatric patients, especially in school-aged children and adolescents, although it may also affect other age groups.[11] Transmission occurs through contact with respiratory tract droplets from infected patients, and the organism may remain incubated for up to 20 days after exposure.[9] Immunity is not long-lasting, and patients may be reinfected multiple times.[9,6] An increase in the incidence of cases has been observed, along with a proportional increase in extrapulmonary manifestations of the pathogen.[9]

Regarding the clinical presentation, approximately one week before mucocutaneous manifestations, most patients present nonspecific prodromal symptoms.[1–4] Two to three mucosal sites are usually affected. Lesions present as hemorrhagic crusts, erosions, and ulcers, associated with local pain,[1,4] as observed in the patient described herein.

Cutaneous lesions are present in a minority of patients, who are classified as MIRM without rash.[1] When present, they are sparse, vesiculobullous, and mainly affect the extremities (46%) and trunk (23%), and may be described as papules, macules, or morbilliform erythema,[1,3] the latter being the type observed in the patient during the course of the disease.

MIRM should be suspected in children with a history of prodromal symptoms preceding the mucocutaneous eruption by approximately one week, as occurred in this patient. Laboratory evidence of *M. pneumoniae* infection supports the diagnosis,[4] including elevated IgM antibody levels, detection of the pathogen in the oropharynx, or culture of the contents of bullous lesions.[1,3,5] In its classic form, diagnostic criteria include: mucocutaneous eruption in one or more sites; presence of vesiculobullous or targetoid lesions in at least two mucosal sites; use of medication without clinical improvement; prodromal symptoms within the previous 7 to 10 days; and clinical, radiographic, or laboratory evidence of an infectious trigger.[1,4]

With regard to these manifestations, approximately 25% of patients present some extrapulmonary sign or symptom, produced by immunomediated effects that have not yet been fully elucidated.[9] In the case described above, the patient was female and within the main age range affected by *M. pneumoniae* infection. The typical clinical picture includes fever, persistent dry cough, asthenia, dyspnea, headache, and odynophagia.[9] The patient presented two of these symptoms—fever and persistent dry cough—and subsequently developed lesions in the oral and nasal cavities. Because extrapulmonary manifestations are uncommon, these lesions were initially evaluated as herpetic gingivostomatitis and symptomatic therapy was instituted. However, herpes virus–related lesions typically begin as small vesicles that evolve into ulcers with a yellowish base and an erythematous halo,[12] which differs from the lesion pattern observed in this patient (Figure 1).

Given that the patient had epidemiological exposure to *M. pneumoniae* and met four of the five criteria for MIRM,[1,4] the diagnosis of infection by the pathogen was considered and treatment was initiated. Recommended investigations include complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Mycoplasma serology, chest radiography, and naso- and oropharyngeal swabs.[6] Mucosal or skin biopsy is not indicated for diagnosis, as it does not reliably distinguish the main differential diagnoses.[7]

Because the patient was hospitalized in a setting with different attending teams and developed a localized erythematous rash after the use of azithromycin, the medication was discontinued due to suspected allergy. A beta-lactam antibiotic was initiated, and it was again considered that the mucosal lesions were herpetic in origin and that the pneumonia was typical, despite progressive improvement of the lip lesions. The beta-lactam was maintained for 72 hours, without further improvement of the lesions, fulfilling the last of the five diagnostic criteria for MIRM. After positive IgM and IgG serology results for *M. pneumoniae*, confirming the diagnostic hypothesis at the laboratory level, macrolide therapy was

restarted with good tolerance, leading the healthcare team to question whether the rash was truly drug-induced or represented a new cutaneous manifestation of the pathogen.

The patient was treated with azithromycin at a dose of 10 mg/kg/day for five days. This medication, as well as clarithromycin, is considered first-line therapy.[9] She returned for outpatient follow-up two days after completion of treatment, with improvement of the lesions (Figure 2) and absence of respiratory symptoms. It should be noted, however, that therapy remains controversial, with variability in dosage and duration of treatment. Severe cases or patients unable to tolerate oral therapy may be treated parenterally.[8,9] Analgesics, fluid replacement, and nutritional support should be used as needed. The use of corticosteroids and immunosuppressants has been studied in severe MIRM.[1]

CONCLUSION:

Based on the reported case and the preceding discussion, it is evident that although this pathogen is very common in pediatrics, with well-known pulmonary manifestations, Mycoplasma-induced rash and mucositis (MIRM) is a recent clinical entity with recognized management but still infrequently applied. Because the condition remains poorly disseminated, changes in treatment may occur for various reasons that hinder appropriate disease management, as occurred in the patient described above, in whom antibiotic switching delayed treatment completion and more effective clinical improvement.

Therefore, it is essential to reinforce knowledge of the extrapulmonary manifestations of this microorganism to ensure that appropriate treatment is not compromised and that patients benefit more rapidly. The importance of laboratory testing in these cases is also emphasized, as it supports confirmation of the suspected diagnosis.

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