

# Oral ulcerations after respiratory symptoms

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## Abstract

*Mycoplasma pneumoniae* (*M. pneumoniae*) is frequently associated with respiratory infections in pediatric patients, but can also cause mucosal and cutaneous lesions. It has a wide spectrum of manifestations, including Kawasaki disease, erythema multiforme, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis and *M. pneumoniae*-induced rash and mucositis (MIRM). This last condition was described as a new entity with mucosal findings consistent with SJS, but without or with sparse cutaneous involvement, preceded by a recognized *M. pneumoniae* infection. The main objective was to describe two possible presentations of this MIRM in order to raise awareness of the diagnostic criteria and proper clinical approach. Authors report the cases of two adolescents with mucosal but no cutaneous involvement that had laboratory confirmation of *M. pneumoniae* infection, either with DNA protein chain reaction or serum enzyme immunoassay. The therapeutic approach included azithromycin course and supportive care, with noticeable clinical improvement and favorable prognosis. These cases corroborate clinical and diagnostic features previously described, which include a predominance of two or more mucosal sites (mainly oral and ocular), relatively sparse cutaneous involvement and evidence of an atypical infection. An accurate diagnosis is of utmost importance for the correct management and prognosis.

## Keywords

Mucositis, *Mycoplasma pneumoniae*, oral ulcer, pediatrics, pneumonia, Stevens-Johnson syndrome.

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## Introduction

*Mycoplasma pneumoniae* (*M. pneumoniae*) is frequently responsible for respiratory infections in pediatric patients, and one in four patients present extrapulmonary complications [1, 2]. It has a myriad of mucocutaneous manifestations, including erythema multiforme (EM), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) [3]. Due to the absent or sparse cutaneous involvement in some patients, Canavan et al. in 2015 proposed a new entity, “*M. pneumoniae*-induced rash and mucositis” (MIRM), which is distinct from SJS, TEN and EM [1-4].

The main aim of this case report was to describe two presentations of MIRM to raise awareness of the diagnostic criteria and proper clinical approach.

## Case description

The first case concerned a previously healthy 15-year-old girl who presented to the emergency room (ER) with a 3-week history of nasal obstruction, rhinorrhoea and dry cough, a 7-day history of diffuse ulcerations of the oral mucosa (lips, palate and gums) (Fig. 1), and conjunctival hyperaemia. She reported no previous medications



**Figure 1.** Diffuse ulcerations of the oral mucosa (lips, palate and gums) in a previously healthy 15-year-old girl.

or fever. Physical examination revealed oral ulceration, partially covered by haemorrhagic crusts, and bilateral conjunctival erythema. No cutaneous involvement was observed. Chest X-ray revealed patchy inflammatory changes confined to the pulmonary interstitium. Laboratory findings included white blood cell (WBC) count 7,740/ $\mu$ L (neutrophils 5,440/ $\mu$ L), C-reactive protein (CRP) 50.4 mg/L, erythrocyte sedimentation rate (ESR) 62 mm/h, and negative results for herpes simplex virus, Epstein-Barr virus, parvovirus and cytomegalovirus serologic tests. The serum enzyme immunoassay showed positive *M. pneumoniae* IgM, despite a negative DNA polymerase chain reaction (DNA-PCR) result for a sample of nasal secretions.

The second case is related to a previously healthy 17-year-old boy who presented to the ER with a 7-day history of fever, cough and rhinorrhoea. One day before admission, he developed oedema and painful erosions of the lips (Fig. 2), as well as conjunctival discharge. Clinical observation revealed blistering and ulcerations of the oral mucosa, along with purulent bilateral conjunctivitis and minor urethral meatus erythema. No cutaneous involvement was described. Chest X-ray findings were similar to the previous patient. Laboratory results were as follows: WBC count 11,110/ $\mu$ L (neutrophils 7,320/ $\mu$ L), CRP 66.2 mg/L, and ESR 42 mm/h. Both the DNA-PCR and enzyme IgM immunoassay were positive for *M. pneumoniae*, and the remaining aetiological investigations were negative.

Both patients were treated with 3 days of azithromycin and supportive care. The second patient required ward admission for intravenous fluids, ophthalmologic evaluation with subsequent neomycin/dexamethasone eye drops, and anaesthetic mouthwash for the oral lesions. Following treatment, both patients presented noticeable clinical improvement and a favourable prognosis.



**Figure 2.** Oedema and painful erosions of the lips in a previously healthy 17-year-old boy.

## Discussion

Atypical pneumonia is a common diagnosis in childhood and adolescence, and *M. pneumoniae* is implicated in approximately 40% of cases. Less frequently, *M. pneumoniae* can be associated with dermatological manifestations, posing a challenge to distinguish MIRM from differential diagnoses of EM, SJS and TEN.

This was the case until 2015, when Canavan established the diagnostic criteria for MIRM, allowing the correct classification of cases with mucosal lesions but with absent or scarce cutaneous involvement, previously classified as “atypical/incomplete SJS” or “Fuchs syndrome”.

In contrast to SJS/TEN, MIRM presents a male preponderance (two-thirds) and a mean age of 11.9 years (standard deviation  $\pm$  8.8 years). In the majority of patients with MIRM, prodromal symptoms including fever, cough and/or malaise will be present the week before the onset of mucosal eruptions [1-6].

The oral mucosa is the most frequently affected site (94%), followed by ocular and urogenital mucosa [1, 3-5]. Therefore, patients can also present purulent bilateral conjunctivitis, photophobia and genital ulcerations [3].

Consistent with the literature, both our patients presented with cough and rhinorrhoea as prodromal symptoms, a predominance of oral and ocular mucosa lesions and no cutaneous involvement. In addition, the two adolescents had laboratory evidence of an atypical infection, as one case had a positive IgM test for *M. pneumoniae* and the second had positive IgM and DNA-PCR for *M. pneumoniae*.

Clinical and diagnostic characteristics of classic MIRM include: (1) predominance of mucositis involving  $\geq$  2 mucosal sites; (2) skin detachment  $<$  10% of body surface area; (3) sparse vesiculobullous lesions or scattered atypical targets; and (4) evidence of atypical infection with either clinical (cough, fever or positive auscultatory pulmonary findings) or laboratory (elevated enzyme immunoassay IgM for *M. pneumoniae*, positive result in oropharyngeal or bullae cultures, positive DNA-PCR and/or serial cold agglutinins) findings [1, 3, 5, 7, 8]. Almost 33% of all MIRM patients do not present significant cutaneous involvement (classified as “MIRM sine rash”), as illustrated in both cases described here [9].

The mechanisms and causal associations involved in MIRM are not completely understood,

but they may differ from EM or SJS/TEN. On the one hand, there is some evidence suggesting cloning of B cells with consequent cutaneous immune complex deposition and complement activation as a possible mechanism for MIRM. On the other hand, delayed hypersensitivity reaction and Fas ligand-mediated toxicity have been described for EM or SJS/TEN. A previous history of herpes simplex virus infection is often associated with EM, and SJS/TEN is usually related to exposure to certain medications, although *M. pneumoniae* is also a possible agent [1, 3, 4].

In case of diagnostic suspicion of MIRM, it is critical to perform an aetiological investigation, which should include chest X-ray and DNA-PCR or enzyme immunoassay IgM for *M. pneumoniae*. The main step for therapeutic management is supportive care, namely pain control and correction of any nutritional and/or hydroelectrolytic imbalances. Although there are no specific guidelines for the treatment of MIRM, the use of antibiotics is universally recommended. There is limited evidence supporting intravenous immunoglobulin and systemic corticosteroids as a first-line therapy [1, 4, 5, 10].

MIRM usually presents an excellent prognosis, with full recovery and uncommon recurrence, as was the case for our patients. Concerning sequelae, mucosal synechiae and pigmentation disorders are the most frequently described [1].

To conclude, MIRM is an entity that should be included in the differential diagnosis of mucocutaneous rash, especially if prodromal symptoms (fever, cough, malaise) and prominent mucosal involvement are present. An accurate diagnosis is of utmost importance for the correct treatment and optimal prognosis.

## Declaration of Ethics

This study was approved by the Ethic Committee of Centro Hospitalar Tâmega e Sousa and complies with the Helsinki Declaration for medical research.

## Informed consent

Informed consent was obtained from the adolescents' legal representative.

## Declaration of interest

The Authors have no conflicts of interest or financial support to disclose. The study did not receive any funding, financial support or material support.

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