Actas Dermosifiliogr. 2016;107(7):e47–e51

ACTAS Dermo-Sifiliográficas

Full English text available at www.actasdermo.org

E-CASOS CLÍNICOS

Mycoplasma pneumoniae-Induced Mucocutaneous Rash: A New Syndrome Distinct from Erythema Multiforme? Report of a New Case and Review of the Literature☆

M. Martínez-Pérez,* A. Imbernón-Moya, A. Lobato-Berezo, M. Churruca-Grijelmo

Servicio de Dermatología y Venereología, Hospital Severo Ochoa, Madrid, Spain

KEYWORDS
Mycoplasma pneumoniae;
Erythema multiforme;
Stevens-Johnson syndrome;
Rash;
Mucositis;
Clinical classification;
Treatment

Abstract Respiratory tract infection due to *Mycoplasma pneumoniae* can provoke cutaneous and mucosal rashes, which have been classified within the spectrum of erythema multiforme or Stevens-Johnson syndrome. This classification is of therapeutic and prognostic importance and has generated intense debate in the literature. A recent systematic review of 202 cases of mucocutaneous rashes associated with *M. pneumoniae* infection concluded that these rashes might constitute a distinct entity, for which the term *Mycoplasma*-induced rash and mucositis was proposed. We describe a patient with acute *M pneumoniae* respiratory tract infection who presented mucosal and cutaneous lesions that were difficult to classify as erythema multiforme or Stevens-Johnson syndrome; the lesions were compatible with the proposed new disease.

PALABRAS CLAVE
Mycoplasma pneumoniae;
Eritema multiforme;
Síndrome de Stevens-Johnson;
Exantema;

Exantema mucocutáneo inducido por *Mycoplasma pneumoniae*: ¿un nuevo síndrome separado del eritema multiforme? Un nuevo caso y revisión de la literatura

Resumen La infección respiratoria por *Mycoplasma pneumoniae* (MP) puede producir erupciones cutáneo-mucosas que se han considerado parte del espectro eritema multiforme o del síndrome de Stevens-Johnson. La clasificación de estas reacciones cutáneas, que tiene importancia pronóstica y terapéutica, ha generado mucha controversia en la literatura. Recientemente, una revisión sistemática de 202 casos de erupciones mucocutáneas asociadas a

☆ Please cite this article as: Martínez-Pérez M, Imbernón-Moya A, Lobato-Berezo A, Churruca-Grijelmo M. Exantema mucocutáneo inducido por *Mycoplasma pneumoniae*: ¿un nuevo síndrome separado del eritema multiforme? Un nuevo caso y revisión de la literatura. Actas Dermosifiliogr. 2016;107:e47–e51.

* Corresponding author.
E-mail address: mrcl_mtnez@yahoo.es (M. Martínez-Pérez).

Mucositis;
Clasificación clínica;
Tratamiento

infección por MP concluye que pueden constituir una entidad distinta para la que se propone la expresión *Mycoplasma-induced rash and mucositis*. Presentamos un caso de infección respiratoria aguda por MP con lesiones mucosas y cutáneas difíciles de clasificar como eritema multiforme o síndrome de Stevens-Johnson, y cuyas características son compatibles con la nueva enfermedad propuesta.

Introduction

Mycoplasma pneumoniae infection affects the skin and mucosas in up to 25% of cases,[1] and can cause erythema multiforme (EM)[2] and Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN).[3] The clinical overlap between these conditions, which has led to long-standing debate in the literature,[4–9] makes diagnosis difficult in some cases.[10,11] An extensive review of 202 cases of *M pneumoniae*-induced EM, SJS, and mucositis without rash was published recently.[12] In their conclusions, the authors proposed a new entity which they called *Mycoplasma-induced rash and mucositis*. We present a case that we found difficult to classify and that was consistent with the new entity described. As suggested by those authors, we believe this entity could be helpful in the diagnosis and treatment of these cases in daily practice.

Case Description

The patient, a previously healthy 16-year-old girl, presented a 7-day history of fever of 38.5 °C, odynophagia, cough, and wheeze. She was diagnosed with acute bronchitis and received treatment with inhaled budesonide and ibuprofen. She was subsequently seen for the rapid onset of lesions on the skin and mucosas. She had not received other drugs and she did not report a history of herpes infection.

Physical examination revealed intense stomatitis with confluent ulcers and scabs affecting all of the lips and the oral, palatine, and pharyngeal mucosas, associated with bilateral conjunctival hyperemia with discharge. Numerous irregular, edematous erythematous plaques with central vesicles and an erythematous halo, giving them the appearance of atypical target lesions, were observed on the skin of the face, trunk, limbs, perineum, and genital mucosa (Fig. 1). The palms and soles were not affected. No tonsillar exudate was observed and there were no palpable lymph nodes in the head and neck. Auscultation of the chest revealed crepitations. Abdominal examination was normal.

The patient was admitted with a clinical suspicion of erythema multiforme major secondary to *M pneumoniae* infection. Laboratory tests were as follows: C-reactive protein, 21 mg/dL; anti-streptolysin O titer, 222 U/mL; white cell count, 22 850 cells/μL (82.3% neutrophils, with no atypical lymphocytes); *M pneumoniae* IgM antibody, 292 U; herpes simplex virus, Epstein-Barr virus, and cytomegalovirus serology, negative. Chest x-ray showed a pneumonia infiltrate in the right upper lobe (Fig. 2). Skin biopsy revealed an intense vacuolar interface lesion, isolated necrotic keratinocytes, and extensive dermoepidermal separation, with no epithelial necrosis (Fig. 3).

Treatment was started with intravenous methylprednisolone, 1 mg/kg/d, clarithromycin, and acyclovir. The acyclovir was withdrawn after the serology results were received. Topical corticosteroids and antibiotics were applied to the conjunctival and oral mucosas, and fluid support and analgesia were administered until the patient's condition improved.

The skin lesions increased for a further 3 days, affecting up to 20% of the body surface, and took on a crusted, purpuric appearance, with lesions simultaneously observed in distinct stages. Some lesions developed flaccid blisters that did not coalesce or rupture. The Nikolski sign was negative and exfoliation did not occur. After 10 days the patient's condition had improved sufficiently for her to be discharged with only a residual hyperpigmentation.

Discussion

M pneumoniae is implicated in up to 40% of atypical pneumonias, particularly in children and young adults.[1] It provokes changes in the skin in up to a fourth of patients, with nonspecific rash being most common, though stomatitis, vaginal ulcers, pityriasis rosea, Kawasaki disease, leukocytoclastic vasculitis, subcorneal pustular dermatosis, Sweet syndrome, thrombotic thrombocytopenic purpura, Raynaud disease, Henoch-Schonlein purpura, and other conditions are also observed.[10] The exact incidence of EM in children and young adults who develop infection due to *M pneumoniae* and other *Mycoplasma* species[13] is unknown, while that of SJS has been estimated at approximately 5%, though these data may be affected by the confusing nomenclature.[10,11] Because of the clinical overlap between these syndromes, EM, SJS, and TEN have for decades been considered part of a spectrum. However, the Severe Cutaneous Adverse Reactions study concluded that EM and SJS/TEN can be separated into 2 distinct groups based on their clinical characteristics.[5] A later multicenter study confirmed the validity of that classification and its correlation with etiologic and prognostic factors,[8] and the 2 conditions are now considered separate entities.[9] It was difficult to confidently classify our patient into 1 of these groups, because the infectious origin, the acute onset, the target morphology of the lesions, and the favorable clinical course supported a diagnosis of EM, while the general symptoms, the central distribution with centripetal spread, and the large area affected by the lesions, together with intense involvement of 3 mucosas, was consistent with SJS. The differences between these conditions are summarized in Table 1.

In a study recently published by Canavan et al.,[12] the authors reviewed the epidemiological and clinical characteristics of the 202 published cases of mucocutaneous rash associated with *M pneumoniae*. Their results, which we