Mycoplasma pneumoniae–induced rash and mucositis as a syndrome distinct from Stevens-Johnson syndrome and erythema multiforme: A systematic review

Theresa N. Canavan, MD,[a] Erin F. Mathes, MD,[b,c] Ilona Frieden, MD,[b,c] and Kanade Shinkai, MD, PhD[b]
Birmingham, Alabama, and San Francisco, California

Background: *Mycoplasma pneumoniae* infection is associated with extrapulmonary complications, including mucocutaneous eruptions. These eruptions, which have been termed either "Stevens-Johnson syndrome" or "erythema multiforme" in the literature, may differ from drug-induced Stevens-Johnson syndrome or viral-associated erythema multiforme.

Objective: We sought to review the literature characterizing morphology and disease course of *M pneumoniae*–associated mucocutaneous disease.

Methods: A comprehensive literature search identified 95 articles with 202 cases.

Results: Patients were often young (mean age: 11.9 years) and male (66%). Cutaneous involvement ranged from absent (34%), to sparse (47%), to moderate (19%). Oral, ocular, and urogenital mucositis was reported in 94%, 82%, and 63% of cases, respectively. Treatments included antibiotics (80%), systemic corticosteroids (35%), supportive care alone (8%), and/or intravenous immunoglobulin (8%). Complications included mucosal damage (10%), cutaneous scarring (5.6%), recurrence (8%), and mortality (3%).

Limitations: Mild cases may not have been published; thus this review may have a bias toward more severe disease.

Conclusion: *M pneumoniae*–associated mucocutaneous disease has prominent mucositis and sparse cutaneous involvement, although cutaneous involvement varies. Because of the distinct morphology, mild disease course, and potentially important clinical implications regarding treatment, we propose a revision of the nomenclature system and suggest the term "*Mycoplasma*-induced rash and mucositis" for these cases. (J Am Acad Dermatol 2015;72:239-45.)

Key words: erythema multiforme; mucositis; *Mycoplasma pneumoniae*; rash; Stevens-Johnson syndrome.

Mycoplasma pneumoniae is a common cause of respiratory tract infections. Although the majority of infections are mild, 25% of patients experience extrapulmonary complications, including severe mucocutaneous blistering complications.[1]

Mucocutaneous eruptions associated with *M pneumoniae* infection are morphologically diverse and include mucositis alone, prominent mucositis with sparse cutaneous involvement, and, less frequently, mucositis with moderate skin involvement. Lesions are characterized as vesiculobullous, targetoid, atypical targets, or macules. Because of the pleomorphic nature of this eruption, *M pneumoniae*–associated eruptions have been labeled under different designations within the spectrum of

From the Department of Dermatology, University of Alabama,[a] and Departments of Dermatology[b] and Pediatrics,[c] University of California.

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Reprint requests: Kanade Shinkai, MD, PhD, Department of Dermatology, University of California, 1701 Divisadero St, Third Floor, Box 0316, San Francisco, CA 94115. E-mail: ShinkaiK@derm.ucsf.edu.

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erythema multiforme, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN). The *M pneumoniae*—associated eruption characterized by mucositis alone has gone by variety of terms including "incomplete Stevens-Johnson syndrome," "Fuchs syndrome," and "*Mycoplasma pneumoniae*—associated mucositis."

In this systematic review of the literature we present the epidemiology, morphology, and disease course of *M pneumoniae*—associated mucocutaneous eruptions based on 95 articles reporting 202 cases.

CAPSULE SUMMARY

- *Mycoplasma pneumoniae* infection is associated with mucocutaneous eruptions typically with prominent mucosal involvement.
- The distinctive morphology, pathophysiology, and disease outcomes of *Mycoplasma pneumoniae*—induced rash and mucositis distinguish it from Stevens-Johnson syndrome and erythema multiforme.
- There is little evidence supporting the best treatment for *Mycoplasma pneumoniae*—induced rash and mucositis.

METHODS

Search strategies

A comprehensive search of the English-language literature was performed on 3 databases: Ovid MEDLINE, PubMed, and EMBASE. Search terms included: "*Mycoplasma pneumoniae*" or "atypical pneumonia" and "Stevens-Johnson syndrome," "erythema multiforme," "toxic epidermal necrolysis," "mucositis," "atypical Stevens-Johnson syndrome," "Fuchs syndrome," or "*Mycoplasma pneumoniae*—associated mucositis." Bibliographies of select publications were reviewed for eligible studies.

Data sources

We included abstracts, case reports, and cohort studies published between 1922 and 2013. Inclusion criteria required a diagnosis of *M pneumoniae* or atypical pneumonia using contemporary diagnostic testing. Cases were included if they provided clinical and/or radiographic evidence of pneumonia (published before the 1940s), positive cold agglutinins (mid-1940s and 1960s), positive complement fixation (mid-1960s to 1990), or documented elevated IgM antibodies against *M pneumoniae* (after 1990). Studies were included if they provided detailed morphology descriptions and/or information on the extent of mucocutaneous involvement. Studies that did not adequately describe the morphology or satisfy the above diagnostic criteria were excluded.

Data extraction

Data collected included age, gender, morphology, extent of mucocutaneous involvement, treatments, and clinical course. Percentages were calculated from available reported information.

RESULTS

In all, 256 potential cases of *Mycoplasma*-associated mucocutaneous disease were identified from 107 reports, of which 202 patients from 95 articles satisfied the inclusion criteria. Twelve articles (54 patients) were excluded because of insufficient morphologic or clinical documentation.[2-13]

Clinical presentation

Patients with *M pneumoniae*—associated mucocutaneous disease were young (mean age: 11.9 ± 8.8 years) with male predominance (66% male) (Table I). Prodromal symptoms were nearly universal, including cough, malaise, and fever preceding the eruption by approximately 1 week (mean: 8 ± 5 days).

Many patients presented with polymorphic lesions. Vesiculobullous was the most common morphology (77%), followed by targetoid lesions (48%), papules (14%), and macules (12%); morbilliform eruptions were reported infrequently (9%). Faint, transient morbilliform[14] or macular[15] eruptions were also reported.

The extent of cutaneous involvement was not ascertainable in all cases[16-21] and only 2 articles[22,23] provided estimates of body surface area. Among cases reporting cutaneous involvement, nearly half (47%) had sparse involvement, characterized by single or a few scattered lesions.[14,15,17,18,24-61] The next most common presentation was severe mucositis alone (34%).[24,30,31,50,54,57,62-85] A minority of reports documented moderate cutaneous involvement (19%),[14,22,23,49,86-105] including 2 cases of TEN-like presentation.[23,97] Among reports describing lesion distribution, acral or extremity predominant distribution was most common (46%), followed by generalized (31%) and truncal (23%). Mucosal involvement was present in the majority of cases. Oral lesions (94% of cases) varied from isolated erosions, ulcers, vesiculobullous lesions, to involvement of the entire buccal mucosa with significant denudation. Ocular involvement (82% of cases) was characterized by purulent bilateral conjunctivitis, and occasionally photophobia and