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CASE IN POINT

PEER REVIEWED

Mycoplasma pneumoniae–Induced Rash and Mucositis: 2 Pediatric Cases

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Mycoplasma pneumoniae–induced rash and mucositis (MIRM) is a newly categorized clinical entity consisting of prominent mucositis and variable skin involvement in patients with a recent mycoplasma infection. This illness is most prevalent in school-aged boys and may be encountered in outpatient and inpatient settings alike. Although hospitalization may be required for management of dehydration, malnutrition, and pain, the overall morbidity and mortality associated with MIRM is low. We present 2 cases of pediatric patients who were recently hospitalized for MIRM and review the literature regarding presentation, pathophysiology, and management of this illness. It is important to be aware of this new diagnosis in order to recognize MIRM, provide supportive care, consider treatment, and effectively counsel patients and families.

CASE 1

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A 16-year-old boy presented with severe mucositis with bullous lesions involving the oral mucosa, lips, and pharynx. He was experiencing an inability to swallow secretions due to severe burning throat pain. He had been also exhibited a low-grade fever with rhinorrhea and a sore throat for the past 3 days. Of note, he had had a previous admission for severe mucositis 3 years prior to presentation, for which he had undergone extensive workup without a clear etiology having been identified. His condition ultimately had improved with supportive care.

At the current presentation, the patient was admitted to the general pediatric service for treatment and evaluation of mucositis of the conjunctivae, oral mucosa, nares, and urethra, as well as a vesicular skin eruption distributed sparsely over his chest, back, and scrotum (**Figures 1 and 2**).

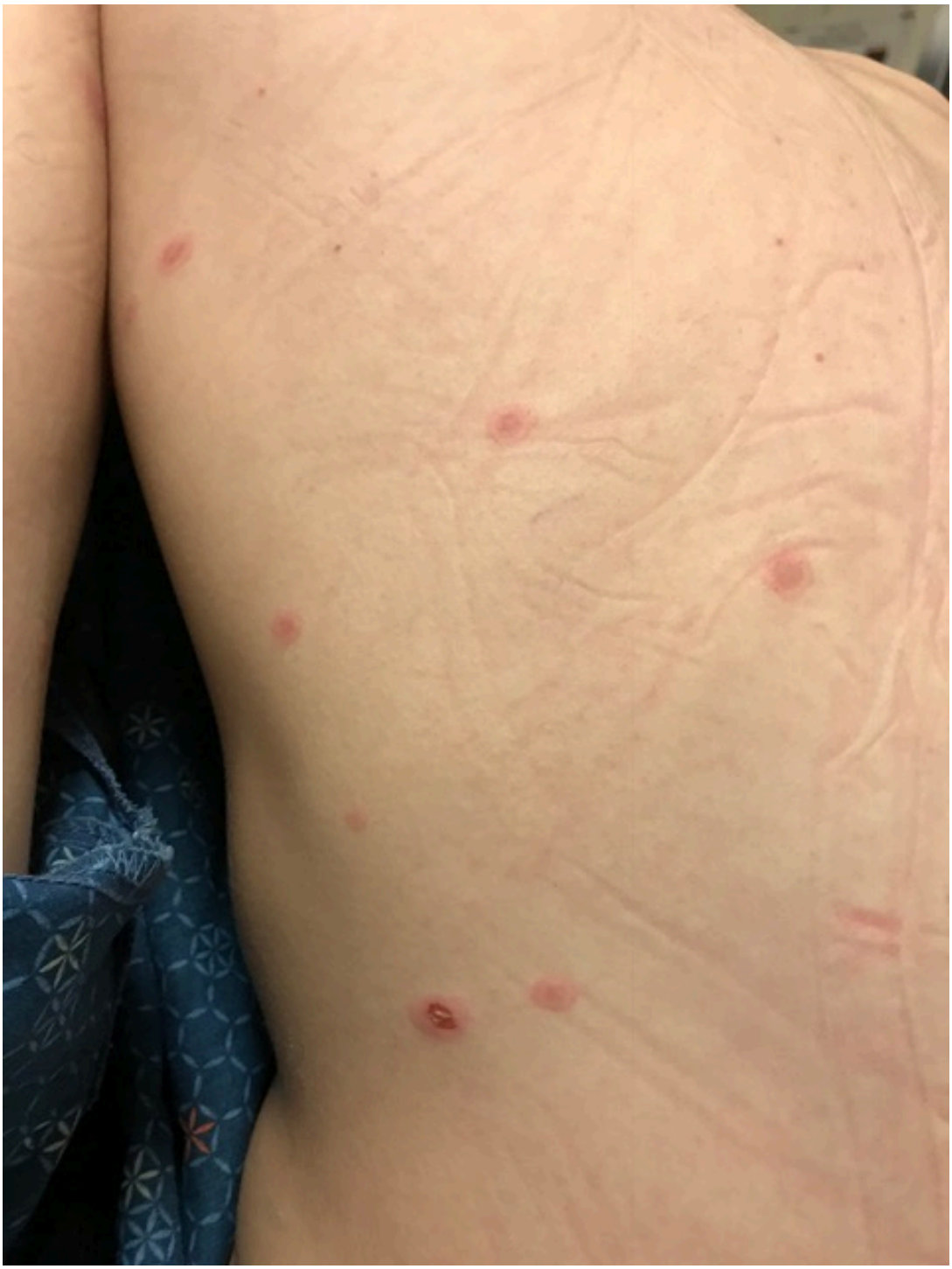


Figure 1. *Skin findings were notable for sparse vesicular lesions and some atypical target lesions with central vesiculation.*

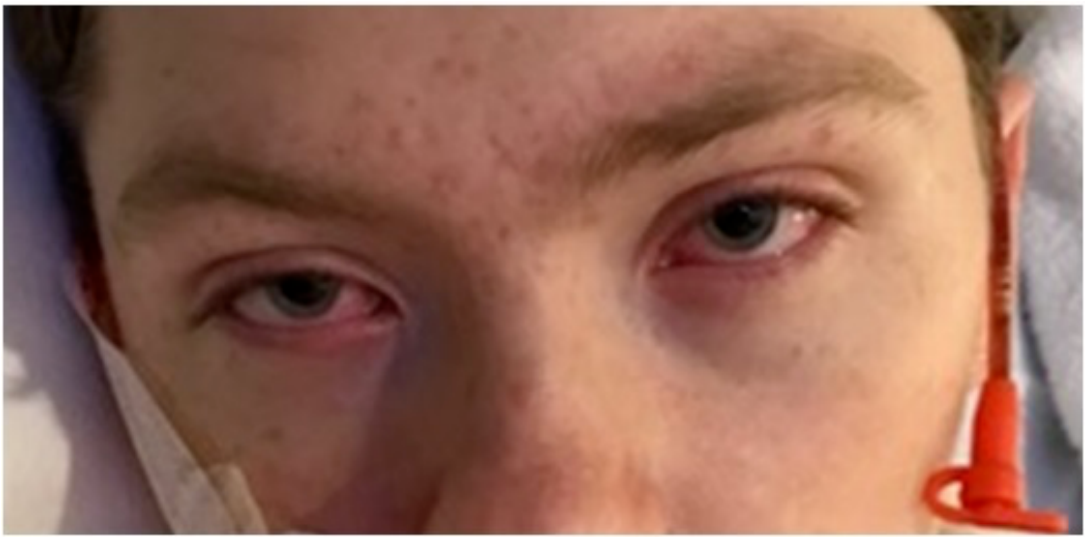
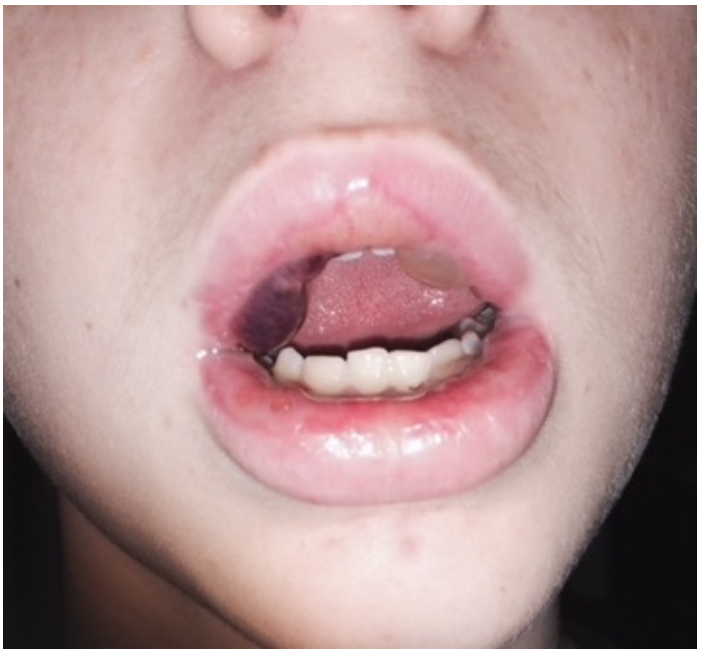


Figure 2. *Ocular findings of erythematous conjunctivae due to mucous membrane involvement.*

A consultant dermatologist suspected MIRM due to the sparsity of the rash and the prodromal viral symptoms. *M pneumoniae* polymerase chain reaction (PCR) results were positive, and the diagnosis of MIRM was made.

The mucosal lesions progressed during his admission from bullae to erythematous ulcerations with crusting (**Figure 3**).



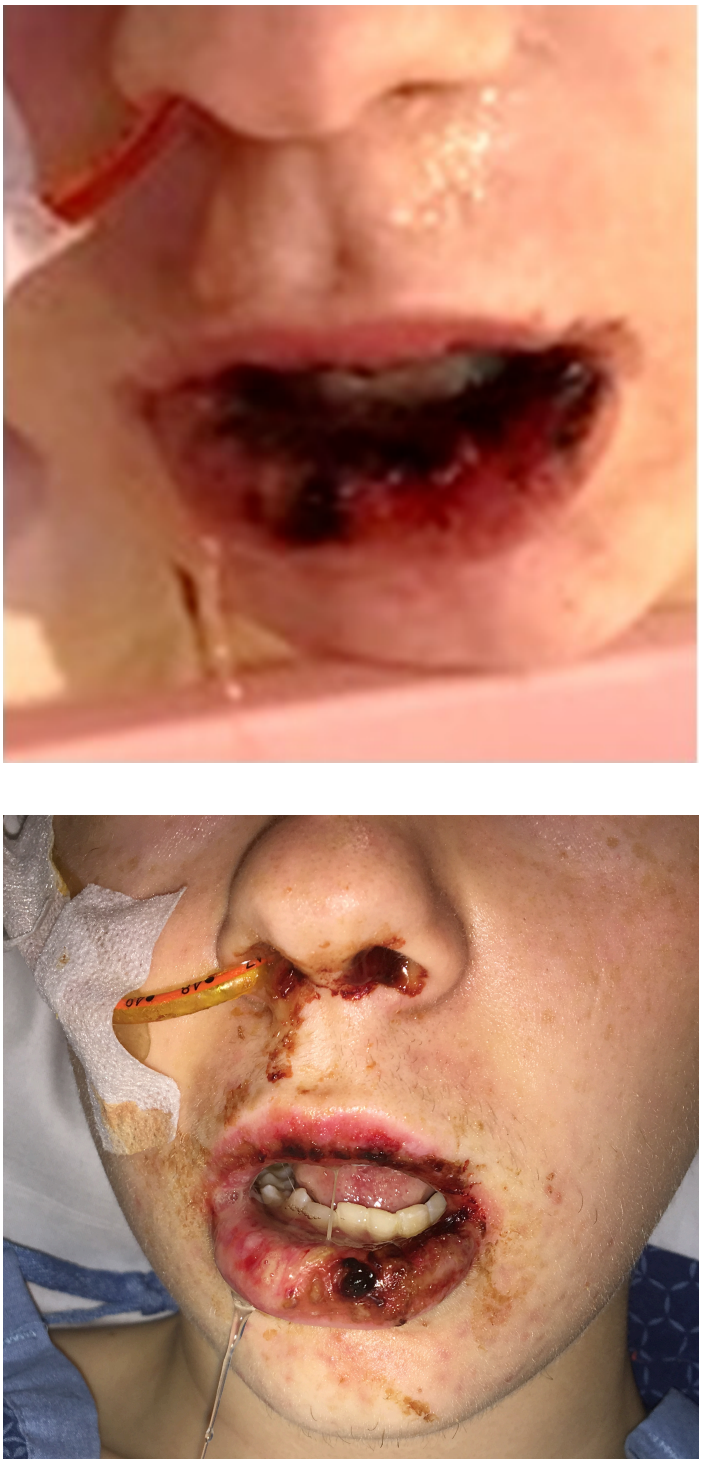


Figure 3. *Progression of oral mucositis from the first 24 hours of symptoms (top), to approximately 4 days of symptoms (middle), to approximately 1 week of symptoms (bottom).*

Due to intolerance of feeding and a previous similar episode of unclear etiology, a gastroenterologist was consulted, and the patient underwent upper endoscopy, which showed multiple ulcerated lesions in the esophagus. The patient was hospitalized for 3 weeks with severe mucositis requiring peripheral parenteral nutrition and intravenous pain management. He received a 5-day course of azithromycin and a dose of intravenous immunoglobulin G (IVIG), after which his mucositis and skin lesions resolved, and he was discharged home.

CASE 2

A 13-year-old previously healthy girl presented with oral and vulvar mucositis. Five days prior to presentation, she had experienced a sore throat, generalized fatigue, and a temperature as high as 38.3°C. Streptococcal pharyngitis test results were negative. She then developed conjunctivitis and began to have more difficulty swallowing, and she was admitted to the hospital due to dehydration and for intravenous pain control.

M pneumoniae PCR results were negative at presentation. The patient's mononuclear spot test results were positive, although more-specific Epstein-Barr virus antibody test results were negative. Despite the negative *M pneumoniae* PCR results, it was thought that her clinical presentation was most consistent with MIRM. This negative test result may have been due to low levels of *M pneumoniae* in the nasopharyngeal swab or improper collection or storage of the sample.

Dermatology, infectious disease, pediatric gynecology, and ophthalmology specialists were consulted during the patient's admission. She received both intravenous and oral corticosteroids, as well as a 5-day course of azithromycin, after which she showed significant clinical improvement and was discharged home after a 1-week hospitalization.

DISCUSSION

Mycoplasma pneumoniae infection classically presents as a respiratory tract infection. However, up to a quarter of patients with Mycoplasma infection experience dermatologic involvement.1 Skin manifestations vary and include erythematous macules, targetoid patches, or vesiculobullous plaques. Severe skin involvement thought to be due to *M pneumoniae* had previously been classified as a variant Stevens-Johnson syndrome (SJS) or erythema multiforme major.2-4 Recent evidence suggests that mucositis and rash associated with *M pneumoniae* may be a separate clinical entity altogether.

CLINICAL PRESENTATION

MIRM is a newer clinical term that is preferred to older terms such as mycoplasma-induced SJS or mycoplasma-induced erythema multiforme major. The new terminology reflects the causal role of mycoplasma in triggering a clinical picture of severe mucositis with variable and often scant skin involvement.

MIRM most frequently affects school-aged children or young teenagers. Boys are approximately twice as likely to be affected as girls.5 Prodromal symptoms including low-grade fever, cough, and rhinorrhea are occur approximately 1 week before skin eruption.5

Skin findings can vary in morphology, with sparse vesiculobullous or targetoid cutaneous lesions being most frequent. Rash is generally less prominent in MIRM compared with SJS.5,6

Mucositis is the predominant clinical finding in these patients, with oral involvement in more than 90% of cases.5 Additional sites of involvement include ocular and urogenital areas.

Proposed diagnostic criteria include less than 10% of body surface area with skin detachment, 2 or more mucosal sites involved, few vesiculobullous lesions or scattered atypical targetoid lesions, and clinical and laboratory evidence of atypical pneumonia (Table).5

Table. Comparison of Clinical Findings Differentiating Erythema Multiforme, SJS, and MIRM

	Description	**Number of Mucosal Sites Involved**	**% Body Involved**	**Additional History**
Erythema multiforme major	*Typical target lesions*: acrally distributed, <3 cm, round, and well defined with 3 zones of color with 1 edematous ring; *atypical target lesions*: edematous and round with 2 zones of color and central vesicles or bullae	Variable	<10%	NA
SJS	*Flat typical target lesions*: widespread round, macular with 2 zones of color and potential for central vesicles or bullae; *macules with or without blisters*: irregular erythematous or purpuric with potential for central vesicles or bullae	>2	<10%	History of medication use
MIRM	*Sparse vesiculobullous lesions* or *atypical target lesions*; possible *typical target lesions*	>2	<10%	Clinical or laboratory evidence of atypical pneumonia

Laboratory evidence of *M pneumoniae* infection can include immunoglobulin M antibodies, cold agglutinin antibodies, or a positive PCR result.5 Interestingly, the patient described in case 1 had significant esophageal bullae noted on endoscopy. Endoscopy is not frequently carried out for patients with a diagnosis of MIRM; therefore, additional areas of gastrointestinal tract mucosal involvement including esophagitis, gastritis, and perhaps colitis may be an underreported finding in patients with MIRM.7 This hypothesis is supported by the frequent feeding intolerance and need for supplemental enteral or parenteral nutrition in many hospitalized patients with MIRM.3

Most patients make a full recovery after their acute mucositis has resolved. The milder course and generally good prognosis differentiate MIRM from SJS, which has higher rates of morbidity and mortality. When complications of MIRM do arise, they most frequently include superficial adhesions due to mucosal healing. Pigmentary skin changes may also occur. Although conjunctivitis and dry eye are the most common ocular manifestation, severe ocular complications can occur, including intraocular or extraocular adhesions, which can lead to vision loss if not treated.8 Approximately 8% of patients will experience a recurrence in MIRM symptoms, similar to the patient described in case 1.5 These recurrences are usually associated with a repeated mycoplasma infection.5

PATHOPHYSIOLOGY

M pneumoniae primarily infects the respiratory epithelium. The bacterium lacks a cell wall, which allows close contact with the host cells and facilitates transfer of the community-acquired respiratory distress syndrome toxin directly into epithelial cells. This toxin induces the production of proinflammatory cytokines, leading to clinical symptoms of a respiratory tract infection. *M pneumoniae* has demonstrated ability to localize within the host's own cells as well as to induce autoantibodies by interacting with the immune system. Proliferation of B cells leading to immune complex deposition in the skin and resulting in activation of the complement cascade has been postulated as being responsible for the skin and mucosal complications of *M pneumoniae* infections.9,10

TREATMENT

Patients with MIRM may be treated as an outpatient or admitted to the hospital if mucositis is severe and supportive care for hydration and/or pain management is needed. Additional therapies such as antibiotics, IVIG, oral or intravenous corticosteroids, and immunomodulatory medications can be considered.11-14 Retrospective review shows a trend toward shorter length of stay for patients receiving intravenous corticosteroids either alone or in conjunction with IVIG.15 Small sample size and retrospective data collection make generalization challenging and causation difficult to interpret. It is unclear whether treatment of the underlying *M pneumoniae* infection changes course of illness, although patients are frequently treated with

pneumoniae infection changes course of illness, although patients are frequently treated with antibiotics once the diagnosis has been made.16 Observational reports of cyclosporine use in SJS and toxic epidermal necrolysis (TEN) show a propensity toward reduction in symptom duration; however, application of this therapy to the milder MIRM phenotype is of unclear benefit.14 Additional studies are needed to investigate the value of these treatment modalities in MIRM.

In our experience, patients with MIRM are frequently admitted for severe mucositis leading to dehydration, malnutrition, or inadequate pain control. Admission for observation may be warranted if there is concern for rapid progression of lesions and an alternative diagnosis of SJS or TEN has not been ruled out. In one review, 83% of patients who were admitted with MIRM required parenteral nutrition due to severe mucositis for an average length of 5 days.3 Consultation with a pediatric ophthalmologist and/or a urologist may also be necessary in cases of severe ocular or genitourinary mucosal involvement to avoid vision loss or mucosal adhesions.8 Consultation with a pediatric dermatologist also is useful in establishing the diagnosis and weighing treatment options.

Supportive care including ocular lubrication, topical and systemic pain control, nutritional support, and hydration are the mainstays of therapy for MIRM. Once patients are stable for outpatient management, pediatric dermatology home follow-up is useful to monitor progression of symptoms. Because MIRM is not related to medication use, patients do not need to avoid any medications in the future.

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