Rapidly Progressive Oral Ulceration in a 12-year-old Girl

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PRESENTATION

A 12-year-old girl with a medical history significant for unvaccinated status presents to the emergency department (ED) with a 1-week history of fever, rash, myalgias, and a new oral ulceration. The patient was well until she went camping with her family and friends. On the second day of the camping trip, she and another child began to feel ill, with subjective fevers and fatigue. The following day she had a fever of 101°F (38.3°C) and began to complain of myalgias and headache. After 2 days at home, the patient was sent back to school. However, she began to feel ill during class and went to the school nurse, who noted “white spots” on her tonsils. The patient was then taken to her pediatrician, who ran a rapid influenza diagnostic test, which was negative, and a rapid group A streptococcus test, which was inconclusive. The patient was subsequently started on amoxicillin–clavulanic acid for presumed streptococcal pharyngitis. After her first dose, the patient began to complain of mouth pain. Her mother saw that she had blistering and ulceration of her lips, tongue, and throat (Fig 1), as well as on the corners of her eyes, so she brought her to the ED.

In the ED she is noted to have bilaterally injected conjunctiva, several small pustular erythematous lesions on her elbow (Fig 2), blistering of her upper and lower lips, oropharyngeal exudates, and blistering of the tongue. A single dose of ceftriaxone is given, and clindamycin is started. Ophthalmology is consulted and notes bilateral conjunctivitis.

The patient is subsequently admitted to the inpatient service. Initial laboratory testing, including a complete blood cell count and urinalysis, is normal except for mild ketonuria and proteinuria.

On physical examination her heart rate is 120 beats/min, respiratory rate is 20 breaths/min, temperature is 103°F (39.4°C), and blood pressure is 112/71 mm Hg, and she is calm. She has significant ulceration of her lips, tongue, and oropharynx. She is also reluctant to open her eyes due to photophobia and pain. Both conjunctivae are injected, and there is a thin, watery discharge bilaterally. Examination findings and serologic test results suggest the diagnosis.

DIAGNOSIS

The patient had positive *Mycoplasma pneumoniae* immunoglobulin (Ig) M of 6,399 U/mL and IgG of 567 U/mL. The character of the lesions, with mucositis, ocular involvement, and *M pneumoniae* antibodies, suggested a diagnosis of *Mycoplasma*-induced rash and mucositis (MIRM).
DISCUSSION

*M pneumoniae* infection is usually associated with respiratory disease. However, more than one-quarter of affected patients experience extrapulmonary symptoms. (1) The potential extrapulmonary manifestations are variable and affect almost every organ system. Cardiovascular effects include pericarditis, endocarditis, cardiac thrombi, and Kawasaki disease. (2) Neurologic effects include stroke, Guillain-Barre syndrome, aseptic meningitis, opsoclonus-myoclonus syndrome, striatal necrosis, disseminated encephalomyelitis, cerebellitis, and acute cerebellar ataxia. (2) This infection has been linked to arthritis and rhabdomyolysis. Enteral involvement has been reported with hepatitis and pancreatitis. (2) *M pneumoniae* has been associated with hematologic manifestations, including autoimmune hemolytic anemia, thrombocytopenic purpura, disseminated intravascular coagulation, and infectious mononucleosis. (2) The sensory organs may be affected through otitis media, hearing loss, conjunctivitis, iritis, and uveitis. The kidneys may be affected with glomerulonephritis, IgA nephropathy, or renal artery embolism. (2) We describe several of the mucocutaneous and dermatologic manifestations in this case, including erythema nodosum, anaphylactoid purpura, cutaneous leukocytoclastic vasculitis, urticaria, and subcortical pustular dermatosis. (2) The literature describes some of the classic dermatologic presentations as ranging from vesiculobullous, as in our patient, to flat macular lesions. (1)

The current understanding of the pathophysiology of these less common presentations is mucosal damage caused by immune complex deposition and complement activation. (1) It has also been noted that molecular mimicry of keratinocyte antigen by *Mycoplasma* P1 adhesin molecule may be responsible for some of the cutaneous findings. (3) In contrast, the accepted pathophysiology of erythema multiforme is related to a type IV hypersensitivity reaction. (4)

Most cases of MIRM have been reported in patients with an average age of 11 years, with a slight male predominance. (1)(5)(6) One week before the onset of rash and mucositis, patients commonly present with a prodrome of upper respiratory symptoms. (7) Onset of mucositis may be varied, but up to 94% of patients show early oral lesions, and up to 82% show ocular lesions. (1) In terms of skin involvement, up to half of reported patients show “sparse, scattered lesions,” although some patients present with mucositis alone. (1) Of note, most patients who present with skin lesions show almost exclusive distribution on the extremities. (1)

The differential diagnosis for mucositis, vesiculobullous lesions, and ocular findings should include systemic juvenile idiopathic arthritis, Fuchs disease, and Stevens-Johnson syndrome/toxic epidermal necrolysis. Note that initially MIRM was classified as a variant of erythema multiforme, but there is strong evidence that it is a separate diagnosis due to differences in presentation and treatment modalities. (2)(6)(8) The Table outlines differentiating features of each similar diagnosis.

Typically, treatment of MIRM consists of systemic antibiotics. The first-line choice is a macrolide such as azithromycin. (5)(13)(14) In cases of macrolide allergy or high community rates of resistance, tetracyclines may be used in patients older than 8 years. (4)(13)(14) Most patients will recover completely within a few weeks to 2 months with this regimen. (15)(11) In severe cases that have failed antibiotic and supportive therapies, some reports note quick resolution after intravenous immunoglobulin administration. (16) If there is ocular involvement, a regimen of topical corticosteroids and topical antibiotics, of which moxifloxacin is a frequent antibiotic of choice, has been shown to be effective. (17) Ascorbic acid drops may be added if involvement becomes severe and the corneas are affected. (18) Treatment
with systemic corticosteroids is controversial because there have been several cases of mucositis severe enough to require hospitalization in which supportive care alone resulted in full recovery. (1)(3)(19) Of note, there have been no randomized studies to date evaluating the efficacy of corticosteroids or intravenous immunoglobulin as treatments for MIPM. Adding corticosteroids to the treatment regimen is based solely on the known pathophysiology of the disease.

**PATIENT COURSE**

Initial interventions were supportive and focused on pain control. The patient required intravenous morphine for several days before her symptoms began to subside. She began to have corneal involvement on day 4 for which the ophthalmologist prescribed corticosteroid drops. On day 5 of hospitalization the patient required nutritional support with nasogastric tube feeding because oral feeding had become too painful. All symptoms began to resolve on day 7 of hospitalization. At the time of discharge her eyes had significantly improved, she was able to take food by mouth, and she had completed a course of azithromycin.

### Summary

- Consider **Mycoplasma-induced rash and mucositis** in the differential diagnosis when a patient presents with mucositis and conjunctivitis.
- **Testing for Mycoplasma pneumoniae** immunoglobulins G and M can confirm this organism as the source of the infection.
- Treatment is mainly supportive and macrolide antibiotics. The role of intravenous immunoglobulin or corticosteroid therapy is unclear.
- Hospitalization may be helpful for nutritional support and pain management.

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**Table. Differential Diagnosis of Mucositis and Rash**

<table>
<thead>
<tr>
<th>DIAGNOSIS</th>
<th>PRESENTATION</th>
<th>PATHOPHYSIOLOGY</th>
<th>DISTINCTIVE FEATURES</th>
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</thead>
<tbody>
<tr>
<td>Juvenile idiopathic arthritis</td>
<td>Macular rash, persistent arthritis &gt;6 wk, diagnosed before age 16 y (9)</td>
<td>Proinflammatory cytokines activate the innate immune system (9)</td>
<td>Koebner phenomenon (exacerbation of rash with minor trauma) (9)</td>
</tr>
<tr>
<td>Fuchs syndrome</td>
<td>Oral mucositis and conjunctivitis with no rash (10)</td>
<td>Not well understood, most likely similar to EM/SJS (1)(6)</td>
<td>Mucositis ± conjunctival injection without skin rash, associated with infection (11)</td>
</tr>
<tr>
<td>Stevens-Johnson syndrome</td>
<td>Distinct, targetoid macules and bullae (6); involves ≤10% of the skin surface area</td>
<td>Cutaneous hypersensitivity reaction; typically due to a drug reaction (4)</td>
<td>Occurs more frequently in adults than in children (1)</td>
</tr>
<tr>
<td>Toxic epidermal necrolysis</td>
<td>Epidermal detachment (12); involves &gt;30% of the skin surface area</td>
<td>Cutaneous hypersensitivity reaction; typically due to a drug reaction (4)</td>
<td>Presence of Nikolsky sign (12)</td>
</tr>
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<td>Erythema multiforme</td>
<td>Significant ocular, genital, and/or oral mucosal involvement in addition to characteristic rash (6)</td>
<td>Type IV (delayed-type) hypersensitivity reaction with possible Fas ligand and granulysin-mediated cytotoxicity (1)(3)</td>
<td>Typical target lesions: well-defined, acral lesions with ≥3 zones of color (6) Atypical target: edematous round lesions with only 2 zones of color and potential central vesicles or bullae (6) Improved prognosis compared with SJS (6)(2)</td>
</tr>
<tr>
<td>Mycoplasma-induced rash and mucositis</td>
<td>≥2 sites of mucosal involvement with minimal skin involvement, sparse/scattered vesiculobullous lesions on extremities and trunk (1)</td>
<td>Immune complex deposition and complement activation secondary to polyclonal B-cell proliferation and antibody production versus keratinocyte and Mycoplasma P1-adhesin molecular mimicry (1)</td>
<td>Secondary to <em>Mycoplasma pneumoniae</em> infection, associated with upper respiratory infection symptoms, more common in children than in adults (1)</td>
</tr>
</tbody>
</table>

EM=erythema multiforme, SJS=Stevens-Johnson syndrome.