Reactive infectious mucocutaneous eruption secondary to SARS-CoV-2

C. Yoonhee Ryder, BS, Elisabeth A. Pedersen, MD, PhD, and Jennifer B. Mancuso, MD
Ann Arbor, Michigan

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INTRODUCTION

Reactive infectious mucocutaneous eruption (RIME) is a recently proposed term used to describe cases of postinfectious rash and mucositis. This entity was previously termed mycoplasma-induced rash and mucositis (MIRM); however, numerous cases have been described with non *Mycoplasma pneumoniae*-associated causes. These patients are typically adolescents and have a prodromal cough followed by severe mucositis of 2 or more mucous membranes, with or without a cutaneous rash. Here, we report a case of RIME secondary to SARS-CoV-2 that was refractory to corticosteroids and improved with cyclosporine.

Abbreviations used:

Ig:	Immunoglobulin
MIRM:	mycoplasma-induced rash and mucositis
PCR:	polymerase chain reaction
RIME:	reactive infectious mucocutaneous eruption

CASE REPORT

A 17-year-old healthy male developed fever, fatigue, and cough and tested positive for SARS-CoV-2 by polymerase chain reaction (PCR). He was diagnosed with COVID-19. He was initially treated at home with ibuprofen. Seven days later, he was presented to the emergency department with pharyngitis and painful oropharyngeal lesions. He was treated symptomatically with mouthwash containing lidocaine and oral nonsteroidal anti-inflammatory medications and discharged. During the next 2 days, he experienced worsening pharyngeal exudate, odynophagia, muffled voice, cervical edema, and fever and presented again to the emergency department. Physical examination revealed mucosal sloughing on the labial surfaces of the lips, tonsillar pillars, and hard and soft palate (Fig 1, *A*). Ocular discharge without conjunctival injection was noted. There were no cutaneous signs or symptoms. Further workup for infection was performed, including oropharyngeal swab RNA-amplified probe assay for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, *Streptococcus A* DNA by PCR, herpes simplex virus 1 and 2 DNA by PCR, and respiratory panel by PCR (parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3, respiratory syncytial virus, *Bordetella pertussis*, *Chlamydophila pneumoniae*, *M pneumoniae*, coronavirus 229e, coronavirus HKU1, coronavirus NL63, coronavirus OC43, human metapneumovirus, human rhinovirus-enterovirus, influenza A, influenza B, and *Bordetella parapertussis*), all of which were negative. *M pneumoniae* IgG and Immunoglobulin M were not detected. HIV antigen and rapid plasma regain were nonreactive. The patient was admitted for severe mucositis. The erythrocyte sedimentation rate was 18 mm and the C-reactive protein level was 16.9 mg/dL, but the results of further workup for symptoms of multisystem inflammatory syndrome in children with complete blood count, comprehensive metabolic panel, troponin, and b-type natriuretic peptide were normal. He was treated with IV methylprednisolone 1 mg/kg/day for 3 days and discharged with oral prednisone 1 mg/kg/day after 5 days in the hospital.

Four days after discharge, he returned to the emergency department with worsening mucositis and dysuria. He again tested positive for SARS-CoV-2 by PCR. He was unable to speak or tolerate oral

From the Department of Dermatology, University of Michigan Medical School, Ann Arbor.
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Correspondence to: Jennifer B. Mancuso, MD, Department of Dermatology, The University of Michigan Medical School, 1500 E. Medical Center Drive, 1910 Taubman Center, Ann Arbor, MI 48109. E-mail: jennbres@med.umich.edu.

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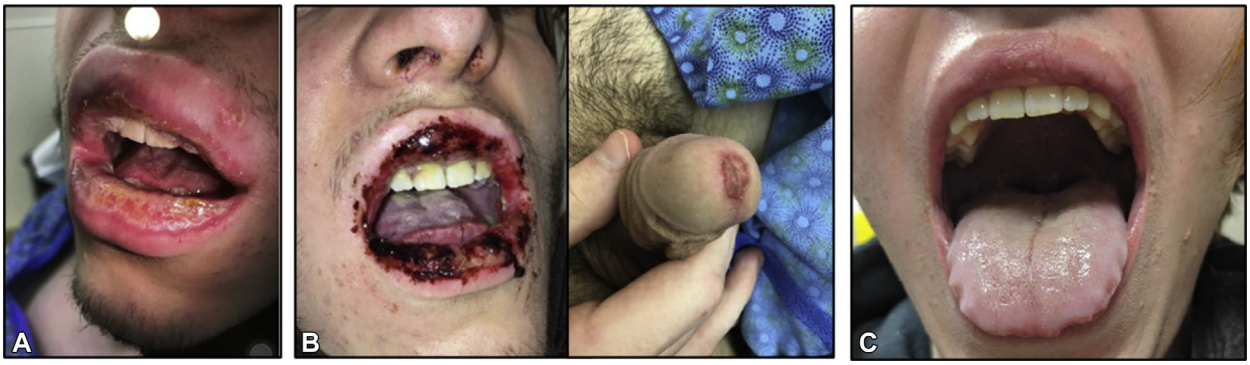

Fig 1. Erosive plaques (9 days following diagnosis of COVID-19) (**A**); hemorrhagic plaques and crusts on the oral, nasal, and urethral mucosa (17 days following diagnosis of COVID-19) (**B**) and complete resolution (26 days following diagnosis of COVID-19) (**C**).

intake due to pain. Physical examination revealed eroded plaques on the labial mucosa, crusting in the bilateral nares, and an erythematous eroded plaque on the periurethral meatus (Fig 1, *B*). No ocular findings were noted. The patient was admitted and started on IV methylprednisolone 1 mg/kg/day. He had worsening oral pain, and subsequently cyclosporine (4 mg/kg/day) was started. After 5 days, his oral intake improved, and he was discharged with prednisone 1 mg/kg/day and cyclosporine 4 mg/kg/day. Three days after discharge, he demonstrated complete resolution of the mucosal lesions (Fig 1, *C*).

DISCUSSION

Mucosal manifestations of COVID-19 are emerging as a complication with a variety of presentations among both adults and children, without clear gender preference.[1-4] A recent cross-sectional study estimated that 11.7% of COVID-19 patients had oral mucosal changes of any kind, with 3.9% having oral mucositis.[4] Here, we describe a case of RIME secondary to COVID-19 with a classic MIRM-like presentation and with complete resolution. MIRM is a well-documented phenomenon, with an estimated prevalence of 6.8% among those demonstrating laboratory evidence of an active *M pneumoniae* infection.[5] More recently, the Pediatric Dermatology Research Alliance proposed the term RIME to encompass other pathogens reported to cause postinfectious reactive mucositis, including *C pneumoniae*, human metapneumovirus, human parainfluenzavirus 2, rhinovirus, enterovirus, and influenza B virus.[6] Now, MIRM is considered a form of RIME induced by *M pneumoniae* infection.[6] RIME is considered a distinct entity from similar conditions with mucocutaneous involvement, such as Stevens-Johnson syndrome/toxic epidermal necrolysis and erythema multiforme.[6] In contrast to RIME, Stevens-Johnson syndrome/toxic epidermal necrolysis is a drug-induced syndrome, and erythema multiforme is a syndrome most frequently induced by herpes simplex virus, which has characteristic targetoid skin lesions with variable mucosal involvement. RIME has predominant mucosal involvement and minor skin manifestations, and the course is often milder than that of Stevens-Johnson syndrome/toxic epidermal necrolysis.[6,7] The patient described had mucositis of 2 mucosal sites (genitourinary and oral) with no cutaneous involvement. All infectious testing was negative except for PCR for COVID-19 virus, implicating COVID-19 virus as the trigger for RIME.

The latency times between symptoms of COVID-19 infection and mucosal eruptions range from 4 days to 12 weeks, with oral lesions appearing 4 to 7 days after systemic symptoms and resolving in 5 to 21 days.[3] Severe and widespread manifestations are associated with older age and immunosuppression.[3] In children, most mucosal symptoms occur with cutaneous reactions, and are more commonly associated with multisystem inflammatory syndrome in children.[1] To date, there is 1 report of oral and urethral erosions and skin lesions consistent with COVID-19-induced RIME[8]; however, this is the first case to show COVID-19-induced RIME in the absence of cutaneous findings.

RIME is considered self-limited, and treatment is supportive.[7] Although RIME has an excellent prognosis, the estimated rate of recurrence is 8%, and the sequelae include scarring and pigmentary changes.[7] The role of treatment with corticosteroids is unclear, and this patient was noted to have progression of symptoms while taking corticosteroids. Cyclosporine may reduce the mean hospital stay of patients with MIRM.[9] This patient experienced complete resolution within 7 days after initiation of cyclosporine. However, it is also possible that this

response may represent natural resolution of the disease.

In conclusion, we describe a case of COVID-19 infection causing a mucosal syndrome consistent with RIME, with complete resolution. Our findings suggest that COVID-19 may induce mucositis in the absence of cutaneous symptoms or multisystem inflammatory syndrome in children.

Conflicts of interest

None disclosed.

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