

CASE REPORT

Reactive infectious mucocutaneous eruption following COVID-19 in an adolescent boy: Case report and review of the literature

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Abstract

Reactive infectious mucocutaneous eruption (RIME) is a mucosal-predominant eruption that usually affects two or more mucosal sites. We present a case of RIME secondary to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and provide a brief review of the literature with a focus on the natural history and response to treatment. This entity may require inpatient management and systemic corticosteroids for symptom control in the pediatric population.

KEYWORDS

COVID-19, exanthema, mucositis, prednisone, SARS-CoV-2

1 | INTRODUCTION

Reactive infectious mucocutaneous eruption (RIME) is a reactive inflammatory mucositis that usually affects two or more mucosal sites. The term *Mycoplasma pneumoniae*-induced rash and mucositis (MIRM) was previously used to describe this eruption; however, reports of MIRM caused by other bacterial and viral infections including *Chlamydia pneumoniae*, enterovirus, rhinovirus, adenovirus, influenza B virus and parainfluenza virus 2 prompted a change in nomenclature.¹ There are no published evidence-based guidelines for the treatment of RIME. We report an additional pediatric case of RIME secondary to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and provide a review of the literature with a focus on the natural history and response to treatment.

2 | CASE REPORT

A healthy 13-year-old Caucasian boy presented to the emergency department with a 5-day history of painful oral erosions and ulcers and impaired oral intake. Two weeks prior to presentation, he had

experienced a fever, sore throat, irritation and redness of the eyes, and swelling of the eyelids and lips. SARS-Cov-2 PCR at that time was positive, and he was diagnosed with COVID-19. The dominant COVID-19 strain during this time was Omicron, and he had previously



FIGURE 1 Diffuse erosion with hemorrhagic crusting of the patient's upper and lower mucosal lips

TABLE 1 Summary of pediatric cases of RIME induced by COVID-19

Publication	Age (years)/ Sex	Involved sites	Type of diagnostic COVID-19 test	Time to lesion development from onset of COVID-19 symptoms	Hospitalization	Systemic therapy	Duration of systemic therapy	Time to complete resolution after initiation of systemic therapy
Mahama et al.	13/M	Lips, oral mucosa, glans penis	SARS-Cov-2 PCR	14 days	Yes, 3 days	Prednisone (1 mg/kg/day PO for 6 days)	6 days	14 days
Bowe et al.	14/M	Eyes, lips, oral mucosa, glans penis	SARS-Cov-2 PCR	9 days	Yes, 14 days	Hydrocortisone (100 mg IV three times a day for 3 days)	At least 3 days	21 days
Bowe et al.	17/M	Eyes, lips, oral mucosa, glans penis	SARS-Cov-2 PCR	8 days	Yes, 4 days	Hydrocortisone (100 mg IV three times a day for 3 days)	At least 3 days	11 days
Holcomb et al.	17/M	Lips, oral mucosa, glans penis	SARS-Cov-2 PCR	3 days	Yes, N/A	Prednisone (1 mg/kg/day PO for 4 days)	4 days	-
Song et al.	15/M	Lips, oral mucosa	SARS-Cov-2 PCR	3 days	No	Prednisone (30 mg PO for 3 days, 20 mg PO for 3 days, 10 mg PO for 5 days)	11 days	-
Ryder et al.	17/M	Lips, oral mucosa (1st visit) Lips, nares, and glans penis (2nd visit)	SARS-Cov-2 PCR	7 days 17 days	Yes, 5 days	Methylprednisolone (1 mg/kg/day IV for 3 days), then prednisone (1 mg/kg/day for at least 2 days)	At least 5 days	-
					Yes, 5 days	Methylprednisolone (1 mg/kg/day IV for at least 5 days) Cyclosporine (4 mg/kg/day PO for at least 5 days)	At least 5 days At least 5 days	7 days

received his second dose of the Pfizer COVID-19 BNT1662b2 vaccine 8 months prior to his diagnosis. Despite resolution of his upper respiratory and ocular symptoms, his lip swelling had persisted and progressed to erosions and ulcerations (Figure 1), and a new erosion had developed on his urethral meatus. Laboratory evaluation revealed negative PCR swabs for herpes simplex virus 1/2 and varicella zoster virus, negative *M. pneumoniae* IgM titers, elevated *M. pneumoniae* IgG titers, negative respiratory PCR panel including *M. pneumoniae*, *C. pneumoniae*, enterovirus, rhinovirus, adenovirus, influenza B parainfluenza 2, and positive SARS-CoV-2 IgG titers. His chest X-ray was unremarkable. No mucosal biopsy was collected.

The patient was diagnosed with COVID-19-associated RIME and admitted for fluid resuscitation and pain control. Topical triamcinolone 0.1% ointment and mouthwash containing viscous lidocaine 2%, diphenhydramine, and aluminum hydroxide with magnesium hydroxide failed to provide sufficient relief after 2 days. He was then started on oral prednisone 1 mg/kg/day and experienced rapid improvement in his symptoms within 24 h. He was discharged after three total days in the hospital with a 5-day prednisone taper. At outpatient pediatric dermatology follow-up 2 weeks later, all lesions had completely resolved.

3 | DISCUSSION

RIME is a recently proposed term to describe a spectrum of postinfectious mucocutaneous eruptions. Etiologies of this condition include *M. pneumoniae*, *C. pneumoniae*, enterovirus, rhinovirus, adenovirus, influenza B, parainfluenza 2, and SARS-CoV-2.² Diagnosis of RIME in the setting of COVID-19 is challenging. In a recent series of 50 pediatric patients hospitalized with COVID-19, 42% of patients had mucocutaneous findings.³ Diagnostic characteristics to help identify RIME include an erosive mucositis affecting at least two sites or vesiculobullous lesions/atypical targets involving less than 10% body surface area, and a noncontributory medication history.⁴ Supporting features are prodromal symptoms of an infectious trigger and histology excluding other diagnoses.⁴

There have been six reported pediatric cases of RIME induced by SARS-CoV-2 infection (Table 1).^{5–8} All reported patients were male, ranging from 13 to 17 years old, and all cases were confirmed by SARS-CoV-2 PCR. There was involvement of both the oral and genital mucosa in all patients, with the exception of one case by Song et al, which was presumed to be recurrent RIME with only oral mucosal involvement. None of the patients had other signs of cutaneous involvement. In a systematic review including 202 patients with MIRM, 47% of patients presented with sparse cutaneous involvement, 19% had moderate involvement, and 34% had no skin involvement.⁹ Data on the frequency of cutaneous involvement in RIME is lacking, so it is unclear if the absence of cutaneous involvement among these patients is characteristic of RIME or RIME induced by SARS-CoV-2. All six cases were treated with systemic corticosteroids, and five out of the six reported cases required hospitalization. Data on the frequency of hospitalization among patients with MIRM or RIME is

lacking, but prominent mucositis is a major cause of morbidity and often leads to hospitalization for additional treatment and diagnostic testing.

Treatment of RIME, regardless of the infectious trigger, is not standardized. Due to the self-limited nature of RIME, supportive care is a cornerstone of management and includes pain control, nutritional support, and wound care.⁹ Topical and systemic corticosteroids are first-line therapies used to truncate the inflammatory response, although there is a lack of prospective data. Targeted antibiotic therapy can be used to address specific underlying infections, and rarely immunosuppressive agents such as cyclosporine and etanercept have been used for severe cases.^{10,11} It is unclear if antiviral COVID-19 therapies such as nirmatrelvir/ritonavir will have any effect on the incidence and natural history of RIME. However, given the historical use of antibiotics for the treatment of RIME induced by bacterial infections, further studies should be completed on the utility of these antiviral therapies in COVID-19-induced RIME.

It has been reported that approximately 35% of *M. pneumoniae*-induced RIME cases are treated with systemic corticosteroids.⁸ In our review of RIME cases induced by SARS-CoV-2 infection, all six patients were treated with systemic corticosteroids and five of six were treated in the hospital setting. Though there are a limited number of cases reported in the literature, these findings suggest that RIME associated with COVID-19 may more frequently require inpatient management and the use of systemic corticosteroids for symptom control. Our patient was fully vaccinated at the time and received his second dose of the Pfizer vaccine 8 months prior to developing RIME; however, vaccination status was not provided in the other reported cases. Inclusion of vaccination status may be helpful in future reports to correlate to clinical severity.

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

CONSENT

We obtained informed consent from the patient's mother to publish the patient's information and pictures.

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- Abbreviation: RIME, reactive infectious mucocutaneous eruption.

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