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Case report

Reactive infectious mucocutaneous eruption (RIME) – A new face of a known entity

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Abstract

Reactive infectious mucocutaneous eruption (RIME) is a serious adverse mucocutaneous reaction that occurs primarily in children and adolescents after a viral or bacterial infection most commonly caused by *Mycoplasma pneumoniae* (formerly known as *Mycoplasma*-induced rash and mucositis [MIRM]). Although MIRM was first described as a new entity in 2015, recent updates to its nomenclature have expanded its scope to include other bacteria and viruses that can cause similar mucocutaneous reactions. While the case presented here involves a mucocutaneous reaction in response to a *Mycoplasma* infection, the updated nomenclature highlights the importance of recognizing and understanding this condition to better integrate it into the diagnosis of future mucocutaneous reactions.

We present the case of a 16-year-old male adolescent who was admitted to the hospital with bilateral phlegmon, aphthous stomatitis, glossitis, bilateral conjunctivitis and papules on both foot soles. He had had a 10-day history of an airway infection, characterized by fever and cough. Diagnostic tests revealed elevated infectious markers and positive serologies for *Mycoplasma pneumoniae*. Based on these findings, the patient was admitted to the Pediatric Ward and diagnosed with RIME. He was treated with ceftriaxone, azithromycin, methylprednisolone, ocular ofloxacin, and a mucositis solution. The patient remained hospitalized for 7 days and showed progressive improvement, with complete resolution of symptoms after 4 weeks.

Through this case, we aim to highlight the signs and symptoms of RIME, which can help ensure timely diagnosis and appropriate management of new cases.

Keywords

Adolescent, mucocutaneous eruption, *Mycoplasma*, stomatitis.

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Introduction

RIME refers to reactive infectious mucocutaneous eruption. It is an adverse and serious mucocutaneous reaction that primarily affects children and adolescents, with a median age of 12 years, although it can also occur in adults. This condition typically develops following a viral or bacterial infection, most commonly due to *Mycoplasma pneumoniae* (*Mycoplasma*-induced rash and mucositis [MIRM]) [1, 2].

In 2015 the term MIRM was introduced to distinguish the reactions caused by *Mycoplasma* from the group of Steven Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and erythema multiforme (EM) [3-5]. Subsequently, it was discovered that these reactions could also appear associated with other viruses and bacteria including: *Chlamydia pneumoniae*, human metapneumovirus, parainfluenza virus type 2, influenza B virus, rhinovirus, enteroviruses (including coxsackievirus), adenovirus, norovirus, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1, 2, 5].

RIME is a distinct clinical entity that does not fall within the spectrum of SJS/TEN, due to its milder course, different pathophysiology, and typically better prognosis [1, 4, 6]. The aim of this report is to emphasize the significance of this new nomenclature in diagnosing additional cases, regardless of the causative agent, based on its characteristic diagnostic features.

Case description

The case involves a 16-year-old adolescent male with a past medical history of epilepsy in infancy, but with no current medications or follow-up care, and no seizure episodes since 2018. The patient presented to the Emergency Room (ER) with a 6-day history of fever, cough, and severe odynophagia. A chest X-ray was performed, revealing bilateral perihilar infiltrates (**Fig. 1**), and he was discharged with symptom management.

Due to persistent symptoms, he returned to the ER 3 days later. He was evaluated by an otolaryngologist (ENT), who diagnosed him with bilateral phlegmon, aphthous stomatitis, and glossitis (**Fig. 2**).

He was treated with a single dose of intravenous ceftriaxone and discharged with ibuprofen.

The following day, the patient was readmitted due to worsening symptoms, including difficulty feeding and bilateral conjunctivitis (**Fig. 3**). On examination, he

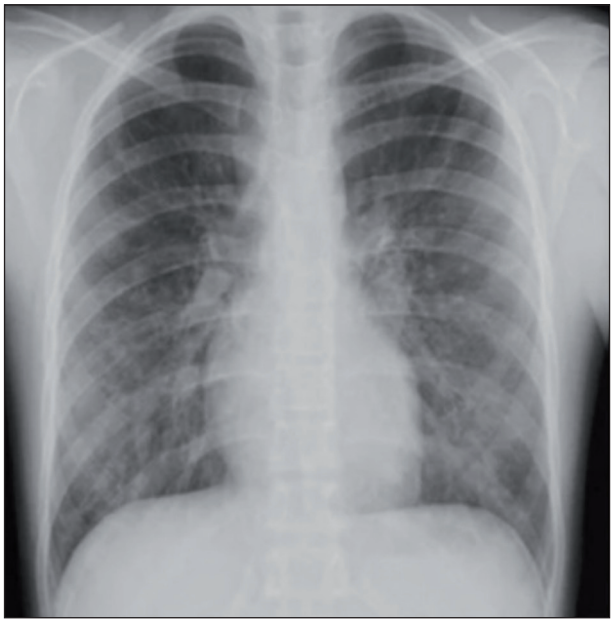

Figure 1. Chest X-ray with bilateral infiltrates.

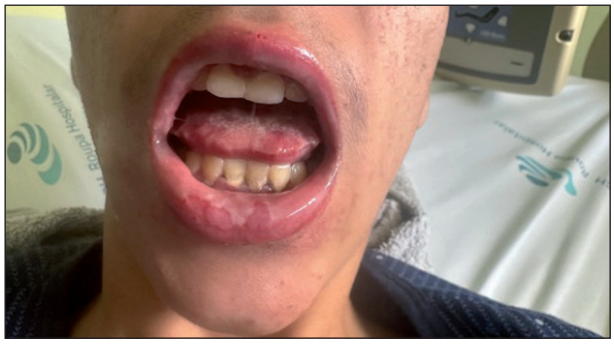

Figure 2. Erosions of lips and oral mucosa.

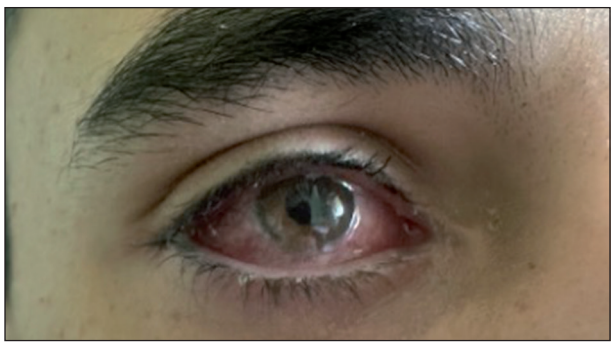

Figure 3. Conjunctivitis.

appeared generally ill (**Figures 4-6**), with bilateral conjunctival hyperemia, difficulty swallowing, a red oropharynx, oral thrush, and purulent tonsils.

Laboratory tests (including a complete blood count with white blood cell differential, basic metabolic panel, coagulation panel, and urinalysis) were performed and revealed elevated inflammatory markers (**Tab. 1**). Serological tests and PCR for *Mycoplasma* were positive, while tests for cytomegalovirus (CMV), Epstein-Barr virus (EBV), parvovirus, and human immunodeficiency virus (HIV) were negative. Blood and ocular cultures were also negative. The patient required admission due to difficulty feeding, and he underwent ophthalmological and ENT evaluations. He was treated for 7 days with ofloxacin eye drops, mouthwash, methylprednisolone, and a 5-day course of azithromycin. After 1 month, the patient was asymptomatic, with no lesions present.

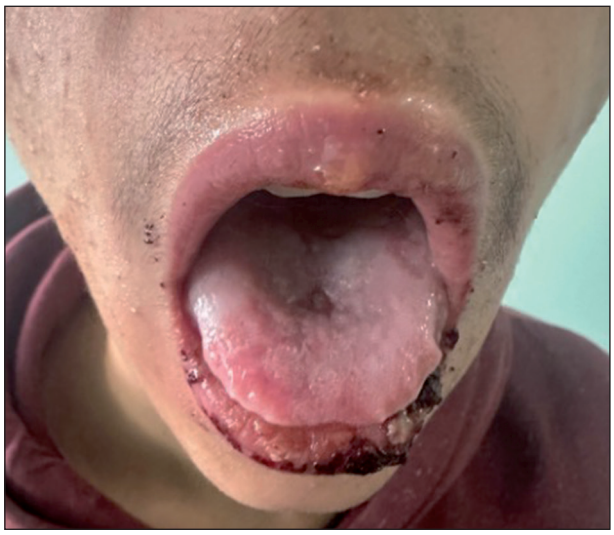

Figure 4. Hemorrhagic crusts.

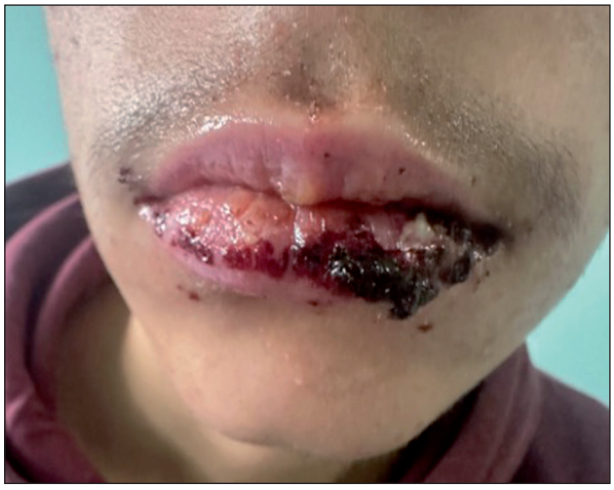

Figure 5. Hemorrhagic crusts.

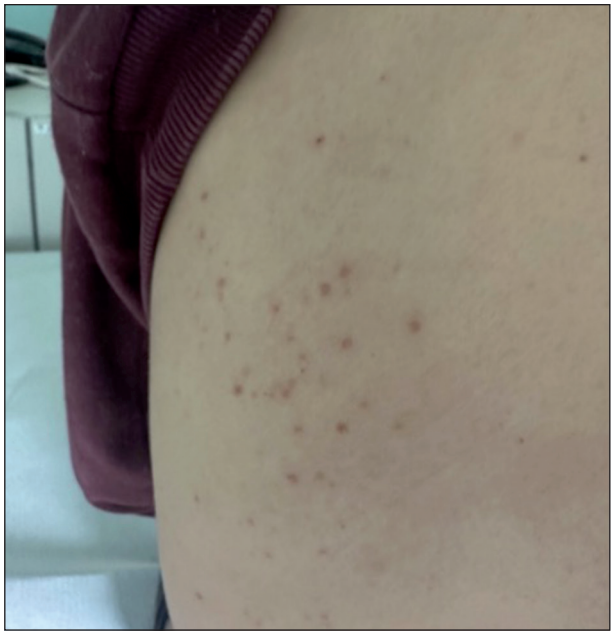

Figure 6. Cutaneous eruption.

Table 1. Laboratory analysis (abnormal results).

Lab	Patient's result	Normal range
Leukocytes	17,300/μL	4,000-10,000/μL
Neutrophiles	14,100/μL	1,800-8,000/μL
AST	46 U/L	5-34 U/L
ALT	78 U/L	< 55 U/L
CRP	140 mg/L	< 5 mg/L

ALT: alanine aminotransferase; AST: aspartate aminotransferase; CRP: C-reactive protein.

Discussion

The inclusion of other causative agents, apart from *Mycoplasma pneumoniae*, and the subsequent introduction of a new entity, became important in distinguishing mucocutaneous reactions from other well-known mucocutaneous entities such as SJS, TEN and EM [7]. These entities are usually more severe, with a worse prognosis and, thus, it is crucial to isolate cases of RIME to prevent unnecessary distress, diagnostic examinations and treatments.

The pathogenesis of RIME is still unknown, although two potential mechanisms have been proposed. The indirect mechanism is the most widely accepted and involves an immune response to an infection that leads to tissue damage through the proliferation of polyclonal B cells and production of antibodies. The direct mechanism involves the bacterium or other infectious agent to locally release inflammatory cytokines, leading to tissue damage. The variability in mucocutaneous involvement, often

affecting distant sites, as well as the time interval over which the lesions extend, makes this mechanism unlikely [1, 4].

It presents with severe mucositis and usually minimal cutaneous involvement, as observed in our patient. It generally affects 2 to 3 mucosal sites, with oral involvement being almost universal, including hemorrhagic crusts and erosions of the tongue and oral mucosa. Most patients also experience ocular involvement, such as bilateral conjunctivitis [1-3, 5]. These findings were observed in our case (**Figures 2-5**). Additional symptoms, such as photophobia, palpebral edema, and urogenital ulcers, may occur in about 60% of patients [1, 3, 4].

The diagnosis of RIME should be suspected when a child presents with a mucocutaneous eruption following a week of prodromal symptoms such as cough, fever, and malaise [3]. If a causative agent is identified through laboratory testing, the diagnosis can be corroborated, particularly if *Mycoplasma pneumoniae* is the identified pathogen.

Although no established diagnostic criteria exist to date, several authors have proposed 5 criteria to aid clinicians in diagnosing RIME. These include:

1. mucocutaneous eruption involving one or more sites, with less than 10% of body surface area affected;
2. scarce vesiculobullous or atypical target lesions;
3. no known medication use in the previous days;
4. a history of prodromal symptoms (cough, fever, malaise) within the last 7 to 10 days;
5. clinical, radiological, or laboratory evidence of a causative agent [1, 2, 4].

An author also suggests including young age as an additional diagnostic criterion due to its higher prevalence among younger populations [3, 4, 8].

Consistent with the literature, our patient met all 5 of the proposed diagnostic criteria, and also met the additional 6th proposed criterion (young age). This helped us differentiate this case from other potential causes and avoid unnecessary investigations in the initial approach.

Currently, there is no established, evidence-based treatment for RIME. Initial management is typically similar to that of other mucocutaneous diseases like SJS/TEN, as distinguishing between them in the early stages can be challenging [7]. This includes prompt diagnostic confirmation, assessment of severity, consultation with dermatology and infectious disease specialists, and the initiation of supportive care. Supportive care includes alternative forms of nutrition in cases of food refusal, application of creams to soothe lesions and reduce pain, use of gauze and petroleum jelly for hemorrhagic crusts, treatment of oral erosions with mucositis solutions, and artificial tears for ocular lesions [1, 2, 4].

Although it has not yet been definitively proven whether antibiotics shorten the duration of illness, it is generally agreed that treatment should begin once there is clinical, laboratory, or radiological evidence of pneumonia [1]. In our case, the patient initially presented with respiratory symptoms, and with his sister recently admitted to the Pneumology Ward for *Mycoplasma* pneumonia, he was promptly started on oral antibiotics. Oral corticosteroids are also commonly prescribed to reduce inflammation and alleviate pain. While evidence supporting their use remains limited, some studies recommend a 5 to 10-day course of prednisone at a dose of 1 mg/kg/day [3]. Our patient was also given corticosteroids, resulting in a noticeable improvement in pain and malaise. Other therapies such as immunomodulators have been proposed to help reduce inflammation and shorten disease duration. However, further research is needed before they can be widely recommended [5, 7]. Therefore, they were not used in this case.

Conclusion

This case underscores the importance of recognizing RIME as a distinct clinical entity which is crucial for preventing unnecessary diagnostic tests and treatments, as the condition typically follows a milder course with a good prognosis compared to the more severe syndromes in this spectrum [2].

In this case, the patient's presentation, including mucositis, ocular involvement, and positive laboratory findings for *Mycoplasma pneumoniae*, met the diagnostic criteria for RIME [1, 2, 4]. Early diagnosis helped avoid extensive and potentially harmful investigations, such as biopsies or unnecessary use of immunosuppressive therapies, which are commonly used for conditions like SJS/TEN [1, 7]. Instead, the patient was managed with appropriate supportive care and antibiotics, leading to a full recovery without complications.

This case highlights the need for further investigation and clinical guidelines to support healthcare professionals in making informed decisions when confronted with suspected mucocutaneous eruptions.

Informed consent

Written informed consent was obtained from the patient's legal guardians.

Declaration of interest

The Authors have no conflicts of interest to disclose. No sources of funding or financial support have been attributed to this paper.

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