ACTA MÉDICA PORTUGUESA
A Revista Científica da Ordem dos Médicos

Reactive Infectious Mucocutaneous Eruption: A Rising Enigma

Erupção Mucocutânea Infeciosa Reativa: Um Enigma em Ascensão

Joana LAGE [1,2,3], Ana LEMOS [1,2], Ana GARCIA [1,2], Tiago SILVA [1,2], Catarina GOUVEIA [1,2]
Acta Med Port 2025 Oct;38(10):648-651 ▪ https://doi.org/10.20344/amp.22792

ABSTRACT

Reactive infectious mucocutaneous eruption is a rare condition that predominantly occurs in pediatric patients following a respiratory infection, most commonly caused by *Mycoplasma pneumoniae*. It is characterized by prominent mucositis, usually with minimal or absent skin involvement. We present the case of a nine-year-old male admitted with severe oral mucositis and a penile lesion compromising bladder emptying. During hospitalization, dispersed cutaneous lesions emerged along with bilateral conjunctival hyperemia. The etiological investigation detected *Mycoplasma pneumoniae* in respiratory secretions, with positive IgM and IgG serology. Treatment included azithromycin, intravenous immunoglobulin and methylprednisolone, resulting in progressive clinical improvement. This case highlights the importance of recognizing reactive infectious mucocutaneous eruption. It can be challenging to differentiate from Stevens-Johnson syndrome, but it tends to have a more favorable clinical course. Early initiation of supportive care and multidisciplinary support are crucial for a good prognosis.
Keywords: Exanthema; Mucositis; Mycoplasma pneumoniae

RESUMO

A erupção mucocutânea infeciosa reativa é uma entidade rara que ocorre predominantemente em idade pediátrica após uma infeção respiratória, na maioria dos casos causada por *Mycoplasma pneumoniae*. Caracteriza-se por mucosite exuberante, com envolvimento cutâneo escasso. Descreve-se o caso de uma criança de nove anos internada por quadro de mucosite oral exuberante e lesão ao nível da glande com compromisso do esvaziamento vesical. Durante o internamento, desenvolveu lesões cutâneas dispersas e hiperemia conjuntival bilateral. A investigação permitiu a deteção de *Mycoplasma pneumoniae* nas secreções respiratórias, com IgM e IgG específicos positivas. O tratamento incluiu azitromicina, imunoglobulina endovenosa e metilprednisolona endovenosa, resultando em melhoria progressiva e recuperação completa sem sequelas. Este caso pretende alertar para o diagnóstico de erupção mucocutânea infeciosa reativa. O diagnóstico diferencial com síndrome de Stevens Johnson e outras toxidermias pode ser difícil, apresentando a erupção mucocutânea infeciosa reativa uma evolução clínica mais favorável. O início precoce do tratamento de suporte e o apoio multidisciplinar são essenciais para um bom prognóstico.
Palavras-chave: Exantema; Mucosite; Mycoplasma pneumoniae

INTRODUCTION

Reactive infectious mucocutaneous eruption (RIME) is a serious mucocutaneous adverse reaction predominantly affecting children and adolescents after respiratory infections.[1]

Epidemiologically, RIME predominantly affects male patients, with a mean age of around 12 years, and often occurs during the winter months.[1] Although *Mycoplasma pneumoniae* is considered the primary causal agent, other pathogens, including *Chlamydia pneumoniae* and various respiratory viruses, such as SARS-CoV-2, have also been implicated.[2-4]

This condition is characterized by pronounced mucositis, typically with minimal or absent cutaneous involvement, distinguishing it from conditions such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), which are characterized by distinct pathophysiological mechanisms and clinical courses.[5] Oral mucosal involvement in RIME is nearly universal and bilateral conjunctivitis and urogenital lesions may be present. As histopathological findings are not pathognomonic, distinguishing this condition from other mucocutaneous conditions can be challenging.[6]

In 2015, the term 'mycoplasma pneumoniae-induced rash and mucositis' (MIRM) was introduced to differentiate mucocutaneous diseases linked to *Mycoplasma* from SJS/TEN.[7] However, due to the potential of other viral and bacterial agents to elicit similar mucocutaneous involvement, the broader classification of 'RIME' was proposed.[4]

CASE REPORT

A previously healthy nine-year-old boy presented with a 10-day history of fever accompanied by dry cough, followed by the appearance of oral mucosal lesions three days before admission. He was first evaluated in the emergency department one week after the onset of symptoms, where he was diagnosed with herpetic gingivostomatitis and discharged with oral acyclovir. As his condition deteriorated, with progressive difficulty in oral intake and a new erosive lesion on the glans, he was readmitted to the emergency department.

1. Pediatric Infectious Diseases Unit. Hospital Dona Estefânia. Unidade Local de Saúde São José. Lisbon. Portugal.
2. Centro Clínico Académico de Lisboa. Lisbon. Portugal.
3. Department of Pediatrics. Hospital Professor Doutor Fernando Fonseca. Unidade Local de Saúde de Amadora/Sintra. Amadora. Portugal.
✉ **Autor correspondente:** Joana Lage. jvclage@gmail.com
Recebido/*Received*: 27/12/2024 - **Aceite/*Accepted*:** 23/04/2025 - **Publicado/*Published*:** 01/10/2025

On clinical examination, the patient exhibited numerous extensive aphthous and vesicular lesions in the oropharynx and a vesicular lesion on the urethral mucosa. There were no cutaneous exanthems nor other significant findings. Due to the extensive oral mucositis with urethritis and inability to tolerate oral intake, hospitalization was warranted.

The initial laboratory findings showed raised inflammatory markers (white blood cell count 12 450/mcL (reference range 3600 – 11 000/mcL), C-reactive protein 59.4 mg/L (reference range < 3 mg/L), with no other abnormal findings. The chest X-ray revealed non-specific bilateral interstitial infiltrates.

On the first day of hospitalization he developed vesicular, bullous, and target-like lesions on the face, trunk, abdomen, and lower limbs, accompanied by bilateral palpebral edema and conjunctival hyperemia, as well as photophobia (Figs. 1 and 2). Hemorrhagic crusting of the lips and erosions on the tongue and oral mucosa were also observed. Due to significant edema and lesions on the glans, the patient underwent bladder catheterization under anesthesia to prevent urinary tract obstruction.

Given the severity of the condition, SJS was initially suspected, leading to the administration of intravenous immunoglobulin on the second and third days of hospitalization. The patient was evaluated by Immunoallergology, and his prior medication history included paracetamol and antihistamines, resulting in an algorithm of drug causality for epidermal necrolysis (ALDEN) score of -1, (indicating that the suspected drug is considered an unlikely cause) which significantly reduced the likelihood of an SJS diagnosis.

Key diagnostic tests detected *Mycoplasma pneumoniae* in upper respiratory secretions by polymerase chain reaction (PCR) and a positive IgM and IgG serology. Other infectious agents, including herpes simplex, enterovirus, adenovirus, influenza, SARS-CoV-2, and *Chlamydia pneumonia* were not detected.

Considering the severe mucositis with minimal cutaneous involvement and evidence of recent *Mycoplasma pneumoniae* infection, the diagnosis of RIME was made. The patient received supportive care, including topical petrolatum jelly on skin lesions, ocular lubricants, daily hyaluronic acid-based solutions for mucosal lesions, saline compresses on the lips and oral mucosa, and oral rinses of aminocaproic acid twice daily. Due to severe pain related to the mucositis, enteral intake became unbearable, requiring the insertion of a central venous access and personalized parenteral nutrition. On day five of hospitalization, due to worsening blistering lesions and mucosal involvement with inability to tolerate oral feeding, methylprednisolone (1 mg/kg/day) was initiated for five days. Five days of azithromycin (10 mg/kg/day) were initially prescribed and on day seven of hospitalization, intravenous amoxicillin-clavulanate 150 mg/kg/day was added for seven days due to suspected superinfection of the cutaneous lesions. The patient was also assessed by the Physical Medicine and Rehabilitation team and the Psychology department.

New cutaneous and mucosal lesions were observed until day six, with limited involvement of both upper and lower extremities. Beginning in the second week, the patient showed gradual improvement in both mucositis and

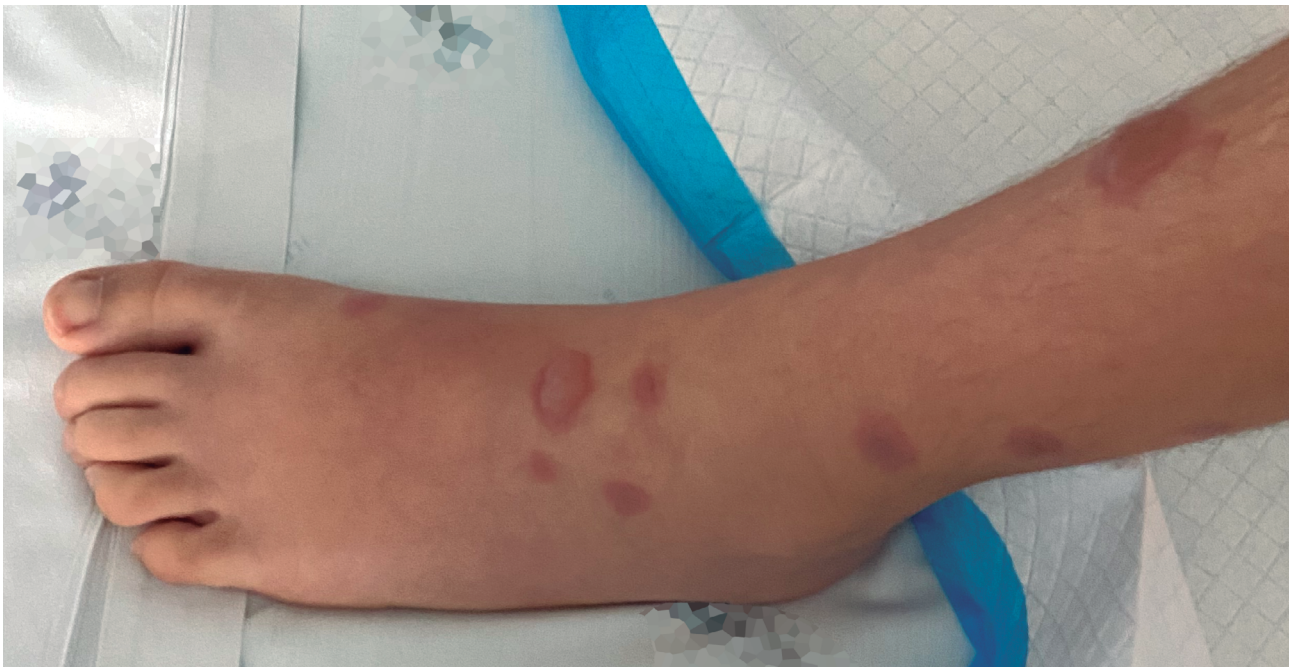

Figure 1 – Vesicular, bullous, and target-like lesions on the lower limb on the third day of hospitalization

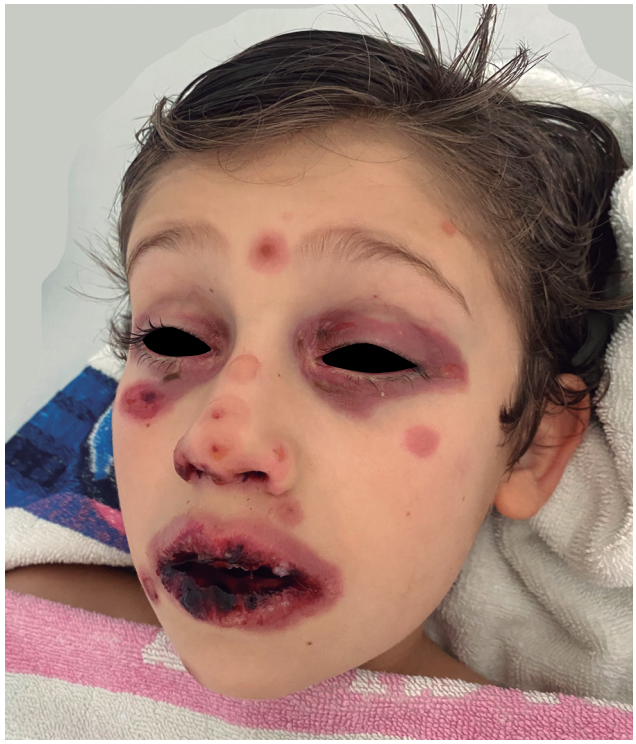

Figure 2 – Extensive mucositis with involvement of the palpebral, conjunctival, nasal and oral mucosa and vesicular and target-like lesions on the face on the fifth day of hospitalization

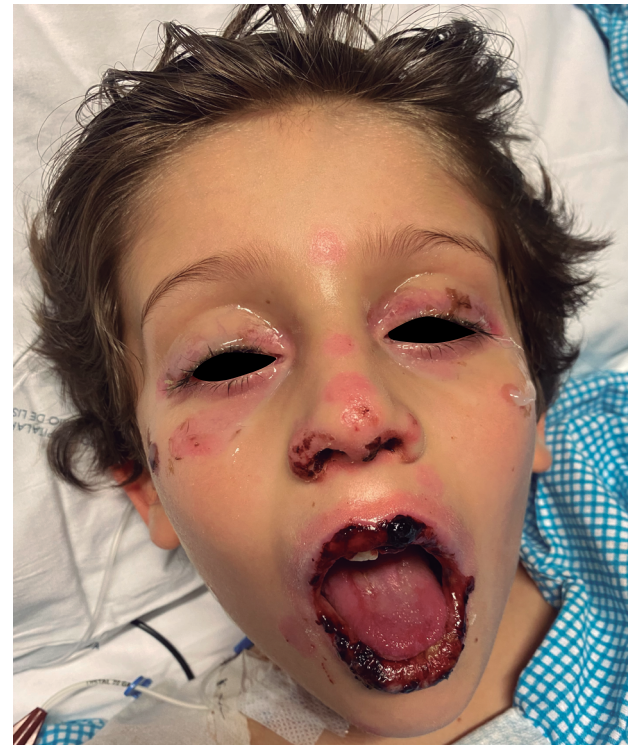

Figure 3 – Improvement of mucositis, characterized by resolution of conjunctival and palpebral hyperemia and significant improvement of lesions affecting the oral mucosa and facial regions on the thirteenth day of hospitalization

rash. (Fig. 3). Parenteral nutrition was suspended on the sixteenth day, and the patient was discharged on day eighteen of hospitalization for outpatient follow-up. The patient exhibited complete recovery, with no apparent sequelae.

DISCUSSION

This case highlights the importance of recognizing RIME, particularly in children who present with severe mucositis following respiratory infections. The identification of RIME relies heavily on the clinical history, including prodromal respiratory symptoms followed by the emergence of mucocutaneous lesions, as demonstrated in our case.[8] Given the potential clinical overlap with conditions such as SJS/TEN, early identification is vital for guiding appropriate management and preventing complications.[7]

Recent reports from the Centers for Disease Control and Prevention (CDC) highlighting a rising incidence of *Mycoplasma pneumoniae* infections in the United States, alongside with similar trends observed across Europe, suggest that this increase may contribute to a corresponding rise in cases of RIME in the pediatric population.[9,10]

The management of RIME is primarily supportive, focusing on symptomatic relief, hydration, nutrition maintenance, and vigilant monitoring for potential complications. Antimicrobial agents, such as azithromycin, target the underlying infection, but their impact on disease duration is unclear. As such, treatment decisions should be individualized based on clinical severity, microbiological evidence, and potential risk of transmission. Similarly, evidence supporting the efficacy of intravenous immunoglobulin or systemic corticosteroids (used in cases of extensive mucosal involvement) is limited and requires careful consideration.[11,12] In our case, IVIG was administered early in the clinical course due to the initial suspicion of Stevens-Johnson syndrome, which prompted an aggressive treatment approach. Some authors suggest a potential immunomodulatory role, particularly in severe or refractory cases, yet no controlled studies have definitively demonstrated improved outcomes with its use in RIME. The overall prognosis of RIME is favorable, with high rates of complete recovery and a low incidence of long-term sequelae.[6] However, recurrence is not uncommon and may occur in 9% - 38% of cases, typically triggered by subsequent infections rather than reexposure to the initial pathogen.[11]

In conclusion, RIME represents a significant, yet often underrecognized, mucocutaneous reaction within pediatric populations. Heightened awareness and understanding

Table 1 – Diagnostic criteria for RIME[12]

Diagnostic criteria - RIME
1 – Mucocutaneous eruption involving one or more sites with less than 10% body surface area involvement.
2 – Presence of vesicular or target-like lesions that are atypical, sparse and dispersed.
3 – Non-suggestive medication history.
4 – Prodromal period (cough, fever, malaise) occurring 7 - 10 days before.
5 – Clinical, radiological or laboratory evidence of an infectious agent.

of its clinical features, diagnostic criteria (Table 1) and management strategies are essential for optimizing patient outcomes. Continued research into the underlying mechanisms, potential genetic predispositions, and effective treatment protocols for RIME is warranted to improve care for affected patients and to further clarify its relationship with other mucocutaneous diseases.

AUTHOR CONTRIBUTIONS

JVL: Literature review and writing of the manuscript.

APL, AMG, TMS: Writing and critical review of the manuscript.

CG: Critical review of the manuscript.

All authors approved the final version to be published.

PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in October 2024.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

PARENTAL CONSENT

Obtained.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

FUNDING SOURCES

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. González C, Croche B, Gómez E. Reactive Infectious mucocutaneous eruption (RIME) in paediatric patients: extrapulmonary mycoplasma pneumoniae involvement. Rev Esp Quimioter. 2024;37:518-20.
2. Mahama A, Kojder P, Thibodeaux Q. Reactive infectious mucocutaneous eruption following COVID-19 in an adolescent boy: case report and review of the literature. Pediatr Dermatol. 2022;40:162-5.
3. Bowe S, O'Connor C, Gleeson C, Murphy M. Reactive infectious mucocutaneous eruption in children diagnosed with COVID-19. Pediatr Dermatol. 2021;38:1385-6.
4. Farhan R, Salim S, Surani A. reactive infectious mucocutaneous eruption (RIME) in COVID-19. WMJ. 2023;122:368-71.
5. Ramien M, Goldman JL. Pediatric SJS-TEN: where are we now? F1000Res. 2020;9:982.
6. Vassalo C, Calabria VR, Isoletta E, Biscarini S, Filippo AD, Brazzelli V. Clinical and microbiological characteristics of reactive Infectious mucocutaneous eruption: a case of 5 patients. JAAD Case Rep. 2021;17:152-6.
7. Canavan TN, Mathes EF, Frieden I, Shinkai K. Mycoplasma pneumoniae–induced rash and mucositis as a syndrome distinct from Stevens-Johnson syndrome and erythema multiforme: a systematic review. J Am Acad Dermatol. 2015;72:239-45.
8. Gonçalves R, Gata L, Brett A. Mycoplasma pneumoniae-associated mucositis. BMJ Case Rep. 2021;14:e239086.
9. Centers for Disease Control and Prevention. Mycoplasma pneumoniae infections have been increasing. 2024 [cited 2024 Oct 18]. Available from: https://www.cdc.gov/ncird/whats-new/mycoplasma-pneumoniae-infections-have-been-increasing.html.
10. Bolluyt DC, Euser SM, Souverein S, Rossum AM, Kalpoe J, Westreenen M, et al. Increased incidence of mycoplasma pneumoniae infections and hospital admissions in the Netherlands, november to december 2023. Euro Surveill. 2024;29:2300724.
11. Maredia H, Eseonu A, Grossberg AL, Cohen BA. Recurrent mycoplasma pneumoniae-associated reactive infectious mucocutaneous eruption responsive to systemic steroids: a case series. JAAD Case Rep. 2021;11:139-43.
12. Ramien ML. Reactive infectious mucocutaneous eruption: mycoplasma pneumoniae-induced rash and mucositis and other parainfectious eruptions. Clin Exp Dermatol. 2021;46:420.