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Research Article

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Expanding Horizons of Mucocutaneous Eruptions: RIME

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ABSTRACT

Reactive Infectious Mucocutaneous Eruption (RIME) is a parainfectious condition characterized by lesions on mucous membranes (oral, genital, and ocular) and, less frequently, skin involvement. It differs from other similar diseases, such as Stevens-Johnson syndrome and DRESS syndrome, in that the trigger is an infection, the course is more benign, and skin involvement is less common. We present two clinical cases with skin lesions compatible with RIME syndrome in 12-year-old males with a history of infectious symptoms. We believe it is important to recognize this entity to appropriately conduct the differential diagnosis between these conditions.

Keywords: Steven-Johnson, RIME, Dress, Mucocutaneous Rash

Introduction

Reactive infectious mucocutaneous eruption (RIME) is a parainfectious condition, which has been described in association with Mycoplasma pneumoniae (the most frequent agent) and other viral infections (influenza, enterovirus, metapneumovirus, SARS-CoV-2, etc.) [1,2]. The patient presents with catarrhal symptoms (fever, cough, general malaise) for one week, followed by lesions on mucous membranes (oral, genital, and ocular areas), and less frequently, skin involvement. This entity has been described more frequently in males, with an average age of 12 years, although cases in adults have also been reported, particularly during winter months 3. It differs from other similar diseases, such as Stevens-Johnson syndrome and DRESS syndrome, in that the trigger is an infection, the course is more benign, and there is usually no skin involvement [1-3].

Case 1: A 12-year-old male patient with a history of allergic rhinitis and dye allergy, who was admitted to the hospital due to painful blisters on the oral mucosa (Figure 1).

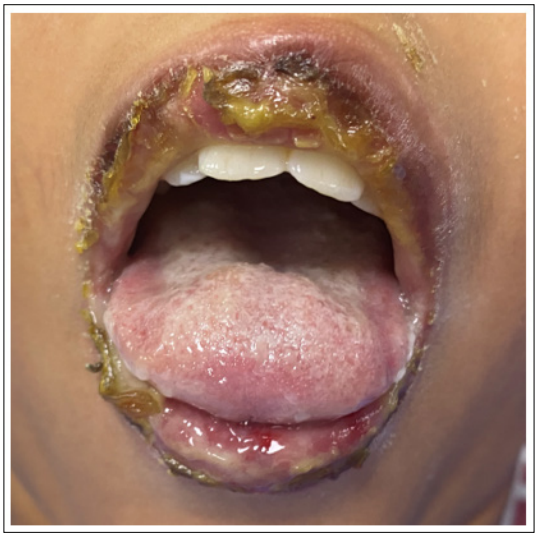

Figure 1: Blistering lesions in the oral area.

It was reported that 5 days before the onset of the condition, the patient had a cough and rhinorrhea, for which he received treatment with ambroxol and rupatadine. Upon admission, the previous treatment was discontinued, and the patient received a

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dose of dexamethasone (8 mg), diphenhydramine, and cefalexin (500 mg).

Laboratory tests (Table 1) showed no alterations in blood counts or coagulation, though there was a slight elevation in acute-phase reactants.

Table 1: Blood analysis of both cases.

	CASE 1	CASE 2
Leukocytes	14.500	17.400
Neutrophils	66.1%	82,7%
Lymphocytes	16.8%	6.8%
Hemoglobin (g/dL)	13.7	13.5
Hematocrit	40.2	41.1
Platelets	452000	727000
PCR (mg/dL)	3.36	8.99
TP segundos	16.7	22
INR	1.22	1.65
TTPa	27.0	91.4

After 24 hours of admission, painful blistering lesions appeared on the genital area (Figure 2).

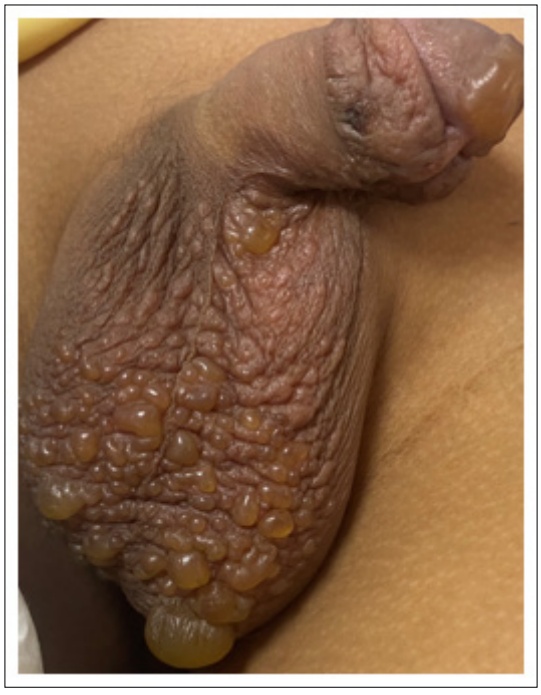

Figure 2: Blistering lesions in the scrotum and penile area.

During hospitalization, a throat swab PCR and serology for Mycoplasma pneumoniae were ordered, both of which were positive, so treatment with azithromycin (500 mg every 24 hours) for 3 days was started. The patient showed favorable progress, without the need for hemodynamic or respiratory support, and no blood transfusions were required. Due to clinical improvement, the patient was discharged with follow-up in dermatology consultations.

Case 2: A 12-year-old male patient with a history of allergic rhinitis who was admitted to the intensive care unit due to painful blistering lesions in the perioral region (Figure 3), upper anterior chest area (Figure 4), upper limbs (Figure 5), and genital area, associated with respiratory difficulty.

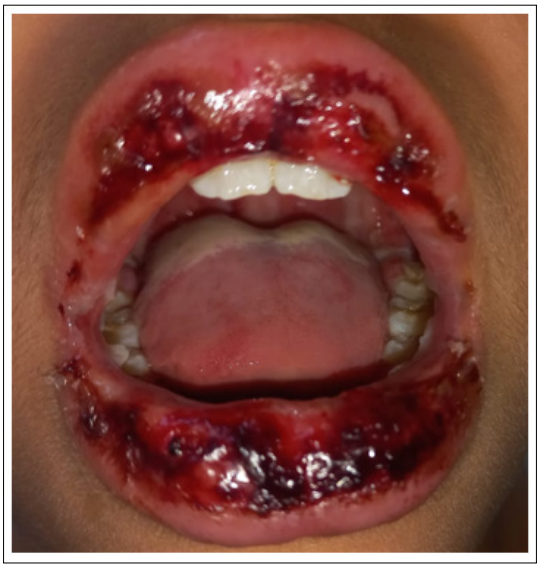

Figure 3: Vesicular-crusted lesions in the perioral region.

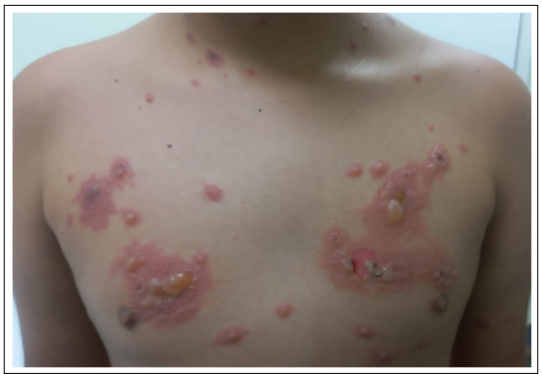

Figure 4: Vesicular lesions on an erythematous bullous base on the trunk.

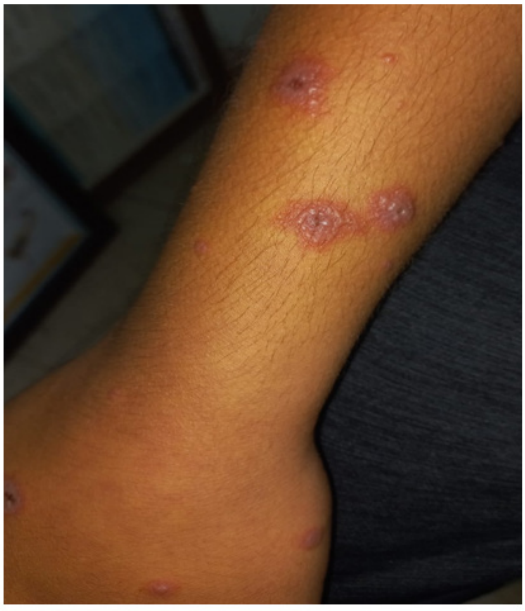

Figure 5: Vesicular lesions on an erythematous bullous base on the upper limb.

The patient's mother reported that he previously had a 10-day history of fever (maximum 38°C) and dry cough. Initially, he received outpatient treatment with amoxicillin, antiviral amantadine, chlorpheniramine, and paracetamol for 5 days. Subsequently, due to persistent catarrhal symptoms, he received outpatient treatment with ceftriaxone, diprofiline, and deflazacort nebulizations for 5 days. After 72 hours of starting the second treatment cycle with ceftriaxone and diprofiline, he developed the previously mentioned skin lesions and dyspnea.

The patient was admitted to the intensive care unit, where he received respiratory support with low-flow oxygen therapy for 3 days. Additionally, laboratory tests on admission showed coagulopathy (Table 1), requiring several blood transfusions with subsequent normalization. An infectious study was conducted, which showed positive Mycoplasma pneumoniae IgM serology, although the PCR for Mycoplasma pneumoniae was negative. He was treated with antibiotics (clindamycin and clarithromycin for 8 days), as well as systemic corticosteroid therapy (methylprednisolone 30 mg for 7 days). The patient showed favorable progress with resolution of the skin lesions.

Discussion

Reactive mucocutaneous infectious eruption (RIME) is an entity within the spectrum of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis (SSJ/NET), although with some significant differences. Therefore, it is important to have a good understanding of both entities to correctly perform differential diagnosis.

RIME is characterized by severe mucositis triggered by a bacterial or viral infection, with *Mycoplasma pneumoniae* being the most frequently described agent. As a result, patients may present prodromal symptoms 7-10 days prior (fever, cough, malaise). It occurs more frequently in children and young males, with an average age of 12 years.

Mucositis is usually present in 2 or 3 regions, with the oral mucosa being the most affected, presenting hemorrhagic crusts on the lips and erosions on the tongue. It can also affect the genital area and the ocular region in the form of mucopurulent conjunctivitis. In some cases, associated skin lesions may be observed, most frequently as vesiculobullous lesions, and less frequently as target lesions or papules. Evidence of prior infection with M. pneumoniae or C. pneumoniae supports the diagnosis, which can be detected through serological studies or PCR on throat swabs. However, it is important to note that IgM serology can remain positive for months or years after the acute infection. Currently, PCR is considered the "gold standard," although it has the drawback that it cannot differentiate between carriers and patients with acute symptoms [4].

In analytical studies, elevated acute-phase reactants such as PCR and ESR may be observed. In cases with a sluggish evolution requiring skin biopsy, no pathognomonic lesions for this syndrome have been found, making it indistinguishable from other entities such as Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. Therefore, routine skin biopsies are not recommended. Regarding the treatment of these patients, a dermatology assessment will be important for local management of lesions. In cases where infection with bacteria such as M. pneumoniae, C. pneumoniae, or S. pneumoniae is confirmed, targeted antibiotic treatment should be started. Additionally, in cases with extensive lesion involvement, immunomodulatory treatment with systemic corticosteroids or intravenous immunoglobulins is recommended [5].

The prognosis for this entity is generally good, with the majority of patients recovering without sequelae and a very low mortality rate compared to SSJ/NET. On the other hand, recurrences have been observed in 9-38% of cases. In summary, the diagnosis of this entity is clinical, suspected in patients with mucositis in two or more regions, affecting less than 10% of body surface area, after a catarrhal illness, and with no history of medication use. It differs from SSJ/NET, which is characterized by severe mucocutaneous involvement after exposure to certain drugs, including antibiotics (amoxicillin-clavulanic acid or cephalosporins) and antiepileptics. The clinical course is more severe, often requiring admission to the ICU for hemodynamic-respiratory support or transfusions [6].

Reviewing the cases of both patients presented (Table 2), in the first patient, since an associated infection was demonstrated, the clinical course was milder, and the patient did not take any medications prior to the condition that have been associated with SSJ/NET, pointing towards a reactive mucocutaneous infectious eruption. However, the second clinical case raises diagnostic doubts, as although the patient had a prior catarrhal illness, they also took several medications associated with SSJ/NET, the course was more severe, and there was greater skin involvement. Regarding the diagnostic tests, only the Mycoplasma pneumoniae serology was positive, which can remain positive for several months after the acute infection. Therefore, in the second case, it is more complicated to make a definitive diagnosis between RIME and SSJ, as it could have been either entity [7].

This often happens in our daily clinical practice; therefore, as physicians, we must overcome uncertainty, review clinical cases carefully, and provide the best possible management for the patient.

Table 2: Description of RIME cases. Diagnosis and treatment review

Case	1	2
Pacient	Male 12 years old	Male 12 years old
Trigger	Catarrhal symptoms 5 days prior	Catarrhal symptoms 5 days prior Notable previous medications: - Amoxicilina - Cefalosporina

Cutaneous/mucosal manifestation	Vesiculocrustous lesions on the oral mucosa and genital area.	Vesiculocrustous lesions on the oral mucosa and genital area. Bullous skin lesions on an erythematous base on the trunk and upper extremities
Microbiological diagnosis	PCR *Mycoplasma pneumoniae* positive. Serología IgM *Mycoplasma pneumoniae* positive.	PCR Mycoplasma pneumoniae negative. Serología IgM *Mycoplasma pneumoniae* positive.
Treatment	- Azitromicina 3 days. - Local treatment of lesions	- Clindamicina y claritromicina 8 days. - Systemic corticotherapy 7 days
Evolution	I do not require hemodynamic or respiratory support. I also do not need transfusions. Resolution of the lesions without residual scarring	Required: - Respiratory support for 3 days. - Transfusions. Resolution of the lesions without residual scarring.

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