RIME without rash associated with *Mycoplasma pneumoniae* infection

RIME sine rash *asociada a infección por* Mycoplasma pneumoniae

Dear Editor,

The term RIME (reactive infectious mucocutaneous eruption) was coined in 2019 to refer to a rare group of para-infectious mucocutaneous eruptions, encompassing both viral (SARS-CoV-2, influenza, herpesvirus) and bacterial aetiologies.[1] Among the bacterial is *Mycoplasma pneumoniae*, which, in 6.8% of those infected, can be associated with this manifestation, previously called MIRM (*Mycoplasma*-induced rashand mucositis).[2] There is a variant without skin involvement, called RIME *sine rash*,[3] as in the case described below.

We present the case of a 19-year-old male with no relevant medical history who presented with a fever of 5 days' duration followed by the appearance 48 h later of necrotic lesions on the lower lip, and subsequent extension to the entire oral mucosa, causing inability to swallow due to severe odynophagia and difficulty in opening his mouth. He had no relevant epidemiological history or drug use. On examination, crusty necrotic lesions with an erythematous background were found on the inner portion of the upper and lower lips (Fig. 1) and, on the soft palate, flat, erythematous punctate lesions, which extended to the oropharynx. No other skin lesions were identified except for an erythematous macular lesion on the glans of less than a centimetre in size. Tests performed initially showed an elevation of C-reactive protein (CRP; 142 mg/l) and leucocytosis with neutrophilia (11,900/mm^3 with 79% neutrophils), and a normal chest X-ray. The patient was admitted for nutritional support treatment and investigation with the following analytical tests: autoimmunity (anti-epidermal basement membrane, anti-epidermal intercellular substance, antinuclear antibodies, extractable nuclear antigen; all negative), viral serologies (Epstein-Barr virus, cytomegalovirus, hepatitis B and C viruses, human immunodeficiency; negative) and exudate study by polymerase chain reaction (PCR) (influenza A, respiratory syncytial virus and SARS-CoV-2, negative). Blood cultures were negative and *punch* biopsy of the lesions was performed. Finally, bacterial serologies were negative for *Chlamydophila pneumoniae* but positive IgM for *M. pneumoniae*. The patient was started on broad-spectrum, then subsequently targeted, antibiotic therapy and systemic corticosteroids, with clinical and analytical improvement, being discharged from hospital after regaining oral tolerance. Subsequently, the buccal mucosa biopsy performed showed data of spongiosis and inflammatory exocytosis associated with reactive epithelial changes, chronic perivascular inflammatory infiltrate and granulation tissue, with negative direct immunofluorescence. After the patient's discharge, full clinical recovery was confirmed and serology showed the appearance of IgG with persistence of IgM for *M. pneumoniae*. The final diagnosis was RIME *sine rash* associated with *M. pneumonia* infection.

This condition predominantly affects males with an average age of 12 years.[4] Although the pathophysiology is not fully understood, a multifactorial immune mechanism is postulated: mimicry between the MP P1 adhesin and keratinocyte antigens, which may lead to the development of a cross-reaction and autoantibodies against the antigens present in the mucosa; the formation and deposition of immune complexes; the polyclonal activation of plasma cells; and genetic susceptibility.[1] Diagnosis is clinical, generally beginning with a prodromal picture (fever, cough, general malaise) followed by the appearance of mucocutaneous lesions one week later, generally polymorphic with a predominance of vesicles and blisters. Diagnostic criteria[4] have been proposed for the classic, severe and RIME *sine rash* forms, the latter variant being: mucocutaneous rash affecting <10% of the body surface; involvement of at least two mucous membranes; mild skin involvement in the form of vesiculobullous lesions, target lesions or rash; and clinical and analytical findings compatible with atypical pneumonia. Although the reason for the different clinical presentations is unknown, it is thought that the presence of multiple genetic subtypes of *M. pneumoniae* could show different patterns of tissue tropism and so result in the diversity.[4]

In the event of clinical suspicion, it is essential to rule out the recent introduction of any drug that could induce conditions such as Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN). It is also recommended to determine C-reactive protein and erythrocyte sedimentation rate and perform chest X-ray, nasopharyngeal swab for respiratory viruses and serology for *M. pneumoniae*, *C. pneumoniae* and herpesvirus. Antibodies to *M. pneumoniae* are often present at the time of clinical symptoms due to the long incubation period. Demonstration of a four-fold increase in titre between a sample from the acute phase and one from the convalescent phase, or titres greater than or equal to 1/32, provides a sensitivity of 90% and a specificity of 88%.[5] Molecular techniques also show high sensitivity and specificity, but they have the limitation of being unable to differentiate colonisation from infection. Skin biopsy, although not showing specific findings, is useful for the exclusion of autoimmune blistering diseases. Differential diagnosis should include drug-induced epidermal necrolysis (SJS and TEN), Kawasaki disease, pemphigus vulgaris, Behçet's disease, and hand-foot-and-mouth disease.[6]

The course of the disease is generally benign with complete recovery, although it is not uncommon for associated comorbidity related to difficulty swallowing (dehydration, weight loss) and neuropsychiatric disorders.[7] In up to 10% of cases, mucosal sequelae may appear, mainly ocular.[4] Recurrence is rare, although there

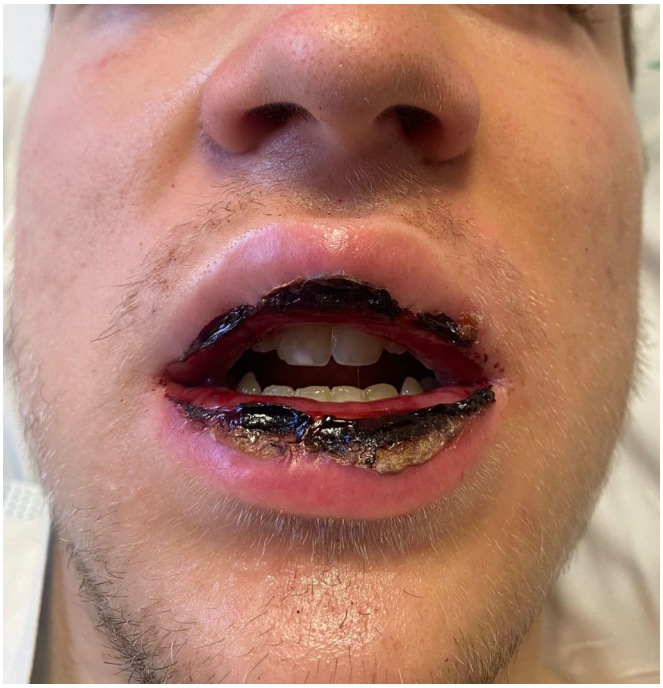

Figure 1. Extensive oral involvement with erosive lesions with haemorrhagic crust on the upper and lower lips associated with significant local oedema.

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is variability between different series both in prevalence (8–38% of cases)[5,8] and in predisposing clinical characteristics.[8,9] Recurrent episodes are associated with shorter recovery times and a lesser or equal degree of mucosal involvement compared with initial episodes.[10]

In terms of treatment, there are currently no clear guidelines, mainly being supportive, prioritising ensuring nutrition and hydration, protection of mucous membranes and pain control. If mucosal involvement is extensive, systemic corticosteroids may be administered (prednisone/methylprednisolone 1 mg/kg/day for 5–7 days).[7] Although the use of antibiotics is recommended, there is no evidence in this regard as, although they reduce infectious complications, their role in the healing of mucocutaneous lesions is unknown.[5] Intravenous immunoglobulins, ciclosporin or TNF-⟨inhibitors have also been used, although there is no evidence to support them.[2]

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References

1. Ramien ML, Bruckner AL. Mucocutaneous eruptions in acutely ill pediatric patients-Think of *Mycoplasma pneumoniae* (and other infections) first. JAMA Dermatol. 2020;156:124–5, http://dx.doi.org/10.1001/jamadermatol.2019.3589.
2. Meyer Sauteur PM, Theiler M, Buettcher M, Seiler M, Weibel L, Berger C. Frequency and clinical presentation of mucocutaneous disease due to *Mycoplasma pneumoniae* infection in children with community-acquired pneumonia. JAMA Dermatol. 2020;156:144–50, http://dx.doi.org/10.1001/jamadermatol.2019.3602.
3. Wang WY, Hu SCS. *Mycoplasma pneumoniae*-associated reactive infectious mucocutaneous eruption sine rash. Am J Med. 2024;137:e111–2, http://dx.doi.org/10.1016/j.amjmed.2024.02.008.
4. 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, http://dx.doi.org/10.1016/j.jaad.2014.06.026.
5. Daxboeck F, Krause R, Wenisch C. Laboratory diagnosis of *Mycoplasma pneumoniae* infection. Clin Microbiol Infect. 2003;9:263–73, http://dx.doi.org/10.1046/j.1469-0691.2003.00590.x.
6. Ramien ML. Reactive infectious mucocutaneous eruption: *Mycoplasma pneumoniae* -induced rash and mucositis and other parainfectious eruptions. Clin Exp Dermatol. 2021;46:420–9, http://dx.doi.org/10.1111/ced.14404.
7. 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, http://dx.doi.org/10.1016/j.jdcr.2021.03.009.
8. Liakos W, Xu A, Finelt N. Clinical features of recurrent *Mycoplasma pneumoniae*–induced rash and mucositis. Pediatr Dermatol. 2021;38:154–8, http://dx.doi.org/10.1111/pde.14472.
9. Pan CX, Hussain SH. Recurrent reactive infectious mucocutaneous eruption: a retrospective cohort study. J Am Acad Dermatol. 2023;89:361–4, http://dx.doi.org/10.1016/j.jaad.2023.03.027.
10. Olson D, Abbott J, Lin C, Prok L, Dominguez SR. Characterization of children with recurrent episodes of Stevens Johnson syndrome. J Pediatric Infect Dis Soc. 2017;6:e140–3, http://dx.doi.org/10.1093/jpids/piw085.

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Endocarditis infecciosa por *Achromobacter xylosoxidans* después de implante de válvula aórtica percutánea: a propósito de un caso

Infective endocarditis due to Achromobacter xylosoxidans *after percutaneous aortic valve implantation: a case report*

Sr. Editor:

El implante valvular transaórtico (TAVI) es el tratamiento de elección en estenosis aórticas graves sintomáticas no candidatas a cirugía, con esperanza de vida > 1 año[1]. La endocarditis infecciosa (EI) post-TAVI (E-TAVI) es una complicación grave e infrecuente con elevada mortalidad. Su incidencia es mayor durante el primer año, con una ratio de incidencia frente al recambio quirúrgico de 0,69 (p = 0,0011)[2,3]. Los microorganismos más frecuentes son *Enterococcus* spp., *Staphylococcus* coagulasa negativos y *Staphylococcus aureus*, siendo poco frecuentes los gramnegativos[3–5].

Presentamos el caso de una mujer de 74 años intervenida por insuficiencia aórtica grave mediante TAVI 3 meses antes en Marruecos que ingresó por fiebre persistente sin foco. En la analítica destacaba una proteína C reactiva (PCR) de 133,80 mg/L, sin leucocitosis ni otros reactantes de fase aguda. En 3/3 hemocultivos procesados mediante el sistema Bact/Alert 3D de Biomérieux se aisló *Achromobacter xylosoxidans*. Se realizaron ecocardiograma transtorácico (ETT) y transesofágico (ETE) que descartaron EI, pautando tratamiento según antibiograma con piperacilina/tazobactam 4 g/500 mg/8 h. La paciente quedó afebril, con hemocultivos de control negativos y fue dada de alta tras 12 días de antibioterapia.

A la semana reingresó por persistencia de fiebre. En la analítica no había leucocitosis pero persistía aumento de PCR (257,40 mg/L) y procalcitonina (1,77 ng/mL). En los hemocultivos se aisló nuevamente *A. xylosoxidans*. Se realizó una tomografía por emisión de positrones (PET-TC) y se repitió la ETE sin hallazgos compatibles con EI, pero ante la alta sospecha se pautó antibioterapia con imipenem 1 g/8 h y se comentó el caso en comité (Endocarditis *team*) que, dada la persistencia de hemocultivos positivos pese a antibioterapia dirigida y debido a la virulencia del microorganismo aislado con una alta tasa de recurrencia, decidió cirugía como la opción más segura.

Se realizó explante de la TAVI bajo circulación extracorpórea y clampaje aórtico. Tras la aortotomía, a la inspección la TAVI presentaba verrugas en la cara ventricular de los velos, que no se visualizaban en la ETE por la sombra del *stent* de la TAVI (fig. 1).