The challenge of diagnosis and treatment of Melkersson-Rosenthal Syndrome: case report

O Desafio do diagnóstico e tratamento da Síndrome De Melkersson-Rosenthal: relato de caso

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Resumo

Objetivo – Relatar os desafios diagnósticos da Síndrome de Melkersson-Rosenthal (SMR), uma doença neuro mucocutânea rara, de etiologia desconhecida, que apresenta uma tríade clássica de edema orofacial, paralisia facial e língua fissurada porém com apresentações clínicas variáveis, muitas vezes levando a diagnósticos tardios ou perdidos. **Métodos** – Trata-se de um relato de caso de uma paciente do sexo feminino, 30 anos, com edema assintomático do lábio superior e língua fissurada. Após avaliação clínica minuciosa e análise histopatológica inconclusiva, a SMR foi diagnosticada com base nos sintomas clínicos e exclusão de outras condições. **Resultados** – A paciente foi inicialmente tratado com corticosteroides, resultando em melhora inicial, mas apresentou instabilidade clínica com subsequentes recorrências dos sintomas. O caso destaca a complexidade da SMR e a necessidade de abordagem individualizada do tratamento, considerando os fatores que contribuem para a instabilidade clínica do paciente. **Conclusão** – A pesquisa contínua e a troca de informações sobre a SMR são essenciais para melhorar o seu manejo e a qualidade de vida dos pacientes afetados.

Descritores: Síndrome de Melkersson-Rosenthal; Paralisia facial; Lingua fissurada, Corticosteroides; Edema labial

Abstract

Objective – To report the diagnostic challenges of Melkersson-Rosenthal Syndrome (MRS), a rare neuro mucocutaneous disease of unknown etiology, which presents a classic triad of orofacial edema, facial paralysis and fissured tongue but with variable clinical presentations, often leading to late or missed diagnoses. **Methods** – This is a case report of a female patient, 30 years old, with asymptomatic edema of the upper lip and fissured tongue. After thorough clinical evaluation and inconclusive histopathological analysis, MRS was diagnosed based on clinical symptoms and exclusion of other conditions. **Results** – The patient was initially treated with corticosteroids, resulting in initial improvement, but presented clinical instability with subsequent recurrences of symptoms. The case highlights the complexity of MRS and the need for an individualized approach to treatment, considering the factors that contribute to the patient's clinical instability. **Conclusion** – Continuous research and exchange of information about MRS are essential to improve its management and the quality of life of affected patients.

Descriptors: Melkersson-Rosenthal Syndrome; Facial paralysis; Cleft tongue; Corticosteroids; Lips edema

Introdução

Melkersson-Rosenthal Syndrome (MRS) is a rare neuromucocutaneous disease of unknown etiology, with an estimated prevalence of only 0.08% in the population[1,2]. It is more commonly observed in females and typically occurs between the second and fourth decades of life[1-3].

The syndrome is characterized by a classic triad of symptoms: orofacial edema, facial paralysis, and fissured tongue. The oligosymptomatic form, which presents with two of these symptoms, is the most common, but a monosymptomatic presentation, characterized solely by edema of the lips, known as Miescher's granulomatous cheilitis, can also occur[2]. The diagnosis of MRS represents a significant challenge for dentists, as the classic triad is not always present, resulting in cases described in the literature without a diagnosis for up to 30 years[3,4].

Orofacial edema is the most frequent clinical manifestation, being acute and painless[1]. It mainly affects the upper lip, either unilaterally or bilaterally, and in some cases, it can involve the eyelids and cheeks[5]. Approximately 77% of MRS patients also present with a fissured tongue, which may be present since birth[3]. Facial paralysis, although less common, affects between 30% to 35% of cases and tends to be recurrent[4-6].

In addition to the classic triad, other signs and symptoms may be associated with MRS, including cutaneous and neurological alterations. The disease can have a chronic and recurrent course, with periods of remission and exacerbation of symptoms[6-8].

To establish the correct diagnosis, a thorough clinical evaluation is essential, including a complete medical history, detailed physical examination, and histopathological analysis of biopsies when necessary. The differential diagnosis should be made with other conditions that present similar orofacial manifestations, such as hereditary angioedema, sarcoidosis, Bell's palsy, and other granulomatous syndromes[7-10].

The treatment of MRS is challenging and varies depending on the severity of symptoms and the individual response of each patient. The use of corticosteroids, immunosuppressants, and biological agents has been reported as therapeutic options in more

severe or recurrent cases. However, there is no standard approach, and treatment should be individualized for each patient[8-11, 12,13].

Case Report

Patient ASL., 30 years old, female, presented to the dental clinic complaining of swelling in the upper lip for about 6 months (Figure 1). The alteration was asymptomatic but affected the patient's facial aesthetics. During the anamnesis, the patient reported not remembering having had similar episodes, denied using any systemic or topical medications, and also denied having allergies to medications or any other substances. Any other information regarding past medical history, dental history, family history, and habits was not relevant to the case.

On clinical examination, a voluminous and painless edema was observed, along with a fissured tongue (Figure 2), leading to a diagnostic hypothesis of Melkersson-Rosenthal Syndrome. Despite knowing that histopathological analysis is conclusive for this diagnosis, after discussion with the patient, we opted for an incisional biopsy on the upper lip mucosa. Histopathological analysis revealed a non-specific chronic inflammatory process that did not contribute to the diagnostic confirmation. Subsequently, a complete blood count, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibodies (ANA), and antineutrophil cytoplasmic antibodies (ANCA) were inconclusive. As the diagnosis of Melkersson-Rosenthal Syndrome is often made based on clinical evaluation and medical history of the patient and the exclusion of other possible pathologies, the definitive diagnosis of MRS was reached.

With the diagnosis, treatment was initiated with Prednisone 20mg once a day and Fexofenadine (Allegra®_ every 12 hours for 7 days. After one week, the patient returned and reported a decrease in lip edema and a sensation of "deflation." Therefore, the Prednisone dosage was increased to 40mg, while Fexofenadine was continued. Upon returning the following week, Fexofenadine was discontinued as the lip started to swell again, increased in volume, and the patient reported headaches. At this point, the Prednisone dosage was reduced to 20mg, and Fexofenadine was resumed. Subsequently, a Prednisone taper was performed, gradually decreasing the dosage (Figure 3).

Due to the limited improvement, a change in therapy was opted, and a new treatment was started with intralesional injection of triamcinolone hexacetonide (Triancil®) combined with 3% Lidocaine (Lidostesin®), injected into the upper lip mucosa every seven days for a month. Initially, the dosage was 1ml, with half triamcinolone and half Lidocaine. The second application was with 2ml, and the third and fourth with 1ml each (Figure 4).

The patient showed slight improvement, but due to the adverse effects that constant corticosteroid use can cause, intralesional injections were discontinued, and this therapeutic protocol was concluded with the use of 5ml of injectable Triamcinolone IM suspension. The patient was discharged, and further observation was advised, with a plan to resume treatment within 4 months. After this period, the patient returned with a stable clinical condition, and she chose to discontinue, at least temporarily, disease control.

Discussion

Melkersson-Rosenthal Syndrome is a rare condition with a highly variable clinical presentation, often complicating accurate diagnosis. The combination of different tests and the exclusion of other conditions are essential for correct diagnosis. Histopathological examinations, complete blood count, erythrocyte sedimentation rate, C-reactive protein, antinuclear antibodies (ANA), and antineutrophil cytoplasmic antibodies (ANCA), and depending on the patient's symptoms, other more specific tests may be requested, such as electrolyte levels, liver enzymes, kidney function, among others[2,3,7,8]. However, in general, the diagnosis of Melkersson-Rosenthal Syndrome is based solely on clinical evaluation and medical history of the patient, as in the case described in this article.

Some authors argue that a biopsy with histopathological analysis is essential to confirm the diagnosis of MRS, especially when the clinical presentation is not classic, and the triad of symptoms is not well-defined. Histopathological analysis can reveal specific characteristics that aid in differentiating the syndrome from other diseases with similar manifestations, thus avoiding misdiagnoses and enabling appropriate treatment[3,5,9,12].

On the other hand, some authors argue that Melkersson-Rosenthal Syndrome is a well-defined clinical condition, and the diagnosis can be established based on typical clinical characteristics, even if the biopsy is inconclusive. They emphasize that the classic triad of orofacial edema, facial paralysis, and fissured tongue is highly suggestive of the syndrome[2,4,8,13].

In the face of this conflict of ideas, it is essential to consider that each case is unique, and the diagnosis of MRS should be approached individually, taking into account the patient's complete clinical picture, symptoms, complementary exams, and response to treatment. The decision to perform a biopsy or not should be made judiciously, weighing the potential benefits and risks for the patient[2,3,7-9]. In the case described here, the biopsy was only performed after a detailed explanation of its advantages and disadvantages to the patient. Despite being aware that it is not mandatory, the patient chose to attempt confirmation through histopathological analysis. However, the result was inconclusive, in line with most of the researched authors.

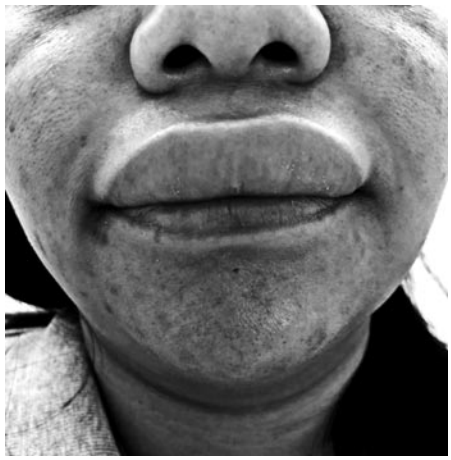

Figura 1. Generalized edema in the upper lip.

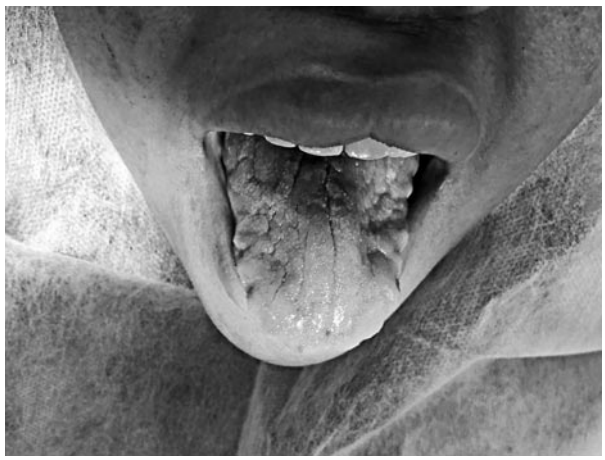

Figura 2. Presence of fissured tongue.

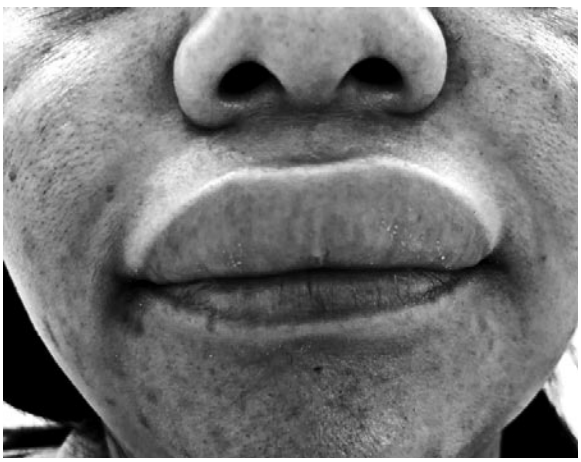

Figura 3. Clinical aspect after using Prednisone. There is an improvement in lip edema.

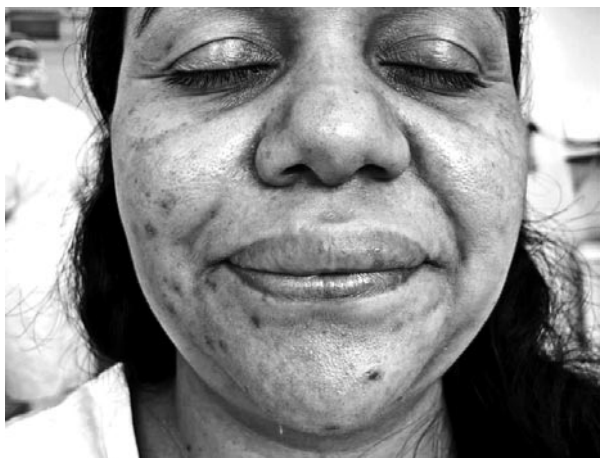

Figura 4. Clinical aspect after using Triamcinolone. Substantial improvement of lip edema is noted.

The literature highlights the use of corticosteroids in various forms as the main therapeutic modality. However, authors also agree on the instability of the clinical condition, with alternating periods of improvement and exacerbation, despite the medication's use. This is particularly important in cases of Melkersson-Rosenthal Syndrome (MRS), as the chronic and recurrent nature of the disease can lead to therapeutic challenges[1,2,10,12].

The fact that the patient initially improved with the use of corticosteroids, as recommended in the literature, indicates that this therapeutic intervention is a valid option and can be effective in controlling the acute symptoms of MRS. However, the instability of the patient's clinical condition, with subsequent recurrences of symptoms even during treatment, highlights that MRS is a complex condition and difficult to manage. Consistent with these findings, the patient described in this report also presented constant variations in her disease response to corticosteroid therapy[2,7,8,11].

In this context, it is crucial to have rigorous and individualized patient follow-up, with treatment adjustments as necessary. This may include optimizing the dose and duration of corticosteroid use, as well as considering other therapies or combined approaches to control symptomatic exacerbations. The literature often does not extensively address this clinical instability, as case reports usually emphasize the diagnosis and initial treatment. However, it is essential to report this instability and the variable response to corticosteroid treatment in your work, as it reflects the clinical reality and the challenges faced in approaching patients with MRS. Furthermore, the possible causes of the patient's clinical condition instability are still poorly studied and understood. MRS is a complex disease, and its etiology is not yet fully clarified. Factors such as genetic, immunological, and environmental factors may be involved in the onset and progression of the disease. Understanding these factors may contribute to the development of more effective and targeted therapeutic strategies[2,3,7,10].

It is crucial to emphasize the importance of continuous research on Melkersson-Rosenthal Syndrome, with the dissemination of more case reports and clinical studies to deepen knowledge about this rare condition and improve its diagnostic

and therapeutic approach. While there is no definitive consensus on the need for a conclusive biopsy for the diagnosis, clinical experience and the judgment of the healthcare professional are crucial for the proper management of the case and the patient's well-being.

Conclusion

Melkersson-Rosenthal Syndrome is a rare and intriguing disease that presents diagnostic challenges to healthcare professionals, especially dentists. In the case described the patient's response to corticosteroid treatment showed initial improvement but exhibited clinical instability, alternating between periods of improvement and exacerbation. MRS and its treatment are extremely complex, and the latter must be performed in an individualized manner, considering possible factors contributing to the instability. In-depth understanding of this syndrome is crucial for early diagnosis and the institution of appropriate treatment, improving the quality of life of patients affected by this condition. Continuous research and information exchange about MRS to improve the management of this challenging condition are fundamental. More studies and case reports are necessary to elucidate the etiology and optimal management of MRS.

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