CASE REPORT

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GRANULOMATOUS CHEILITIS OF MIESCHER AND LINGUA PLICATA AS AN OLIGOSYMPTOMATIC FORM OF MELKERSSON–ROSENTHAL SYNDROME: CASE REPORT AND REVIEW OF LITERATURE

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Abstract. Introduction: *Granulomatous cheilitis of Miescher (GHM) is a rare chronic disorder that presents with recurrent swelling of one or both lips, frequently accompanied by erythema and edema of the whole face. The association of cheilitis with fissured tongue and facial paralysis is known as Melkersson–Rosenthal syndrome. It is a condition with a characteristic manifestation, unknown etiology and difficult treatment.* ***Clinical Case Description:*** *We present the case of a 49-year-old woman who was admitted in our dermatology department with orofacial edema for the last 10 years and fissured tongue. No family history data on medication, food, insect allergy, atopy, asthma or associated comorbidities were reported. The diagnostic workup included clinical investigation, histopathology of skin, laboratory tests and a CT scan of the head to exclude abnormalities of n. facialis canals in reference to Melkersson–Rosenthal syndrome. The patient was treated with dexamethasone 4 mg/24 h and ceftriaxone 2 g/24 h without improvement. As a second line, dapsone therapy was initiated with gradually increasing dosage with methemoglobin levels monitoring.* ***Discussion:*** *There is still no effective therapy for this condition, although various symptomatic therapies targeted to avoid relapses, especially in the edematous stage, exist. The aim of the treatment is to improve the clinical symptoms and quality of life. The spontaneous vanishing of the disease is very rare but such cases has been reported.*

Key words: *Melkersson–Rosenthal syndrome, granulomatous cheilitis of Miescher, lingua plicata*

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INTRODUCTION

Granulomatous cheilitis of Miescher (GHM) is a rare chronic disorder that presents with recurrent swelling of one or both lips, frequently accompanied by erythema and edema of the whole face. The association of granulomatous cheilitis, lingua plicata (LP) (or fissured tongue) and facial paralysis is known as Melkersson–Rosenthal syndrome (MRS). The syndrome is named after Ernst Melkersson, who described a 35-year-old female patient with recurrent facial edema and facial nerve paralysis [1]. In 1931, the German neurologist Rosenthal reported

three patients who had fissured tongue, in addition to orofacial edema and facial paralysis, and suggested a relationship between the triad of symptoms, which subsequently became the syndrome [2].

Genetic factors, hormonal disorders, and infections are suspected as etiological factors. Various allergens have been suggested to play roles in disease pathogenesis such as cinnamon or benzoate [3]. Although few cases of MRS are monogenic, mutations of FATP1 and SCN1A genes were reported [4, 5].

MRS is associated with various underlying diseases such as sarcoidosis, Down's syndrome, psoriasis, diabetes mellitus and Crohn's disease [6, 7]. In addition, patients may complain of migraines, headaches and dizziness, tinnitus, deafness, facial paresthesia, excessive tearing of the eyes and visual disturbances.

CLINICAL CASE DESCRIPTION

A 50-year-old female patient was admitted to our dermatology department with persistent swelling of the upper and lower lips, accompanied by facial erythema. The patient denied having any past and accompanying diseases, or family predisposition. No allergies to foods, medications or insects have been identified, as well as no alternation in the general condition of the patient was observed. Previous repeated therapies with corticosteroids and antihistamines were administered with mild improvement of erythema and no effect on lip swelling.

The clinical examination revealed pathological changes involving the skin of the face, upper and lower lips, and tongue, which were presented by centrofacial erythema and orofacial edema – more pronounced on the upper lip (Figure 1 A and B) and lingua plicata with deep fissures (fissured tongue) (Figure 2).

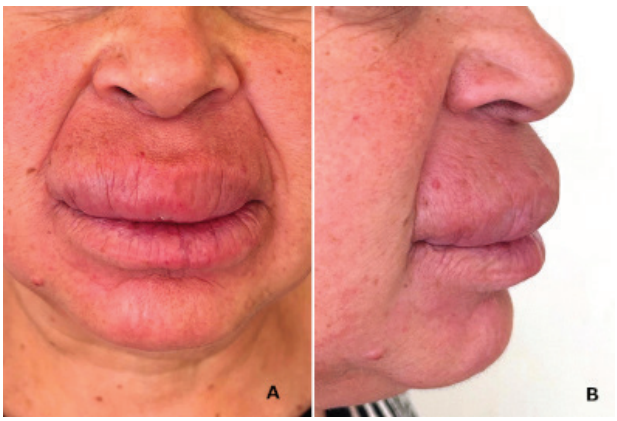

Fig. 1. Centrofacial erythema and edema on both lips. A) Full face; B) – In profile

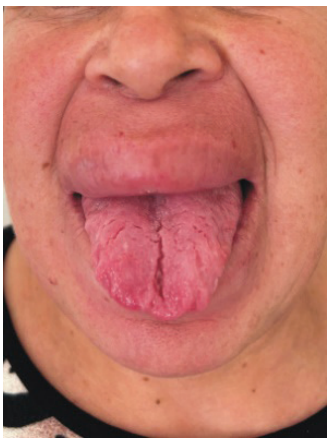

Fig. 2. Significantly fissured tongue (lingua plicata)

The routine laboratory examinations as complete blood count, serum biochemistry, urine analysis and liver function test were within normal ranges, except for the erythrocyte sedimentation rate (51 mm/h) and C-reactive protein (12.5 mg/L).

Histological examination of the specimen of our patient showed normal epidermis without any granulomatous process in the dermis. The presence of occlusive perivascular round cell infiltrates around the blood vessels in the upper dermis and pronounced solar elastosis was observed (Figure 3).

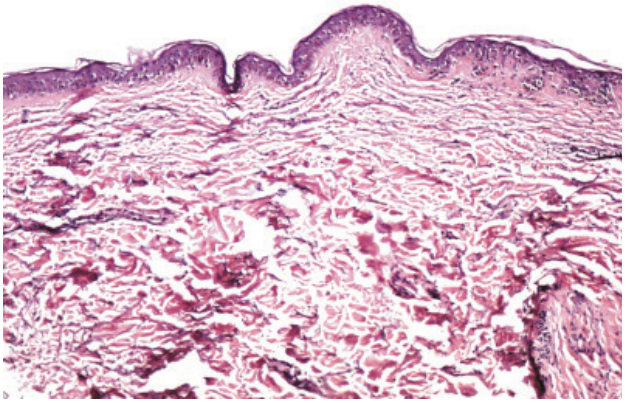

Fig. 3. The histology of lesional skin showing edema, perivascular inflammatory infiltrates, and solar elastosis in dermis (H&E 100x)

Computed tomography (CT) of the pyramidal eminences of the left and right facial nerve canals was performed finding no abnormalities in their sizes, shapes and contours (Figure 4).

During the hospitalization, systemic treatment with antibiotics and corticosteroids was carried out with discrete improvement. After dehospitalization, an oral therapy with 25 mg dapsone was started with an increase in daily dosage with regular monitoring of methemoglobin and glucose-6-phosphate-dehydrogenase levels. During the first month of treatment, there was a slight improvement in the lip erythema

and edema. At the third month, the patient felt well and a significant decrease in edema was observed. However, since the methemoglobin level was elevated, the dapsone treatment was discontinued and replaced by doxycycline 100 mg/24 h.

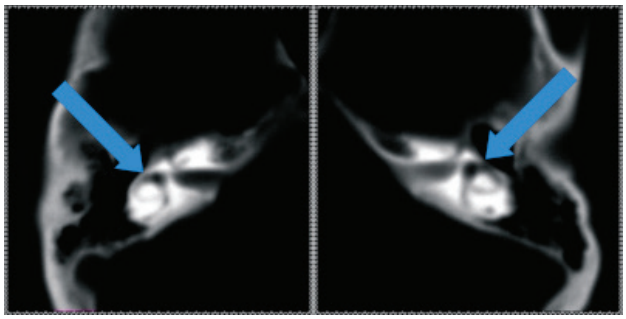

Fig. 4. CT of the pyramidal eminences of the left and right facial nerves canals

DISCUSSION

Melkersson–Rosenthal syndrome is a rare inflammatory condition, characterized by the classic triad of orofacial edema, fissured tongue, and facial palsy. The incidence of MRS is between 0.2 and 80 cases in 100,000 population per year, and affects predominantly women [8]. However, less than 30% of patients present with the complete triad, while others are oligosymptomatic, as our patient [9].

The isolated affection with lip swelling was initially described by the Swiss dermatologist Miescher in 1945 as „cheilitis granulomatosa“ [10]. Granulomatous cheilitis of Miescher is characterized clinically by persistent labial edema and histologically by localized granulomatous inflammation and no signs of systemic granulomatous diseases [11]. It typically affects the upper lip; however, lower lip, periorbital tissues, cheeks, and chin may also be involved [7]. Edema is the most commonly reported first symptom; however, facial paralysis may preside the swelling of the lips by years [12]. The differential diagnosis includes angioedema, Crohn's disease, sarcoidosis, and various granulomatous infectious.

Histopathological examination of skin in early stages of MRS reveals dermal edema, fibrosis, vasodilatation and perivascular lympho-plasmocytic inflammatory infiltrates. The most important findings are defined granulomas; however, their absence does not rule out the diagnosis of the MRS [13], as in our case.

Lingua plicata presents clinically with fissures that are more than 2 mm deep, and/or cobblestone-like protuberances on the dorsum of the tongue [14]. It is considered as development malformation, which affects between 0.5 to 5% of general population [14]. The incidence of LP among MRS case series varies between 30 and 100% of patients [14, 15] and remains unexplained.

The missing symptom in our patient was facial nerve paralysis. CT investigation was performed to establish the pathological changes in the bone structures of the facial nerve canal; however, it showed no abnormalities. In contrast, in a study of 21 MRS patients, who underwent multiplane tomography of facial nerve canals, abnormalities in the width, shape, and convexity of the bone structures in 76% of the patients were found [15].

In terms of therapy, there is still no consensus accepted for the treatment of MRS. Non-steroid anti-inflammatory drugs and corticosteroids are used as first line therapy, reducing tissue edema in 50% of patients and the frequency of relapses by 60–75% [16]. Intralesional corticosteroid administration showed significant reduction of labial edema, as well as diminished recurrences after 6 months [17]. Combined therapy with intralesional betamethasone and oral doxycycline was found useful in some patients with MRS [18].

Dapsone, a sulfone derivate used for the treatment of leprosy, was found effective in few cases with MRS, because of its anti-inflammatory activity [19, 20]. The main disadvantage of such therapy was the frequently provoked dapsone-associated methemoglobinemia, ranging from cyanosis to severe dyspnea and anemia [21]. Single cases with partial effect or complete remission after clofazimine, infliximab and adalimumab therapy were also reported [22, 23].

Surgery is recommended to decompress the facial nerve and reduce tissue edema; however, its effectiveness has not been established [24, 25]. Surgical approach aimed at removing part of m. orbicularis oris and the coarse edematous tissue has been proposed [24]. Helium-neon laser ablation is an alternative procedure to cheiloplasty [26]. Both the procedures can cause loss of sensation in the affected lip and do not affect the recurrence of the disease. There are rare cases, reported in the literature, of spontaneous resolution of symptoms.

CONCLUSIONS

In conclusion, we present a patient, who has fulfilled two of the three criteria for MRS. The disease was successfully controlled with various therapeutic modalities. Despite therapeutic options, the treatment of patients with MRS remains challenging, the response and outcomes are individual, and the main goal is to improve the patient's quality of life.

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Ethical statement: *This study has been performed in accordance with the ethical standards as laid down in the Declaration of Helsinki.*

Consent for publication: *Consent form for publication was signed by the patient and collected.*

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