Melkersson-Rosenthal syndrome: Appropriate response to the combination treatment with intralesional triamcinolone injection and oral azithromycin

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Conflict of Interest: None to declare

Received: 1 February 2015
Accepted: 5 March 2015

Melkersson-Rosenthal syndrome is an uncommon disorder which is presented by a triad of lip swelling, facial nerve palsy, and a fissured tongue. A number of treatments have been reported for this syndrome with variable outcomes. We have reported a 38-year-old female patient with lower lip swelling and a fissured tongue on clinical examination. She was also suffering from facial nerve paralysis since 8 years ago. A significant improvement of the signs was achieved with a combination of intralesional corticosteroid injection and oral azithromycin. Although our patient showed the triad, she had an atypical clinical course due to the initiation of syndrome with facial nerve palsy, resulting in a delay in definite diagnosis of her disease. The anti-inflammatory and immuno-modulatory effects of azithromycin and the therapeutic properties of the intralesional injection of corticosteroid have an important role in managing this syndrome.

Keywords: Melkersson-Rosenthal syndrome, azithromycin, corticosteroid, facial nerve palsy

Iran J Dermatol 2015; 18: 140-143

INTRODUCTION

Melkersson-Rosenthal syndrome (MRS) is an uncommon condition with unknown etiology which shows a classic triad, including recurrent orofacial edema, facial nerve paralysis, and a fissured tongue [1,2]. In MRS, the age at presentation is widely varied but the mean age is 33.8 to 39 years, and females are more involved than males [2-4]. The complete classical presentation of MRS is rare and seen in only 25% to 40% of the patients [3]. The histopathologic hallmark of the disease is epithelioid noncaseating granulomas, but other findings include lymphedema and perivascular lymphocytic infiltration [5].

Although many drugs, including systemic or intralesional injection of corticosteroids, various antibiotics, immunosuppressants, immunomodulators, etc., and surgical intervention, alone or in combination, have been suggested for the management of this syndrome, most of them are not satisfactory treatments [4-9]. Azithromycin is a macrolide antibiotic and is used to treat many dermatoses because of its anti-inflammatory and immunomodulatory effects [10].

Since MRS is rare with different clinical presentations, studies are difficult to carry out, limiting our understanding of the syndrome and its therapeutic options.

We reported this case in order to improve the understanding of the syndrome, and to attract the attention of the researchers. Our case was referred with a full-blown presentation but an unusual

clinical course. She was treated with a combination of intralesional corticosteroid injection and oral azithromycin.

CASE REPORT

A 38-year-old female patient was admitted to the Hajdaie Dermatology Clinic with persistent, non-painful swelling of the lower lip since 2 years ago. Clinical examination of the lower lip showed non-tender edema without any pebble sensation on palpation, mild fissuring, erosion, and crusting. Mild swelling of the upper lip and oral mucous membrane, numerous deep grooves (lingua plicata) were seen. As for the past medical history, she reported unilateral facial nerve palsy on the right side since 10 years ago (Figures 1 and 2). Chest-X-ray showed no abnormality, and the PPD test was non-reactive. Based on the clinical findings, clinical diagnosis of MRS was suggested and a biopsy from the lower lip was performed for a definite diagnosis.

Histopathology revealed a perivascular inflammatory cell infiltration of lymphocytes, plasma cells, and histiocytes. Lymphatic channels were widely dilated with inflammatory cell collections, but well-defined granulomata were not seen (Figures 3 and 4). Clinical and histopathologic findings confirmed the diagnosis of MRS.

The patient had received multiple treatments such as oral and intralesional corticosteroid, dapsone, azathioprine, clofazimine, tetracycline group, and erythromycin, single or in combination, but she had not responded appropriately to them. We first prescribed oral azithromycin alone without any adequate response, but later combination

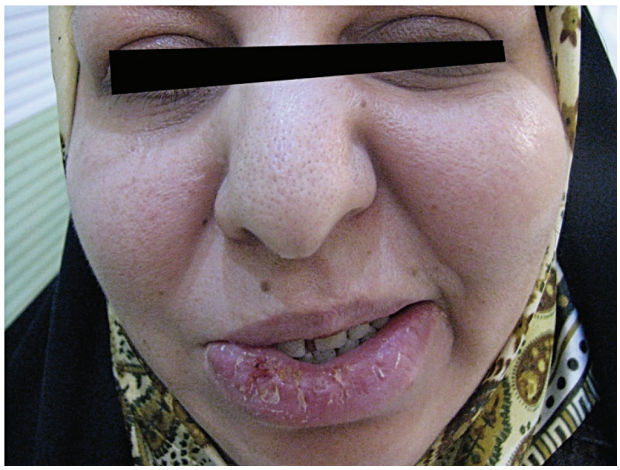

Figure 1. Swelling, crusting, and erosion on the lower lip and facial palsy of the right side.

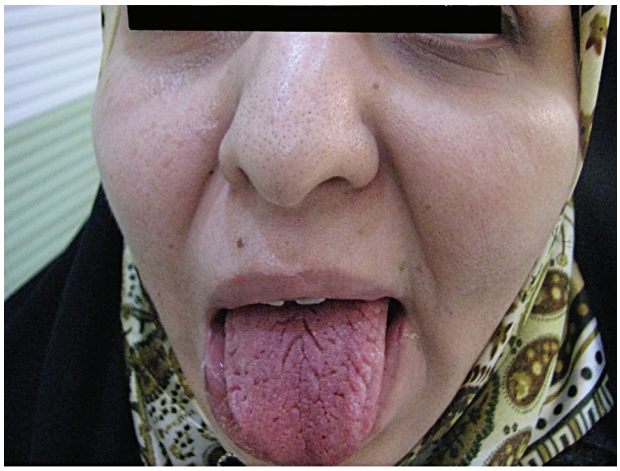

Figure 2. Fissured tongue with multiple grooves on the tongue.

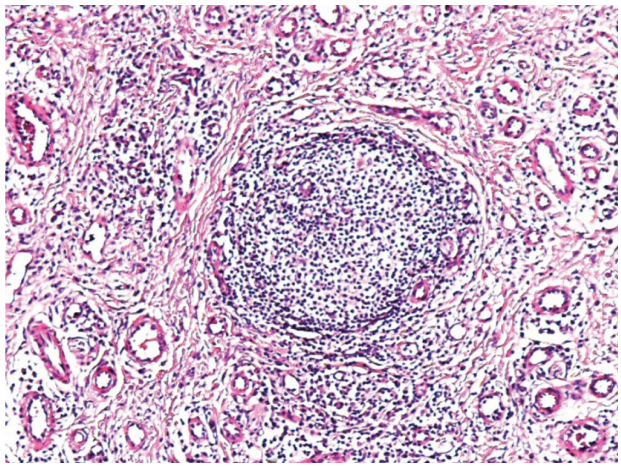

Figure 3. An infiltration of inflammatory cells with dilated lymphatic channels (H & E, ×100).

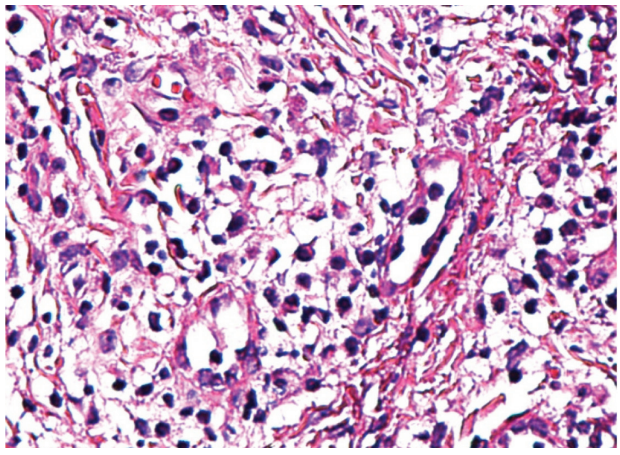

Figure 4. Dilated lymphatic channels surrounded by lymphocytes and plasma cells (H & E, ×400).

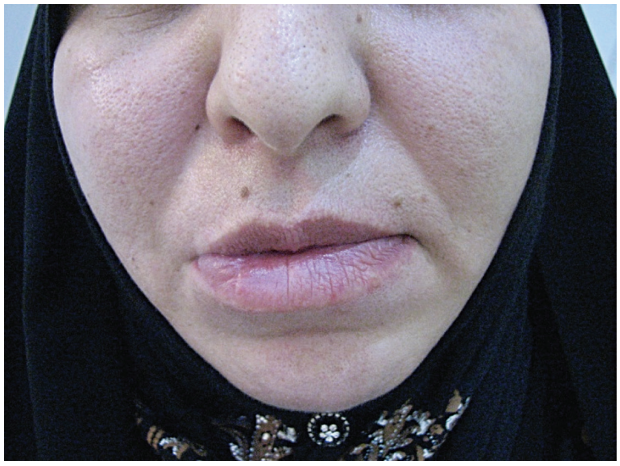

Figure 5. Significant improvement of the lower lip swelling after treatment.

therapy with intralesional triamcinolone injection every month and oral azithromycin, 250 mg three times a week, for 3 months resulted in a significant reduction of her lower lip swelling (Figure 5). Recurrence was not seen during a 1-year follow-up with this combination therapy.

DISCUSSION

Cheilitis granulomatosa (CG) may present as a mono-symptomatic type (Miescher granulomatosa) or as one sign of the typical triad of MRS. However, CG can occur as part of systemic diseases such as Crohn's disease, sarcoidosis, and infectious granuloma [1,8,9].

The cause of MRS is unknown but many factors such as autoimmunity, infection, genetic predisposition, food additives, and neurotrophic factors are implicated in its pathogenesis [9].

The earlier and dominant manifestation of MRS is orofacial edema that is usually present as the swelling of the lips or CG, which most commonly involves the upper lip. Lower lip, and cheek involvement occurs less frequently. The forehead, eyelids, and scalp are involved less commonly [2-4,9]. In a number of studies, facial nerve palsy has been seen in 19.4% to 47% of the patients and a fissured tongue has been reported in about half of the cases [2-4].

Extra- orofacial involvement has been seen in the dorsal aspect of the hands and feet, and back area [2,3]. Most cases of MRS occur in incomplete forms and a full-blown presentation is occasionally seen [2-4,9].

Although multiple medications such as systemic or intralesional corticosteroids, non-steroidal anti-inflammatory drugs, metronidazole, acyclovir, clofazimine, tetracycline, doxycycline, lymecycline, dapsone, tranilast, thalidomide, adalimumab, infliximab, azathioprine, and methotrexate, single or in combination, have been suggested for this syndrome, they have failed to sufficiently control it [4,6-9].

Although our patient had the classic triad of MRS, she had an atypical clinical course because the illness initially started with unilateral facial palsy, and she developed swelling of the lower lip about 8 years later. The patient had fissured tongue at the time of presentation to our clinic and she was not informed about this sign. If MRS initiates with the lip swelling, because these patients visit dermatologists and they are familiar with this syndrome, they are usually diagnosed very soon. But the onset of MRS with facial palsy most often results in its very late diagnosis; therefore, in this situation, careful examination and follow-up as well as evaluation of its signs and symptoms such as a fissured tongue can be helpful in its early diagnosis.

We believe anti-inflammatory and immunomodulatory properties of azithromycin, in addition to anti-inflammatory, immunosuppressive, and anti-proliferative effects of intralesional corticosteroid injection, have a significant role in the treatment of this syndrome, especially in its resistant forms.

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