Melkersson-Rosenthal Syndrome: a rare familial case with granulomatous cheilitis and fissured tongue in both father and son

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Sri Lanka Journal of Dermatology, 2017, **19**, 46-49

Abstract

Melkersson-Rosenthal Syndrome (MRS) is a rare condition with an unknown aetiopathogenesis. Infectious, genetic and inflammatory aetiologies are implicated in MRS, but familial cases of MRS are exceedingly rare. There are several case series in literature where MRS was associated with rosacea. Recurrent facial nerve palsy, recurrent facial swelling and fissured tongue constitute the classic triad in MRS. Diagnosis is often difficult as the classic triad of features are present in only 25-30% of cases. We report the rare occurrence of MRS in both father and son. Index patient who is a 23 year old male had concurrent rosacea also treated with doxycycline has resulted in improvement of both facial swelling and rosacea. He has had a history of facial nerve palsy three years back, followed by progressive swelling of lips and tongue. Swelling of lips and tongue was initially fluctuating and later became persistent. Patient also developed mild photosensitivity, persistent erythema over the nose and conjunctival injection for one year duration. Skin biopsy revealed granuloma, and, slit skin smears from the lips were negative for acid fast bacilli. The diagnosis of granulomatous cheilitis secondary to MRS with concurrent rosacea was made and was treated successfully.

Introduction

Melkersson-Rosenthal syndrome (MRS) is a rare neurological disease with mucocutaneous manifestations[1]. MRS has a recurrent and progressive course. Classic triad of MRS include progressive lip swelling (cheilitis granulomatosa or Meischers cheilitis), Fissured tongue (lingua plicata or scrotal tongue) and facial nerve paralysis[1]. In most cases the diagnosis is delayed as the presentation is incomplete (most cases are oligosymptomatic or monosymptomatic). The classic triad of features are seen in 25-30% of cases[2]. There is a clear female preponderance and it can present at any age. The average age at presentation is 39 years.

Underlying aetiology of MRS is uncertain but infectious, genetic, inflammatory and autoimmune factors are implicated. MRS is known to be symptomatic of Crohn's disease, sarcoidosis and rosacea. Familial aggregation of MRS has been observed and the possible genetic association with de novo autosomal t(9; 21) (p11; p11) translocations[1] are seen in some of these patients. Underlying process is a chronic granulomatous inflammation (which is recurrent in early MRS and persistent in later stages) affecting the mucocutaneous tissue and orofacial innervation. Early histopathological changes include variable perivascular lymphocytic infiltrate and subepidermal oedema. In an established infiltrate, formations of non-caseating granulomas are seen in the dermis and in the subcutaneous tissue.

In monosymptomatic cases the commonest presentation[3] is recurrent or persistent lip swelling. Non-caseating cheilitis granulomatosa (CG) belongs to the orofacial granulomatosis group and is known to precede the diagnosis of Crohn's disease by many years especially in children. Plicated tongue is characterized by development of deep grooves on the dorsal and the lateral surface of the tongue. It is a benign condition and can be seen in healthy subjects. Fissured tongue is common in patients with MRS and is also seen in psoriasis, Sjogren syndrome and chronic granulomatous disease[1]. Lower motor neurone type facial nerve paralysis seen in MRS is indistinguishable to Bell's palsy[3] and it can precede granulomatous cheilitis by several years. Rarely MRS can be associated with other cranial nerve palsies and dysautonomia[3].

In a patient with recurrent orofacial oedema presence of at least one feature: idiopathic facial nerve paralysis or fissured tongue is adequate to make a definitive MRS diagnosis.

Case report

Authors report a case of a 23 year old Sri Lankan male presenting to the Base Hospital Nawalapitiya who was later referred to Teaching Hospital Kandy

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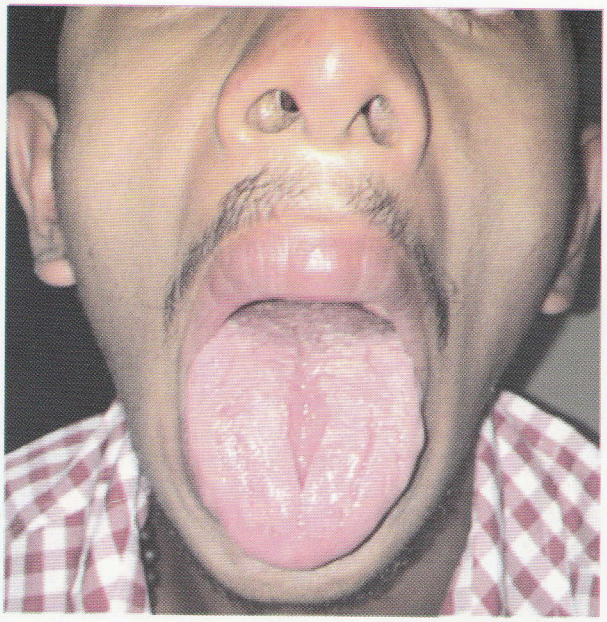

Figure 1. *Macroglossia and granulomatous cheilitis in the son.*

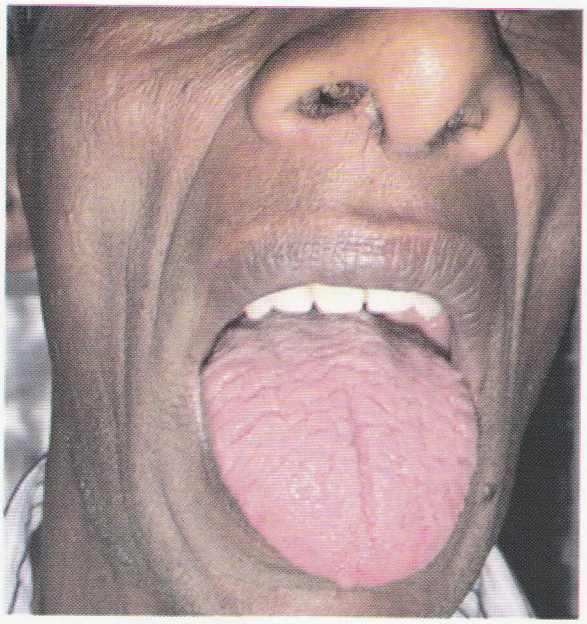

Figure 2. *Macroglossia with fisures in the patient's father.*

for evaluation of persistent, non-pruritic, painless swelling of the lips of 3 year duration. Symptoms started with no preceding trigger with sudden onset left side lower motor neurone facial nerve palsy which at that time was managed as Bell's palsy with complete resolution over several weeks. Shortly after this patient has noticed recurrent swelling of the lips and at the time of presentation patient has had persistent asymptomatic lip swelling for 1 year duration. The lips were enlarging slowly and progressively reaching 3-4 times the normal size. There was no associated numbness, ulceration or urticarial skin lesions associated with lip swelling. Patient did not give a history of contact with leprosy and did not come from a leprosy high endemic area. There were no features to support sarcoidosis. Patient's bowel habit was normal and did not show any features of malabsorption to suggest Crohn's disease. The patient also reported a change in tongue morphology with progressive enlargement of the tongue and development of deep fissures on the dorsolateral surface. There were no features of leprosy, sarcoidosis or dysautonomia. The family history was positive for fissured tongue in the father.

On examination there was firm homogenous symmetrical swelling of upper and lower lips. There was macroglossia with deep furrows and fissures affecting the dorsolateral aspect of the tongue. There were no cranial neuropathy and dysautonomia. There was no reduction in facial sensation and the regional nerves were not thickened. The patient was clinically diagnosed to have classic MRS with the complete triad of clinical features.

Examination of patient's father revealed macroglossia with fissured tongue and was a monosymptomatic case of MRS

Skin histology done at base hospital, Nawalapitiya revealed granulomatous dermatitis, and the patient was planned to be started on multi drug therapy (MDT) for leprosy when the patient was referred to Teaching Hospital Kandy (THK) for a second opinion. Repeat skin biopsy was performed and slit skin smear was done. Wade-Fite stain for acid fast bacilli was negative.

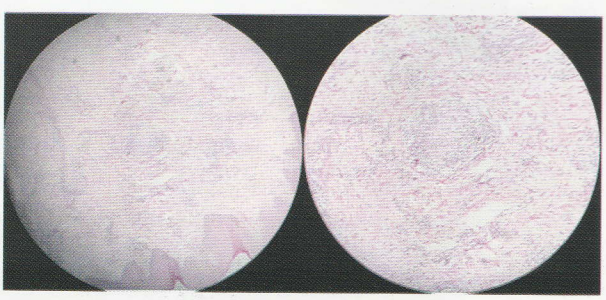

Figure 3. *×10 and ×40 showing non caseating granulomatous inflammation.*

Patient also had mild erythema and telangiectasia over the face and redness of conjunctiva suggestive of rosacea. The possibility of concurrent granulomatous rosacea as a possible cause for granulomatous cheilitis was entertained. As a result patient was started on anti-inflammatory antibiotic doxycycline 100 mg bid with significant improvement over next few months.

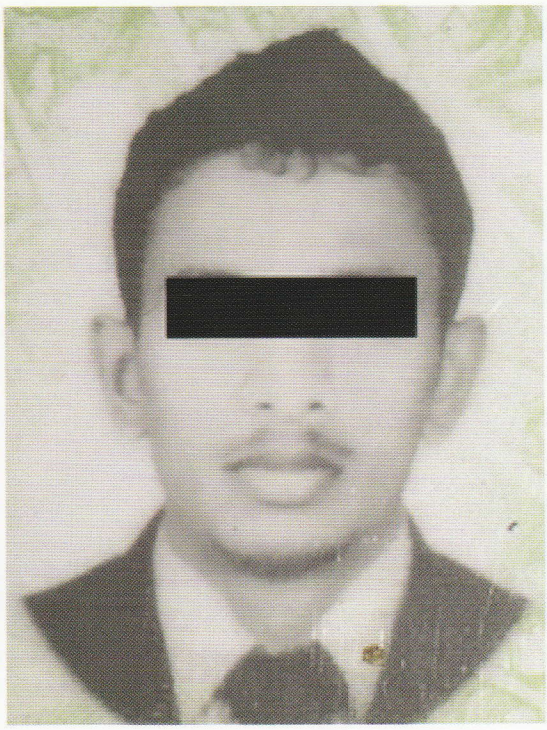

Figure 4. *Patients appearance at 18 years of age before developing symptoms.*

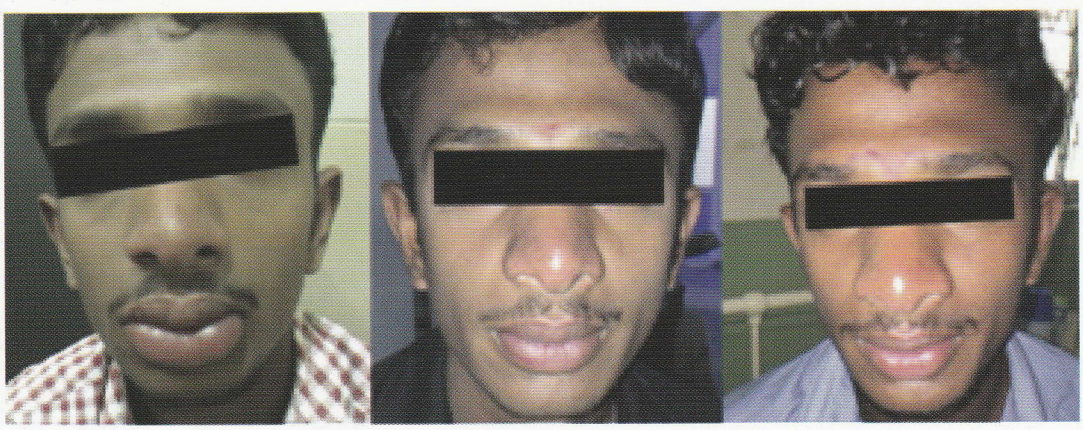

Figure 5a. *Improvement of granulomatous cheilitis with treatment.*

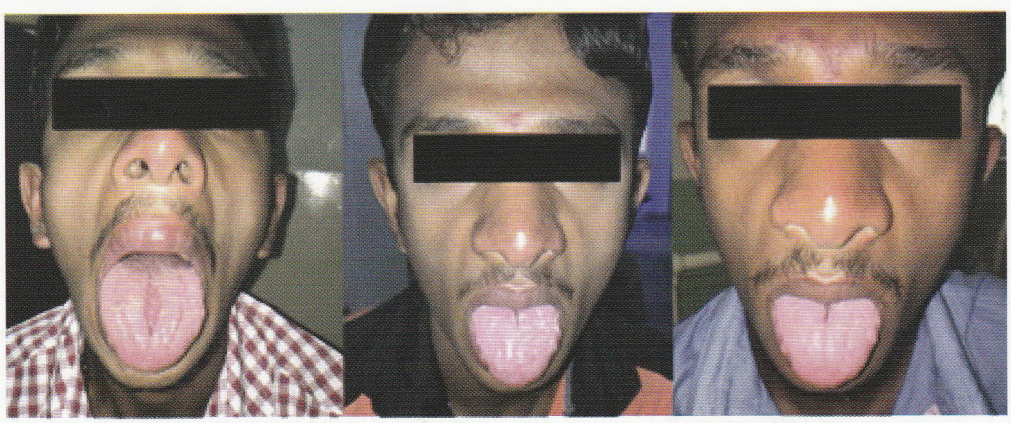

Figure 5b. *Improvement of macroglossia is less marked.*

Discussion

MRS is a rare clinical condition showing granulomatous inflammation. Histology is not required to make the diagnosis of MRS. Common causes of granulomatous cheilitis include Crohn's disease, rosacea and sarcoidosis. There are case reports of leprosy presenting with lip swelling. Thus in the Sri Lankan setting, leprosy should not be overlooked as a cause for granulomatous cheilitis. Facial sensory loss is a late feature in leprosy, as facial sensory innervation has great overlap. Therefor its absence should not be used to exclude leprosy. Alternative methods such as slit skin smears and fite stain should be utilized to exclude leprosy. Cases of familial MRS is very rare but as there are now identified genetic loci for MRS, the presence of family members with MRS gives added support to the diagnosis.

Granulomatous cheilitis is the most commonly encountered clinical feature of MRS. It often poses management problems and the most commonly used treatment is topical and intra lesional corticosteroids[4-5]. Often the effects of intralesional corticosteroids are temporary and repeated injections are required. None-the-less this treatment modality circumvents the systemic toxicity of glucocorticoid treatment to an extent. The dose of intralesional triamcinolone varies between 10 to 20 mg and the gap between injections quoted in studies varies from weeks to months.

Anti-inflammatory and immunomodulatory antibiotics are also used to treat granulomatous cheilitis. Antibiotics[5] that have recently gained popularity for this include minocycline (100 mg daily) and roxithromycin (150-300 mg daily). Due to availability in the hospital our patient was treated with long term doxycycline 100 mg bid monotherapy with good response in lip swelling and granulomatous cheilitis. Oral metronidazole[5] 750-1000 mg daily has also shown good response.

Patients with granulomatous cheilitis in association with Crohn's disease improved with infliximab[4] 3-5 mg/kg dosing were reported. Methotrexate 5-10 mg per week is also effective in treating granulomatous cheilitis.

Surgical debulking is resorted to when there is severe deforming facial and lip swelling. There is considerable morbidity associated with surgical management as there can loss of normal sensation of the lips can be lost which will interfere with feeding and speaking.

Patients with fissured tongue will benefit from good oral hygiene, avoiding irritant foods and intermittent use of anti-inflammatory alkaline solutions.

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