CASE REPORT

Clinicopathological significance of Melkersson-Rosenthal syndrome

Shruti Bohra,¹ Pratik B Kariya,² Seema Dinesh Bargale,² Shital Kiran³

¹Department of Oral Pathology and Microbiology, Sharad Pawar Dental College, Wardha, Maharashtra, India

²Department of Pedodontics and Preventive Dentistry, KM Shah Dental College and Hospital, Vadodara, Gujarat, India

³Department of Pedodontics and Preventive Dentistry, Karnavati School of Dentistry, Gandhinagar, Gujarat, India

Correspondence to

Dr Shital Kiran,
drshitalkiran@yahoo.com

Accepted 19 July 2015

SUMMARY

Melkersson-Rosenthal syndrome (MRS) classically shows a triad of orofacial swelling, fissured tongue and facial palsy, more commonly the oligosymptomatic form. The orofacial swelling is characterised by swollen reddish-brown non-pruritic lips and facial oedema. In one-third to one half of patients, fissured tongue is seen, which also aids in diagnosis. The histological finding of MRS includes non-caseating, sarcoidal granulomas, but their absence does not exclude the diagnosis. All these findings together form a basis for a cautious search for confrontational reasons for the symptom complex of MRS.

BACKGROUND

Melkersson-Rosenthal syndrome (MRS) is considered to be a rare syndrome. Hornstein¹ estimated the incidence to be 0.08%. MRS is a non-caseating granulomatous disease showing (in complete or incomplete form) a triad of facial paralysis, orofacial oedema and fissured tongue (scrotal tongue, lingua plicata or furrowed tongue). Orofacial swelling is the most consistent and dominant feature of MRS. In a review by Zimmer *et al.*,² in patients diagnosed with MRS, orofacial swelling was the most frequent initial presenting sign. Most commonly, the lips are affected, with swelling sometimes confined only to the lips. Cheilitis granulomatosa (or granulomatous cheilitis) is a chronic inflammatory granulomatous swelling of the lips; it is also referred to as Miescher cheilitis and considered a monosymptomatic form of MRS.³ MRS usually presents in a monosymptomatic or oligosymptomatic form. This unique case presents an adolescent girl with a clinicopathological correlation of MRS.

CASE PRESENTATION

A 16-year-old girl presented to our dental department with generalised gingival enlargement as well as swelling in the upper and lower lips for the past 8–9 months. She was apparently normal 9 months previously, when she had an episode of fever that lasted for 8 days and subsided with medication taken from a local clinician. This was followed by episodes of remission and exacerbation of gingival enlargement with swelling of the upper lip with pus discharge and bleeding.

On examination, the patient's face was bilaterally asymmetrical, with swelling on the right side. Both upper and lower lips were swollen (figure 1). On palpation, the swelling was a normal temperature, non-painful, non-pitting and rubbery in consistency.

The patient's face was flattened on the left side; the mandible was deviating on the right side on opening of the mouth. On intraoral examination, generalised gingival enlargement was noticed covering the cervical one-third of almost all the teeth (figure 2). The teeth present were central incisors to second molars in all four quadrants. The tongue had deep grooves and fissures. A long and prominent central groove was evident extending in a straight line on the dorsum of the tongue, with numerous small grooves and fissures running laterally from the middle third of the tongue (figure 3).

An initial diagnosis of angio-oedema was made. Diphenhydramine hydrochloride, 100 mg, was administered intramuscularly followed by a course of diphenhydramine hydrochloride, 50 mg orally, four times a day. After 24 h, no noticeable reduction in facial swelling was seen. Therefore, re-evaluation of the diagnosis was necessary. As a result of this history, recurrent cheilitis granulomatosa consistent with MRS was added to the differential diagnosis.

INVESTIGATIONS

A biopsy specimen of the affected lip area was sent for histopathological examination, confirming the

Figure 1 Extraoral photograph showing swollen upper and lower lips.

CrossMark

To cite: Bohra S, Kariya PB, Bargale SD, *et al.* *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-210138

Figure 2 Intraoral photograph showing generalised gingival enlargement.

final diagnosis of MRS. On histopathological examination, the mucosa consisted of parakeratinised, hyperplastic, stratified squamous epithelium overlying collagenous connective tissue. Within the connective tissue there were discrete aggregations of lymphocytes, generally with a perivascular distribution; however, there was evidence, in the central foci, of histiocytes consistent with granulomatous lesions. The histological findings were consistent with cheilitis granulomatosa (figure 4).

TREATMENT

Treatment consisted of application of lip gloss to prevent cracking of the exposed mucosa, along with oral corticosteroids in tapering doses, analgaesics, warm compresses, vitamins, antibiotic eye drops and active as well as passive physiotherapy. Vitamin B₁₂ in the form of methylcobalamin was prescribed because it aids in healing as well as improves the recovery time of facial nerve function.

Figure 3 Intraoral photograph showing deep grooves on dorsal surface of the tongue.

Figure 4 Photograph showing histological presentation of cheilitis glandularis at low power (10x) and high power (40x).

OUTCOME AND FOLLOW-UP

No further treatment was deemed necessary except continuation of the patient's regular biannual preventive recall appointments.

DISCUSSION

MRS classically shows a triad of orofacial swelling, fissured tongue and facial palsy. An oligosymptomatic form of this syndrome is more commonly known as Miescher cheilitis.³ MRS may often go undiagnosed for some days, as in the present case. Rossolino, in 1901, was the first to describe this particular association of oedema of the face, facial nerve palsy and scrotal tongue; the syndrome was named after Melkersson and, later, Rosenthal.⁴ In 1928, Ernst Melkersson, a Swedish physician, described a 35-year-old woman with facial oedema and paralysis. Shortly after, in 1931, Curt Rosenthal, a German neurologist, described three patients who had fissured or plicated tongues in addition to orofacial swelling and facial palsies, and proposed a link between the triad of symptoms.⁵ Subsequently, the triad of clinical findings came to be known as MRS.

MRS does not appear to have an obvious predilection for either sex, although some claim that it is slightly more common in females.^{6–8} Although MRS is reported as commonly found during the second to fourth decades of life, there are many published reports of MRS in children and preadolescents; Roseman⁷ described a case of MRS in a 7-year-old girl, Cohen⁸ described four cases of MRS in children younger than the age of 11 years and Yuzuk⁹ described the case of a 13-year-old girl who presented with the oligosymptomatic form, or labial

oedema, coupled with fissured tongue. No particular racial predilection has been noted in MRS.

Aetiology of this disease remains largely unknown.¹⁰ In granulomatous cheilitis, the normal architecture of the lips is altered by the presence of lympho-oedema and non-caseating granulomas in lamina propria. T_H1 immunocytes produce interleukin 12, RANTES/MIP-1 α and granulomas. Expression of protease-activated receptors 1 and 2 occurs in orofacial granulomatosis. Human leucocyte antigen (HLA) typing may show HLA-A2 or HLA-A11.¹¹ The pathogenesis of MRS was suggested by Hornstein,¹ who suggested that abnormal regulation of the autonomic nervous system leads to excessive permeability of the facial cutaneous vessels. From this abnormal circulation, non-specific antigens then stimulate the perivascular cells to form granulomas. Obstruction of perivascular vessels by granuloma has been proposed as a causative factor in the swelling.¹

Initially, a patient with MRS usually reports painless facial swelling that has persisted for a long time. Further investigation may reveal a history of previous episodes of swelling associated with facial paralysis or fissured tongue that the patient has never noticed. The most common symptom of MRS is recurring orofacial swelling in which the upper lip is more often affected. In this case, swelling of both lips was observed. Other areas affected by orofacial swelling in MRS in order of frequency are cheeks, nose, eyelids, the alveolar process and chin.^{2 12} Zimmer *et al*² reported orofacial manifestations in 42 patients with MRS who were examined at their clinic among 220 reviewed cases reported in the literature between 1965 and 1990. They found that 82% of patients presented labial swelling, whereas swelling in other areas of the face apart from the lips was 40%; 24% had Bell's palsy, and 59% had fissured tongue. Other areas of intraoral swelling were, in order of frequency, the gingiva (11%), buccal mucosa (16%), palate (8%) and tongue (7%).

The swelling of the face, including the lips, is described as recurrent, non-tender, non-pitting and firm, but not of hard consistency. The orofacial swelling is usually sudden and, in most cases, precedes facial paralysis by weeks, months and even years.^{2 5 6} The first episode of oedema, sometimes accompanied by fever and mild constitutional symptoms (as seen in the present case, eg, headache, visual disturbance), usually subsides completely in hours or days. Recurrences can range from days to years, each recurrent episode lasts longer and is more pronounced, and swelling may ultimately become permanent.^{2 5 6}

The facial paralysis associated with MRS is frequently indistinguishable from Bell's palsy. The site affected by paralysis usually corresponds to the site of swelling. As in the present case with facial swelling, the paralysis is on the right side. Each recurring episode is more profound and lasts longer.^{6 13 14} Other neurological presentations associated with MRS are altered taste, migraine headaches and trigeminal neuralgia.^{2 5 6 13 15} Fissured tongue (eg, lingual plicata) is usually found at birth and therefore considered an incidental finding of MRS. Nevertheless, fissured tongue is 10 times more likely to be found among individuals diagnosed with MRS than in the general population.^{2 6 15} Miyashita¹⁶ described MRS in a 56-year-old woman who was afflicted with cheilitis granulomatosa caused by lingual candidiasis of a fissured tongue. The oedematous lesion, on histopathological investigation, is a non-caseating epithelial cell granuloma with perivascular mononucleated lymphocytic infiltrate. Fibrosis of the granulomas is typical in long-term and recurrent lesions.^{1 2 17}

Differential diagnosis includes Crohn's disease, sarcoidosis, Ascher's syndrome, allergic angio-oedema, leprosy and tuberculosis.^{1 5 15 17-19} In laboratory studies, a serum ACE test may be

performed to help exclude sarcoidosis. Reactions to food additives, metals and oral antigens, which may be associated with some cases of granulomatous, are excluded by using Patch tests.²⁰ If found positive, patients are advised to avoid the allergen. Imaging studies such as gastrointestinal tract endoscopy, radiography and biopsy may be used to differentiate MRS from Crohn's disease. Chest radiography, gallium or positron emission tomography scanning may be helpful in excluding sarcoidosis and tuberculosis. Orthopantomogram helps in ruling out presence of a chronic dental abscess.

A final diagnosis of MRS is made from the clinical history and histopathological assessment of the oedematous tissue, which usually includes the lip. When biopsy of the oedematous tissue is difficult or not warranted, then a history of recurrent idiopathic facial swelling associated with at least one of the following two entities, idiopathic facial paralysis or fissured tongue, is sufficient to make a positive diagnosis of MRS.

Treatment of MRS is aimed at the facial swelling and paralysis. Because the aetiology and pathogenesis of MRS are not well understood, treatment continues to be empirical and, in most cases, unsuccessful. Fortunately, the swelling and the paralysis are both self-limiting, and usually go into remission on their own. Treatment with oral prednisone or nerve decompression has been shown to be effective.^{1 5 6} Also, interlesional injections with triamcinolone hexacetonide suspension have been shown to provide temporary benefit.¹² Plastic surgery may be considered in the case of permanent fibrotic lesions. Nevertheless, thorough documentation by many dentists eventually allowed MRS to be included in the differential diagnosis. This case highlights the importance of good history taking, regular follow-up and thorough documentation, for proper patient management.

Learning points

- Concomitant presence of orofacial swelling, fissured tongue and facial palsy, or any one of these, may be a case of Melkersson-Rosenthal syndrome (MRS).
- A final diagnosis of MRS is made from the clinical history and histopathological assessment of the oedematous tissue.
- MRS may recur intermittently and can become a chronic disorder.

Contributors SB, PBK, SDB and SK contributed significantly to the conception and design, analysis and interpretation of the data, writing of the manuscript and reviewing the article for important intellectual content.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Hornstein OP. Melkersson-Rosenthal syndrome: a neuro-muco-cutaneous disease of complex origin. *Curr Probl Dermatol* 1973;5:117-56.
- 2 Zimmer WM, Rogers RS, Reeve CM, *et al*. Orofacial manifestations of Melkersson-Rosenthal syndrome: a study of 42 patients and review of 220 cases from the literature. *Oral Surg Oral Med Oral Pathol* 1992;74:610-19.
- 3 Rogers RS III. Melkersson-Rosenthal syndrome and orofacial granulomatosis. *Dermatol Clin* 1996;14:371-9.
- 4 Magid ELS, Galala ELE. Melkersson-Rosenthal syndrome; review of the literature and report of a case. *J Laryngol Otol* 1973;87:898-902.
- 5 Green RM, Rogers RS III. Melkersson-Rosenthal syndrome: a review of 36 patients. *J Am Acad Dermatol* 1989;21:1263-70.

- 6 Orlando MR, Atkijns JS Jr. Melkersson-Rosenthal syndrome. *Arch Otolaryngol Head Neck Surg* 1990;116:728–9.
- 7 Roseman B, Fryns JP, Van DBC. Melkersson-Rosenthal syndrome in a 7-year-old girl. *Pediatrics* 1975;61:490–1.
- 8 Cohen HA, Cohen Z, Ashkenasi A, *et al.* Melkersson-Rosenthal syndrome. *Cutis* 1994;54:327–8.
- 9 Yuzuk S, Trau H, Levy A, *et al.* Melkersson-Rosenthal syndrome. *Int J Dermatol* 1985;24:456–7.
- 10 Tilakaratne WM, Freysdottir J, Fortune F. Orofacial granulomatosis: review on aetiology and pathogenesis. *J Oral Pathol Med* 2008;37:191–5.
- 11 Ketabchi S, Massi D, Ficarra G, *et al.* Expression of protease-activated receptor-1 and -2 in orofacial granulomatosis. *Oral Dis* 2007;13:419–25.
- 12 Miele FA Jr. The big lip. Diagnostic and treatment considerations. *Gen Dent* 1994;42:258–9.
- 13 Graff-Badford SB. Melkersson-Rosenthal syndrome—a review of the literature and a case report. *South Afr Med J* 1981;60:71–4.
- 14 Balatiieh AB, Pillai KG, Maisour M, *et al.* An unusual case of the Melkersson-Rosenthal syndrome. *Oral Surg Oral Med Oral Pathol* 1995;80:289–92.
- 15 Winnie R, DeLuxe DM. Melkersson-Rosenthal syndrome: review of literature and case report. *Int J Oral Maxillofac Surg* 1992;21:115–17.
- 16 Miyashita M, Baba S, Suzuki H. Role recurrent oral candidiasis associated with lingua plicata in Melkersson Rosenthal syndrome. *Br J Dermatol* 1995;132:311–12.
- 17 Minor MW, Fox RW, Bukant SC, *et al.* Melkersson-Rosenthal syndrome. *J Allergy Clin Immunol* 1987;80:64–7.
- 18 Kano Y, Shiohara T, Yagita A, *et al.* Association between cheilitis granulomatosa and Crohn's disease. *J Am Acad Dermatol* 1993;28:801.
- 19 Lloyd DA, Payton KB, Guenter L, *et al.* Melkersson-Rosenthal syndrome and Crohn's disease: one disease or two? Report of a case and discussion of the literature. *J Clin Gastroenterol* 1994;18:213–18.
- 20 Fitzpatrick L, Healy CM, McCartan BE, *et al.* Patch testing for food-associated allergies in orofacial granulomatosis. *J Oral Pathol Med* 2011;40:10–13.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow