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Melkersson-Rosenthal syndrome

Ioannis Chatzistefanou, Petros Zikos, Grigorios Venetis, Konstantinos Vahtsevanos, Konstantinos Antoniades

Ioannis Chatzistefanou, Petros Zikos, Grigorios Venetis, Konstantinos Vahtsevanos, Konstantinos Antoniades, Department of Oral and Maxillofacial Surgery, "G. Papanikolaou" General Hospital, Aristotle University of Thessaloniki, 54124 Thessaloniki, Greece

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Correspondence to: Ioannis Chatzistefanou, MD, DDS, Department of Oral and Maxillofacial Surgery, "G. Papanikolaou" General Hospital, Aristotle University of Thessaloniki, 54124 Thessaloniki, Greece. ioannis.chatzistefanou@gmail.com
Telephone: +30-231-760124
Fax: +30-231-760124

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Abstract

Melkersson-Rosenthal syndrome (MRS) is a rare, non-caseating granulomatous disorder of unknown etiology and undefined diagnostic criteria. The classical triad of recurrent orofacial edema, relapsing facial paralysis, and fissured tongue, is not frequently seen in its complete form, and many patients remain misdiagnosed or undiagnosed for years. The purpose of this study is to review the findings in the literature describing the Melkersson-Rosenthal syndrome with aim to identify its clinical and histopathological characteristics and correlate them with definitive diagnostic criteria and effective treatment modalities. A systematic review and analysis of more than 100 publications met eligibility criteria performed by the authors. Orofacial edema of unknown etiology is the most typical clinical feature of the Melkersson-Rosenthal syndrome. Its coexistence with of facial nerve palsy or fissured tongue could be characterized as an oligosymptomatic MRS. Many investigators suggest cheilitis granulomatosa as a monosymptomatic form of MRS, while patients with facial palsy and fissured tongue, without orofacial edema, should not be considered having MRS. Histological evidence is not necessary. Corticosteroids are generally accepted as the mainstay treatment.

Key words: Melkersson-Rosenthal syndrome; Orofacial swelling; Cheilitis granulomatosa; Facial nerve palsy; Fissured tongue

Core tip: Orofacial edema of unknown etiology is the most typical clinical feature of the Melkersson-Rosenthal syndrome. Many investigators suggest cheilitis granulomatosa as a monosymptomatic form of melkersson-Rosenthal syndrome (MRS). The coexistence of orofacial edema with facial nerve palsy or fissured tongue could be characterized as an oligosymptomatic MRS. Patients with facial palsy and fissured tongue, without orofacial edema, should not be considered having MRS. Histological evidence is not necessary. Corticosteroids are generally accepted as the mainstay treatment.

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INTRODUCTION

Melkersson-Rosenthal syndrome is a rare pathological entity of unidentified pathogenesis and equivocal diagnostic criteria[1]. All three classical melkersson-Rosenthal syndrome (MRS) signs of orofacial edema, facial nerve palsy and fissured tongue[2], as described by Melkersson[3] and Rosenthal[4], are not frequently encountered and many patients remain misdiagnosed or undiagnosed for years due to indefinite syndrome sub-classification[2,5-8].

The annual incidence of MSR is ranging between 0.2 and 0.3 in 100000 per year among various published studies[2,6,7,9-11], but the rarity of the disease in conjunction with the difficulty in diagnosis makes these estimations quite precarious. Although MRS may affect all age groups[12], typically at least one of its symptoms appears before the fifth decade of life[10,13]. Many studies show a slight predilection for females[2,7,13], while equal female: male ratio[10] or male predominance[14] has also been reported.

The etiology of Melkersson–Rosenthal syndrome still remains unidentified. Although Crohn's disease, sarcoidosis, herpes viruses' infection, allergic reactions, and autoimmune diseases have been considered as possible causes of the syndrome[2,9,10,12,15-28], a definite pathogenetic association failed to be demonstrated by solid scientific evidence. Familial inheritance has also been assumed[5,8,15,29].

The purpose of this study is to review the associated with Melkersson-Rosenthal syndrome literature citations with aim to identify its clinical and histopathological characteristics and correlate them with definitive diagnostic criteria and effective treatment modalities.

STUDY STRATEGY

A systematic review and analysis of more than 100 publications met eligibility criteria performed by the authors. The search of literature references based on the MEDLINE with subject keywords included five main categories: Melkersson-Rosenthal syndrome, orofacial edema, cheilitis granulomatosa, facial paralysis and fissured tongue. Most of these studies have been conducted at departments of dermatology, oral and maxillofacial surgery, oral pathology and plastic surgery.

RESEARCH

Diagnosis

The most dominant manifestation of MRS is asymptomatic orofacial granulomatous edema[5,10,13,14,19,20,24,25,30]. Lip localization (cheilitis granulomatosa) is perhaps the most frequently encountered type of the MRS associated edema[10,12,14,30,31] while cheeks, tongue or eyelids involvement has also been reported[2,10,13,14,30]. The patients may experience recurrent short episodes of the edema for many years, which gradually becoming more persistent[3,8,10]. It may clinically mimic angioedema, but it last longer and it does not respond to antihistamines administration[32].

Unilateral or bilateral peripheral facial nerve palsy, indistinguishable from Bell's palsy, is another commonly encountered manifestation of MRS[7,13,17,30-33]. Facial nerve involvement could become permanent after recurrent episodes of shorten duration[13]. Palsies of other cranial nerves have also been reported[34].

The fissured tongue (lingua plicata), although found in one third to one half of MRS patients, could valuably assists in diagnosis[9,13,19,20,23-25,30,32,35]. Fissured tongue is defined the presence of at least 2 mm deep and 15 mm long grooves crossing the dorsum or margins of the tongue[36].

MRS patients may also experience recurring episodes of acute anterior uveitis[2,37]. Gastrointestinal symptoms[2], trigeminal neuralgia, psychotic episodes, migraine[9,12,23-28,30,31,38] or longstanding immunologic and autoimmune disturbances[35], may also be encountered.

The associated with the MRS histopathological findings include non-caseating granuloma, giant cells and/or lymphocyte infiltration, and fibrosis[2,5,10,12,26], but their present is not necessary for the final diagnosis[12,34,39]. However, biopsy proofs could crucially assist in diagnostic process and therefore repeated biopsies during an acute edema episode are generally recommended in case of strong clinical suspicion of MRS with negative or inconclusive histopathological report[5,12,13,32,39].

Imaging investigations and dermatology, immunology, gastroenterology, and ophthalmology consultations are also recommended during differential diagnosis, in order other pathologic entities to be excluded[5,20,21,23,40-42].

Sub-classification of MRS

The diagnosis of a complete MRS requires the simultaneous or not presence of orofacial swelling, facial nerve palsy and fissured tongue[2-4,12]. However the complete form of the syndrome is found in no more than 20% of overall MRS cases[5,9,10,12-14,17,20,30].

The majority of literature evidence demonstrates orofacial edema, as the most important diagnostic feature of MRS, affecting almost all patients[12,14,34]. Many investigators suggest cheilitis granulomatosa as a monosymptomatic form of MRS[10,12,17]. The coexistence of orofacial edema with facial nerve palsy or fissured tongue could be characterized as an oligosymptomatic MRS[5,9,20,23,25]. Other minor and more rare signs and symptoms could also be considered as additional diagnostic criteria of the oligosymptomatic form of the syndrome[2,30,34]. Patients with facial palsy and fissured tongue, without orofacial edema, should not be considered having MRS[12,43].

Management

Although there is no consensus in therapeutic approach, corticosteroids are generally accepted as the mainstay in MRS management[9,13,20,23,25,35]. Systemic or intralesional corticosteroid administration has been demonstrated

to keep orofacial edema under control, while pain relievers and/or antibiotics may be also be indicated in some cases[44,45]. In case of unacceptable aesthetic consequences, associated with the orofacial edema, facial reconstructive surgery could be taken under consideration[5,31,46].

Corticosteroids are also considered to be the treatment of choice for MRS associated facial nerve paralysis[9,13,23,25,27]. Massage and electrical stimulation have also been described but remain of uncertain efficacy[8,46]. Follow-up of the patients diagnosed to have MRS should be in a regularly base due to its chronic and gradually progressive nature.

CONCLUSION

Melkersson–Rosenthal syndrome is a recurrent and gradually progressive pathologic entity of indefinite classification. Even though the etiology still remains unknown and various treatment modalities are often unsatisfactory, it could be relieving to the patients and the involved physicians to have MRS diagnosed.

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