Melkersson-Rosenthal syndrome: a retrospective study of 44 patients

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Abstract

Conclusion: When patients with recurrent facial paralysis are encountered, otolaryngologists should check for fissured tongue, and question those patients about orofacial edema, minor symptoms, and family history. Histologic evidence is not necessary for the diagnosis of Melkersson-Rosenthal syndrome (MRS), while coronary high-resolution CT (HRCT) reconstruction of temporal bone and food allergen detection may be beneficial. Prophylactic decompression of the facial nerve for patients with appropriate electrophysiological indication may prevent further facial palsy attacks. Objectives: The objective of this study was to analyze the clinical features of a group of patients with MRS with major complaints of facial palsy treated at the Department of Otorhinolaryngology, and to comment on MRS from the perspective of otolaryngologists. Methods: A retrospective review of patient database for the last 6 years in the Department of Otorhinolaryngology in Beijing Shijitan Hospital was performed to find patients diagnosed with MRS. Results: A total of 44 MRS patients were included in this study. The mean age at onset was 14.1 years. A total of 13 (29.5%) patients had family history, 17 (38.6%) revealed broadened fallopian canal on coronary HRCT reconstruction of temporal bone, and 20/23 (87.0%) patients showed positive results in food allergen detection. Thirty-one patients accepted subtotal facial nerve decompression and only one patient had facial palsy recurrence on the same side as the operation.

Keywords: Recurrent facial nerve palsy, orofacial edema, fissured tongue

Introduction

Melkersson-Rosenthal syndrome (MRS) is a common cause of recurrent peripheral facial paralysis. It is a rare, noncaseating granulomatous disease marked by the triad of recurrent nonpitting orofacial edema, fissured tongue, and recurrent peripheral facial paralysis [1].

MRS patients treated at departments of otorhinolaryngology mostly have complaints or histories of facial paralysis. However, previous studies were mainly from the departments of dermatology and oral-maxillofacial surgery, which treated MRS patients mainly troubled by edema. Only 5% of the related articles were published in otorhinolaryngology journals [2] and this has influenced the existing knowledge about MRS [3].

In the present study, we performed a retrospective review of the patient database for the last 6 years in the Department of Otorhinolaryngology in Beijing Shijitan Hospital to find patients diagnosed with MRS. All medical records of the MRS patients were reviewed in detail and we comment on MRS from the perspective of otolaryngologists, trying to share our experiences with other otolaryngologists.

Material and methods

To identify patients with MRS (diagnosis code G51.2 according to the international statistical classification
of diseases and related health problems, ICD), we retrospectively assessed the records of 1070 inpatients with peripheral facial nerve palsy at the Department of Otorhinolaryngology in Beijing Shijitan Hospital from June 2007 to June 2013. Those cases caused by facial neuroma, intracranial tumor, recurrent Bell’s palsy, Ramsay Hunt syndrome, Guillain-Barre syndrome, leukocythemia, infection or some other possible etiologies were ruled out.

The medical charts were meticulously reviewed for MRS patients. The clinical data noted included brief personal information, the onset and the course of the disease, imaging findings, allergies, differential diagnostic procedures, comorbidities, and family histories. Applied treatment modalities and responses to therapy were also recorded. After discharge, patients were followed up for at least 6 months at the outpatient clinic.

The study protocol was approved by the Beijing Shijitan Hospital Ethics Committee.

Results

Of the 1070 inpatients with peripheral facial nerve palsy during this period, 44 were diagnosed with MRS, including 24 (54.5%) women and 20 (45.5%) men. The mean age at onset was 14.1 years (range 1–50 years) (Figure 1). The mean interval from the onset to the diagnosis of MRS was 8.6 years (range 1 month to 55 years).

There were 20 (45.5%) patients characterized with MRS in its complete form, including 13 females and 7 males. All the patients came with complaints or histories of facial nerve palsy, among which 2 patients had 1 episode (both had orofacial edema and fissured tongue), 22 patients had 2 episodes, and 20 had more than 2 episodes. In addition, it was found that all eight patients whose onset ages were above 22 years had two episodes. For the 42 patients who had more than 1 episode, 22 were contralateral and 20 were ipsilateral. Among the 20 ipsilateral patients, 9 were found on the left and 11 on the right. Fissured tongue was found in 33 patients and orofacial edema in 31 patients (Table I). Furthermore, 23 (52.3%) patients had obvious minor symptoms (craniofacial neurovegetative troubles not including the typical triad of MRS) of MRS (Table II), among whom 17 patients had more than 1 minor symptom.

A total of 13 (29.5%) patients had family history. One patient had concomitant hypertension, one had diabetes mellitus, and another had both hypertension and diabetes mellitus. High-resolution CT (HRCT) reconstruction of temporal bone was carried out for all patients and 17 (38.6%) demonstrated broadened fallopian canal. With the approval of patients, ELISA was applied to detect allergen-specific IgG antibody of 14 kinds of food in 23 patients (including 5 patients without orofacial edema) and it was determined that 20 (87.0%) patients showed positive results, 15 (65.2%) patients had intolerance to eggs, and 11 (47.8%) patients had intolerance to milk.

The treatment consisted of subtotal decompression of facial nerve, systemic corticosteroids, medicine to improve microcirculation (oral administration of extract of horse chestnut seeds as tablets,}

### Table I. Primary symptoms of 44 patients with Melkersson-Rosenthal syndrome (MRS).

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>Facial nerve palsy</th>
<th>Orofacial edema</th>
<th>Fissured tongue</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 (45.5%)</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>11 (25%)</td>
<td>+</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>13 (29.5%)</td>
<td>+</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Total 44 (100%)</td>
<td>31 (70.5%)</td>
<td>33 (75%)</td>
<td></td>
</tr>
</tbody>
</table>

### Table II. Secondary symptoms in 23 of 44 patients with Melkersson-Rosenthal syndrome (MRS).

<table>
<thead>
<tr>
<th>Secondary symptoms</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periauricular pain</td>
<td>13 (29.5%)</td>
</tr>
<tr>
<td>Abnormal gustation</td>
<td>11 (25.0%)</td>
</tr>
<tr>
<td>Dry eyes</td>
<td>9 (20.5%)</td>
</tr>
<tr>
<td>Excessive tearing</td>
<td>7 (15.9%)</td>
</tr>
<tr>
<td>Hyperacusis</td>
<td>3 (6.8%)</td>
</tr>
<tr>
<td>Hypoacusis</td>
<td>3 (6.8%)</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>3 (6.8%)</td>
</tr>
<tr>
<td>Migraine</td>
<td>1 (2.3%)</td>
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</table>
Thirty-one patients with appropriate electrophysiological indication, whose electroneurography showed more than 90% degeneration of the facial nerve, accepted subtotal facial nerve decompression. In the surgery, we decompessed the facial nerve from the stylomastoid foramen to the labyrinthine segment by the transmastoid approach. During the operations it was observed that the most swollen part of the facial nerve was the mastoid segment in 26/31 (83.9%) patients and the labyrinthine segment in 3/31 (9.7%) patients. In addition, chorda tympani with two roots were witnessed in three patients. The mean follow-up period was 3.2 years (range 6 months to 6 years), while we failed to follow up six patients after more than 6 months of regular review, including four who underwent operation and two who had conservative therapy. After the operation, the most of the patients were fully or almost recovered [4], and recurrences of facial palsy were found in three patients, all of whom were female. Two cases recurred on the opposite side to the operation, and one on the same side. Besides the 31 patients who underwent surgery, the other 13 (including 5 patients who had more than 90% degeneration, but rejected operation) accepted conservative management, which proved to be effective and without adverse effects.

**Discussion**

MRS is a rare disorder of unknown etiology, undefined incidence, and inconsistent classification. Hornstein estimated an incidence of 80 in 100 000 per year [1], while Kanerva et al. proposed that the annual incidence of MRS was 0.3 in 100 000 [3]. The sex distribution of this syndrome is controversial. Most authors claim no sex domination, while some authors claim that MRS appears more frequently in females [5]. In the present study, there were 24 females and 20 males, with a slightly higher female presence. MRS may present at any age. Most researchers pointed out that the onset occurred predominantly during the second decade of life and rarely occurred in children [6]. In the present study, the mean age at onset was 14.1 years, which is significantly lower than previous reports of 25–40 years [3,7] and 18 (40.9%) patients experienced the onset in the first decade of life (Figure 1). The divergence may be due to disagreement about the definition of the onset of MRS. It is obvious that facial palsy is the most impressive symptom among the triad. Therefore, once the diagnosis of MRS was confirmed, we regarded the first episode of facial palsy as the onset of MRS. Moreover, it was found that age at onset was above 22 years in only eight (18.2%) patients, and all the eight patients had only experienced two episodes. We may generally assume that the incidence and frequency of MRS declines with the increasing of age.

Although infectious agents, genetic factors, allergic reactions, and benign lymphogranulomatosis have been implicated as possible causes of MRS, the etiology and the mechanism are still not known [8]. Smeets et al. considered MRS to be an autosomal dominant disease, located at chromosome 9p11 [9]. However, at present available studies do not provide sufficient evidence to support a genetic background of MRS. In the present study, 13 (29.5%) patients had a family history, including eight cases with paternal inheritance, two with maternal inheritance, and three with biparental inheritance. In addition, three cases of fissured tongue were all reported from fathers. We may assume that MRS is probably paternal inheritance dominated.

The occurrence of swollen lips histologically characterized by noncaseating granulomas is called granulomatous cheilitis, which many believe is the oligosymptomatic form of MRS. Food intolerance has been implicated as a possible etiologic agent of granulomatous cheilitis, and elimination diets have led to improvement in some patients [10]. In the present study, 20/23 (87.0%) patients showed food intolerance. The percentages of intolerance to eggs and milk were 65.2% and 47.8%, respectively, which were significantly higher than that of the general Chinese population at 29.6% and 13.8%. However, we believe that the influence of food intolerance can only be verified by dietary exclusion [11]. Food allergen detection was helpful to screen patients who may benefit from diet limitation.

Studies have demonstrated that temporal bone HRCT reconstruction is useful in detecting facial nerve abnormalities and can provide accurate anatomic details to surgeons [12]. In the present study, temporal bone coronary HRCT reconstruction of 17 patients indicated broadened fallopian canal. Swollen facial nerve was seen in 29 of the 31 operated patients. The authors hold the view that these data support genetic, infectious, anatomic, and immunologic factors in the pathogenesis of MRS in our patients.

It is difficult to diagnose MRS because of commonly seen abortive cases. Moreover, there are no acknowledged diagnostic criteria and there is no specific diagnostic test. Some authors propose that MRS can only be certainly diagnosed when there is at least one major symptom (e.g. recurrent orofacial edema or facial nerve palsy) and the histologic features of typical noncaseating granulomas. They insist that histological evidence is mandatory [13], while...
others suggest that the presence of the triad is sufficient [2]. As otolaryngologists, we hold that biopsy is not necessary because MRS is a clinical syndrome. Furthermore, as shown in the present study, the concomitant minor signs have proved to be useful for the diagnosis when incomplete symptoms occur. Previous studies suggested that comorbid systemic diseases except migraine were found in more than one-third of cases of MRS [8], whereas in the present study, there were only three cases with concomitant hypertension or diabetes mellitus. We did not find a strong connection between MRS and these diseases.

The presence of the complete triad is reported in 8–25% patients [14], and 25–50% of MRS patients suffered from facial nerve palsy [1,15,16]. In the present study, 20 (45.5%) patients were characterized with MRS in its complete form and all patients had facial palsy. We believe that the noticeable disparity results from the fact that previous studies were mainly from departments of dermatology and oral-maxillofacial surgery and patients in the department of otorhinolaryngology mostly had complaints or histories of false palsy, which is less common among the triad. Therefore, the percentage of complete MRS in our study was higher. Kanerva et al. studied differences in MRS patients treated at the Departments of Otorhinolaryngology and Dermatology of Helsinki University Central Hospital and reached the conclusion that the clinical picture of MRS with facial palsy differed from that of edema-dominated MRS. They proposed that MRS could be divided into two separate forms according to the aggressiveness of the edema [3]. We hold the same opinion based on our experience. It is noticeable that before coming to otolaryngologists, many Chinese people with complaints of Bell’s facial palsy had received acupuncture treatment, which usually led to facial swelling. It frequently resulted in a misdiagnosis. Therefore, when patients with facial palsy and facial swelling are encountered, otolaryngologists should examine and question those patients carefully.

Management of MRS can be controversial because of the unknown etiology and inconsistent classification. Currently, there is no standard therapy and the treatment remains largely symptomatic. It is widely accepted that the fissured tongue is usually asymptomatic and requires no treatment [17].

Treatment is aimed at management of the facial paralysis and cosmetic reduction of established facial swelling. According to the literature, corticosteroid therapy, either systemic or intralesional, might be the initial choice of treatment for MRS [2]. In those MRS patients with unsightly lip swelling, reconstructive surgery may be the choice, but the swelling is likely to recur. Although some authors consider that prophylactic decompression of the facial nerve through its bony canal should be performed to prevent a further attack [18,19], others hold a conservative attitude in the treatment of facial palsy in MRS [17]. In view of the progressive and recurrent nature of facial palsy in MRS, we consider that surgical subtotal decompression for patients with frequent and progressive facial palsy is reasonable. Among the 31 operated patients, recurrence of facial nerve palsy on the same side as the operation was found in only 1 (3.2%) patient after operation. Hence, we believe that prophylactic decompression of the facial nerve for patients with appropriate electrophysiological indication may prevent further attacks.

This study does have several inevitable limitations. This cohort is subject to selection biases, such as Berkson bias and referral bias. The sample was not large enough and the clinical data were reviewed retrospectively. Additionally, it is possible that some monosymptomatic patients were misdiagnosed and not included in our study. Furthermore, some patients were receiving two or more treatments simultaneously, limiting assessment of the efficacy of any treatment independently. In view of the limitations of this retrospective study, further investigations are needed.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References


