Melkersson-Rosenthal syndrome revisited as a misdiagnosed disease

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Abstract

Purpose: We aimed to attract our college’s attention to the Melkersson-Rosenthal syndrome (MRS), which has been an infrequently encountered subject in otolaryngology journals during the last 10 years.

Materials and methods: A retrospective review of the last 10 years’ patient database was performed to find patients with MRS. The medical files, treatment charts, and radiological and histopathological records of these patients were reviewed.

Results: The study group consisted of 3 MRS patients who had been misdiagnosed for 9, 10, and 16 years. Two of them have had the symptoms since adolescence. All of them presented orofacial edema and fissured tongue, whereas first two also had recurrent facial paralysis. Characteristic histopathological features were noted in 1 patient. Electromyography (EMG) was done in 1 patient who underwent facial decompression. All patients responded to either systemic or intralesional corticosteroid treatment.

Conclusions: In the daily practice of an otolaryngologist, it is not usual to diagnose a patient as having MRS. We consider that this is partly because of misdiagnosis. We therefore believe that this study will supply an additional aspect to otolaryngologists, in the scope of recurrent facial paralysis and orofacial edema in both children and adults.

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1. Introduction

Melkersson-Rosenthal syndrome (MRS) is a rare, non-caseating granulomatous disease that is characterized by a triad of facial paralysis, orofacial edema, and lingua plicata (scrotal tongue, or fissured or furrowed tongue). The classic triad of MRS is not frequently seen in its complete form, whereas oligosymptomatic forms are more common [1-4].

The etiology and the mechanism of the disease are still not known; however, infectious diseases, genetic causes, allergy, and benign lymphogranulomatosis have been implicated as possible causes of the syndrome [5-7].

Characteristic histopathological features of MRS are lymphoedema, noncaseating epitheloid cell granulomas, multinucleated Langhans-type giant cells, perivascular mononuclear inflammatory infiltration, and fibrosis [7]. Identification of these features can be difficult, but their absence does not exclude the diagnosis [8,9].

Treatment of choice for MRS varies from center to center. Both surgical and medical treatment modalities for patients with MRS have been reported [1,2,4,10-12].

In this study, we presented MRS patients who were misdiagnosed for at least 9 years. In the light of the data of patients and the body of literature on the subject, we intended to comment on the current diagnosis, histopathological features, and clinical course and current treatment of this underdiagnosed disease. Because MRS has been a rarely encountered entity in otolaryngology journals during last 10 years, we also aimed to attract our colleges’ attention by revisiting the syndrome as a misdiagnosed disease.

2. Materials and Methods

A retrospective review of the last 10 years’ patient database was performed to find patients with MRS. The
medical files, treatment charts, and radiological and histopathological records of these patients were reviewed. The onset and the course of symptoms, differential diagnostic procedures, histopathological findings, and applied treatment modalities were meticulously noted. Patients who were diagnosed as having MRS in their first admission were not included in the study group.

3. Results

The study group consisted of 3 MRS patients who were admitted to our clinic in 1997, 2006, and 2007, respectively.

3.1. Patient 1

A 44-year-old woman presented with recurrent right peripheric facial paralysis (PFP). According to her medical files, 10 years ago, she had admitted to our outpatient clinic with swollen lip and House-Brackmann (HB) grade 6 PFP. In her first attack, she was given 1 mg/kg methyl prednisolone for 20 days. After getting the result of severe axonal degeneration on EMG, facial nerve decompression via transmastoid approach was performed. During the 2-month follow-up, PFP had regressed to HB grade 3. The patient had recurrent attacks of facial nerve paralysis on the same side 1, 3, and 7 years after the surgery, and in every attack, the paralysis regressed to HB grade 3 after corticosteroid treatment.

In her last visit, HB grade 6 PFP on the right side, edema of both upper and lower lips, and furrowed tongue were noted at the same time. She noticed that lip edema is recurrent and simultaneous with her PFP.

No abnormality was found in audiological examinations or temporal magnetic resonance imaging (MRI). Internal medicine, dermatology, and immunology consultations resulted in no specific pathology. In the histopathological examination of upper lip biopsy, lymphocytic infiltration and submucosal edema were noted; the lymphocytic infiltration was predominantly seen in perivascular or perilymphatic regions. The pathologist reported it as chronic inflammation going on for a long time; however, non–necrotizing granulomatous inflammation consisting of Langhans-type giant cells and epitheloid histiocytes could not be found.

Based on these findings, she was diagnosed as having MRS 10 years after her first attack of PFP. Her PFP regressed to HB grade 3 after 3 weeks of corticosteroid treatment and physical therapy. Three months after the treatment, control purposed biopsy was taken, and significant regression of inflammation was noted on the histopathological investigation. During the follow-up, the symptoms had completely regressed at the sixth month, except grade 3 PFP, and none of the symptoms have recurred during the last 3 years.

3.2. Patient 2

A 32-year-old man was admitted to our outpatient clinic for swollen lip. On the physical examination, marked lower lip edema and fissured tongue were noted (Figs. 1 and 2.). The patient had a history of recurrent PFP during the last 16 years: in 1990 (right side), 1991 (right), 1993 (left side), 1994 (left), and 2002 (right). All of these attacks were simultaneous with perioral edema and diarrhea. His previous PFP attacks were diagnosed as Bell palsy by different physicians and regressed with medical treatment and physical rehabilitation. He had no PFP attacks for the last 5 years. However, he had progressive perioral edema with recurrent diarrhea and burning sensation in his right eye and ear for 6 months. The patient had a history of smoking 15 pack/years, and his family history was unremarkable. No abnormality was found in the laboratory tests, audiological examinations, chest x-ray, or temporal MRI.

He was consulted to a gastroenterologist for colonoscopy, and no finding was noted on histopathological examination of colonoscopic biopsy specimen. Uveal ectropion with patchy atrophy in his iris stroma was noted by the
ophthalmologist who also noticed that the patient was suffering from simultaneous visual loss during his previous PFP attacks.

He was diagnosed as having MRS, 16 years after his first attack of PFP. He underwent intralesional corticosteroid treatment. After topical anesthesia, 3 injection points were marked on the lips. Using a tuberculin syringe, 0.1 mL of triamcinolone (10 mg/mL) was injected into each site. Ice pack was applied periorally for 10 minutes. These injections were repeated once a week for 1 month. Marked regression of lip edema was noted 1 month after the last injection. During 1-year follow-up, PFP or perioral edema did not recur.

3.3. Patient 3

A 21-year-old male patient presented to our outpatient clinic with perioral edema. Physical examination revealed marked edema of the upper lip and fissured tongue. He had recurrent attacks of perioral swelling and occasionally had periorbital edema as an accompanying symptom since he was 12-year-old. Moreover, he has had hives, rhinitis, and conjunctivitis. He never had PFP, and his family history was noncontributory.

He was treated and followed up by different specialists in dermatology, immunology, and allergy. Sarcoidosis and some venereal and connective tissue diseases were ruled out for the differential diagnosis. The patient also had history of bloody diarrhea. Colonoscopy ruled out inflammatory bowel diseases. The histopathological examination of our upper lip biopsy revealed non caseified granulomatous morphology (Fig. 3): granulomatous cheilitis, which was well matched with our clinical findings. Control biopsy was not taken because of his fear of further facial deformity.

Intralesional corticosteroid injections were performed in the same fashion that was described for the second patient,
4. Discussion

Melkersson-Rosenthal syndrome is a rare disorder that is seen more commonly in Europe than America, yet it is unclear whether this is an artifact [2, 13, 14]. The etiology of MRS is still unknown, although genetic factors, infectious agents, allergic reactions to various foods and food additives, and autoimmune diseases have all been considered in the etiology of MRS [2-4, 10, 11, 15-17]. Several reports of familial occurrence have supported the theory of genetic origin [5, 18, 19].

The diagnosis of MRS is often difficult because the presence of the complete triad of symptoms is reported in 8% to 20% of patients [1, 4]. Patients may exhibit all components of the triad simultaneously or at different times. In a patient with persistent or recurrent orofacial edema, the presence of at least one of the findings of idiopathic facial paralysis or lingua plicata is sufficient to make definitive diagnosis of MRS [2, 4, 10, 11]. The most dominant manifestation of MRS is facial edema, which is acute, diffuse, painless, nonpitting, and mostly confined to the lips [1, 3, 4, 10, 15]. The upper lip is affected more frequently, and the edema tends to be recurrent and lasts from hours to several weeks [7, 20]. It usually mimics angioedema; however, it is more persistent than angioedema, and it does not respond to antihistamines and can lead to fibrosis of the involved tissues [21]. The classic triad of MRS was present in the first two of our patients; however, in the second patient, the first 5 attacks were with a complete triad, but the last attack was without facial paralysis. In all attacks, they have orofacial edema, which gradually recovered after treatment.

Facial paralysis associated with MRS may occur months to years before or after the onset of facial edema [20]. Relapses of PFP are frequent but eventually recover in most patients, as in our 2 patients. Peripheric facial paralysis may be unilateral or bilateral, and it may be partial or complete. Our patients presented complete paralysis in all PFP attacks. One of them had bilateral but not simultaneous PFP.

Lingua plicata has been accepted to be congenital in 30% to 80% of reported patients [21]. This anomaly is present in only 0.5% to 5% of the general population, and it is considered as a developmental malformation [1-4, 10-12, 15]. All of our patients had fissured tongue, but their family histories were noncontributory.

Temporal MRI revealed no pathological finding in our patients with recurrent PFP, and chest x-ray was normal in all patients. Although there is no specific radiological finding for MRS, chest x-ray and temporal and cranial computed tomography or MRI can be used to exclude other diseases.

The histopathological investigation of the swollen lip or facial tissues reveal the characteristic findings, including edema, noncaseating epithelial cell granulomas, multinucleated Langhans-type giant cells, perivascular mononuclear inflammatory infiltration, and fibrosis [7]. Because MRS is a clinical syndrome, histological evidence is not necessary [8, 9]. However, biopsy may help to diagnose MRS and to rule out Crohn disease and sarcoidosis [21], as it did in two of our patients.

Melkersson-Rosenthal syndrome is associated with some other findings, including trigeminal neuralgia, paresthesias, ocular palsies, blepharospasm, epiphora, keratitis, psychic episodios, and migraine [2, 6, 10, 11, 15]. In the differential diagnosis of MRS, Crohn disease, sarcoidosis, granulomatous blepharitis, cheilitis, contact dermatitis, facial trauma, and Bell palsy are considered [4, 11, 17, 22-24]. Two of our patients had severe diarrhea in all of their attacks. However, no pathological finding was found on colonoscopy, and biopsies from colon and oral mucosa lacked any ulceration or cobble stoning. The same patients also experienced burning sensation and discharge on their eyes. The consultant ophthalmologist noted uveal ectropion and patchy atrophy in iris stroma for our second patient and conjunctivitis for the third one. Sarcoidosis is not considered in any of our patients regarding the lack of pulmonary symptoms, normal x-rays, and nondiagnostic consultation notes.

The modality of treatment in MRS is another issue of controversy. Facial edema may temporarily be regressed by systemic and intralesional corticosteroids. Antihistamines, antibiotics, salazosulfapyridine, and irradiation have been reported to be not useful for facial edema [25, 26]. Initial choice of treatment in facial nerve paralysis should be medical treatment [1, 2, 6, 10, 11]. However, decompression of facial nerve throughout its bony canal may be indicated for patients with recurrent or persistent attacks of facial paralysis despite medical treatment [27]. Furthermore, in severe cosmetic complaints associated with persistent excess tissue or the appearance of upper lip, reconstructive surgery can be the treatment of choice [20]. Corticosteroid therapy was the initial treatment for our patients. In addition, facial decompression was performed for our first patient, and intralesional steroid injection was applied into the edematous lips of the last 2 patients. Respecting the patients’ data and the literature on the subject, we got the impact that MRS patients are not appropriate candidates for facial decompression. Hence, we consider that corticosteroid therapy, either systemic or intralesional, might be the current and noninvasive treatment of choice for MRS.

In the daily practice of an otolaryngologist, it is not usual to diagnose a patient as having MRS. Although 2 of our patients have had the symptoms since adolescence and they have been treated by different physicians, they could be diagnosed as having MRS 9 and 16 years after the onset of symptoms. Much more interpretation of the outcome from such a small number of patients would not be expressive, but we consider that this is partly because of misdiagnosis. We recommend that when a patient with recurrent facial paralysis is encountered, he/she should be examined and
questioned for recurrent or persistent orofacial edema. Also, the reverse should be considered for a patient with recurrent orofacial edema. Lingua plicata should be searched in both situations. Then, when MRS is diagnosed, we recommend consultations to dermatology, immunology, gastroenterology, and ophthalmology to rule out other diseases with similar symptoms and to figure out accompanying problems. Lastly, these patients should be followed up regularly because of the chronic progressive course of MRS.

We searched MRS in PubMed and found 140 articles published between 1997 and 2007. However, only 7 (5%) of them were published in otolaryngology journals. We therefore believe that this study will supply an additional aspect to otolaryngologists, in the scope of recurrent facial paralysis and orofacial edema.

References