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Case Report

The Importance of the Dental Factor in the Pathogenesis of Melkersson-Rosenthal Syndrome

Przemyslaw Kustra*

Department of Conservative Dentistry with Endodontics, Jagiellonian University of Medical College, Poland

***Corresponding Author:** Przemyslaw Kustra, Department of Conservative Dentistry with Endodontics, Jagiellonian University of Medical College, Poland.

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Abstract

Melkersson-Rosenthal syndrome is a clinical entity characterized by swelling of facial soft tissues, while the histological picture shows granulomatous infiltration. The patient, aged 23, presented to the dental office referred by a dermatologist with a diagnosis Oedema labii inferioris ad dextram for consultation and potential treatment. Unsuccessful dermatologic treatment for 1 month, discontinued due to increased gastrointestinal side effects, and the progression of recurrent edema into a persistent form caused the patient to be referred for re-examination for foci of infection in the oral cavity. Based on the clinical and histological picture, the diagnosis of incomplete presentation of Melkersson-Rosenthal syndrome was made. The following treatment plan was established: endodontic retreatment of teeth 15 and 46, replacement of amalgam fillings with composite fillings, treatment of carious lesions, and restoration of missing teeth in the upper arch. Since the successful revision of a root canal treatment of tooth 46, no swelling of the lower lip has been observed. With more than a year of follow-up of the patient, it can be concluded that the etiologic factor of Melkersson-Rosenthal syndrome was a dentoalveolar infection focus.

Keywords: Dental; Pathogenesis; Melkersson-Rosenthal Syndrome

Introduction

The term *orofacial granulomatosis* is applied to a group of clinical entities with a common feature of chronic swelling of the soft tissues of the face and oral cavity, as well as granulomatous infiltration in the histological picture [1]. These include Melkersson-Rosenthal syndrome (MRS) in addition to sarcoidosis, Crohn's disease, and Miescher's granulomatous cheilitis [2,3].

The typical form of MRS includes a triad of symptoms: swelling of the lips, sometimes recurrent and often unilateral facial nerve palsy, and fissured tongue or *lingua scrotalis* [4]. The development of MRS-type lesions occurs in people of different ages, usually in early childhood or adolescence, with 50% of cases affecting people around the age of 20, especially women [5,6]. Cases of familial occurrence of the condition have also been described [7,8]. Many times the syndrome is monosymptomatic or incomplete, involving one or two of the three classic symptoms [5].

The most common symptom is swelling of the lip or both lips, considered by some authors an oligosymptomatic presentation of the syndrome [9,10]. According to Klauss and Brunsting, as well as Knychalska-Karwan, MRS can involve recurrent swelling not only of the lips, but also affecting the mucosa of the cheeks, palate, uvula and peritonsillar area [11,12]. Secondary leukoplakia sometimes develops on top of these proliferative oral lesions. Pisanty and Sharaw [13], as well as Hornstein [14] described the occurrence of gingival lesions, which was confirmed by Worsaae and Pindborg on 30 cases of patients with MRS [15], as well as by Knychalska-Karwan [12]. Edematous lesions can also occur around the eyes and eyelids, nose, forehead, parotid glands, and sometimes even in the anal area [16,17]. The swellings appear suddenly, with no apparent cause, and subside after a longer or shorter period of time. Swelling of both lips, or one, more often the upper lip, is a consistent symptom of Melkersson-Rosenthal syndrome. It often precedes facial nerve palsy - total or partial [18,19]. It occurs most often unilaterally and, according to some authors, in 40-50% of cases [19], while others describe nerve VII palsy in 90% of MRS patients studied [20].

Fissured tongue is not among the permanent symptoms and occurs in 20-40% of cases. Occasionally, patients with Melkersson-Rosenthal syndrome have impaired taste (*ageusia*), inadequate saliva secretion (*hyposialgia*) or complete lack of saliva secretion (*asialgia*) [19].

The clinical picture of MRS is sometimes accompanied by symptoms affecting other organs as well. These can include symptoms of damage to cranial and autonomic nerves, neuro-vegetative centers in the brainstem, migraine headaches, sensory disturbances in the peripheral parts of the upper and lower extremities, and psychiatric disorders. In addition, it has been found that MRS can coexist with premenstrual syndrome, Crohn's disease, peptic ulcer disease, as well as dysphagia and epilepsy [21,22].

MRS histological features include perivascular infiltration of lymphocytes, histiocytes, and plasma cells, as well as granulation tissue composed of epithelioid and giant cells without features of necrosis. Early lesions show swelling of the connective tissue lining, while chronic lesions demonstrate connective tissue fibrosis and proliferation [4,5].

The pathogenesis of Melkersson-Rosenthal syndrome is not precisely explained, and is likely to be polyetiological in nature. The involvement of genetic, infectious, allergic, and immunological factors, as well as anatomical and functional abnormalities in the autonomic system have been suggested. Difficulties in determining the causes of the development of MRS are probably due to the low incidence of cases of the fully symptomatic, classic clinical picture. The presence of a sparse number of symptoms, sometimes with a non-specific histological picture, creates significant diagnostic, therapeutic and prognostic difficulties.

Treatment of patients with Melkersson-Rosenthal syndrome is difficult due to an etiology that has not yet been clarified. Often it is only symptomatic and requires multidisciplinary treatment. Reports in the literature emphasize the important role of eliminating sources of infection in the oral cavity, as well as the use of antibiotic and anti-allergic treatment [12]. Some authors also suggest taking antirheumatic drugs, antimycobacterial drugs, corticoids and ACTH, or even insulin therapy.

In the past, local treatment consisted of X-irradiation, injections of corticosteroids (triamcinolone), while in chronic cases, where lip swelling persisted, surgical treatment (mucosal excision) and cryotherapy were used.

B. Urbaniak presents a treatment regimen for patients in an article on the long-term results of Melkersson-Rosenthal syndrome therapy [19]. This therapy includes both symptomatic and cause-specific interventions. In accordance with these guidelines, patients with MRS were initially subjected to the oral sanitization with elimination of foci of infection, together with antimicrobial prophylaxis. Additionally, topical protective preparations were applied in the form of ointments, and physical therapy (Kromayer quartz lamp irradiation, hydrocortisone and vitamin C iontophoresis) was introduced. Close cooperation with an internist, ENT specialist, neurologist and rheumatologist was provided. Systemic treatment was started with the administration of vitamin preparations to replenish their deficiencies, raise general immunity and improve metabolism. Anti-inflammatory, anti-edema and antihistamine drugs were also administered. In the absence of treatment effects, stronger anti-inflammatory, immunosuppressive and anti-allergic drugs (steroids) were used, while betamethasone (Bedifos, 3.5-5 mg) was injected locally. Some patients were given tranquilizers. Using the treatment regimen described above, significant improvement was achieved, with 66.7% of patients experiencing complete resolution of symptoms.

Case Presentation

The female patient A. Z., aged 23, presented to the office in October 2004, referred by a dermatologist with a diagnosis *Oedema labii inferioris ad dextram* for consultation and potential treatment. The first symptoms of the disease, in the form of periodic swelling of the lower lip, were observed by the patient in May 2004. Swelling of the lip was greatest in the morning, decreasing slightly throughout the day. Apart from this, the patient reported no complaints from other organs.

Due to recurrent swelling of the lower lip, initially diagnosed as Quincke's edema, the patient was treated by a dermatologist with antihistamines, corticosteroids and an elimination diet, excluding salicylates and benzoates from food.

The results of the laboratory tests performed (ESR, blood count, absolute eosinophilia, transaminases, bilirubin, blood glucose level, ASO, CRP protein, Waaler-Rose test, C3 and C4 complement component levels, urinalysis) were within normal limits. No parasites were found in the feces. Bacteriological examination of throat swab was negative. No pathological changes were found in the gynecological or neurological examination, and the allergic history was negative. A previous dental consultation revealed a tooth with a necrotic pulp (24), with no periapical lesion visible on x-ray.

Unsuccessful dermatologic treatment for 1 month, discontinued due to increased gastrointestinal side effects, and the progression of recurrent edema into a persistent form caused the patient to be referred for re-examination for foci of infection in the oral cavity.

An extraoral examination revealed swelling of the lower lip vermilion on the right side (Figure 1). The enlarged lip was soft, with cushion-like cohesiveness, non-painful, and free of inflammatory changes.

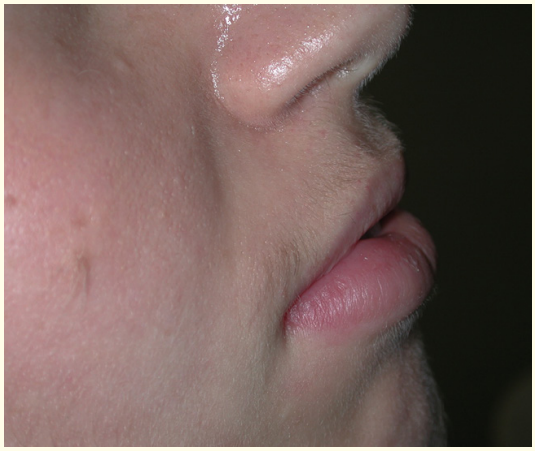

Figure 1: An extraoral examination revealed swelling of the lower lip vermilion on the right side.

Intraoral examination revealed

- Fissured tongue (Figure 2).
- Missing teeth in the upper arch.
- Low attachment of the upper lip frenulum.
- A fresh post-extraction wound in the area of tooth 24.
- Tooth 48 tilted mesially, forming a deep bony pocket.
- Multiple amalgam restorations.
- Carious lesions.
- Crowding in the lower arch (Figure 3).

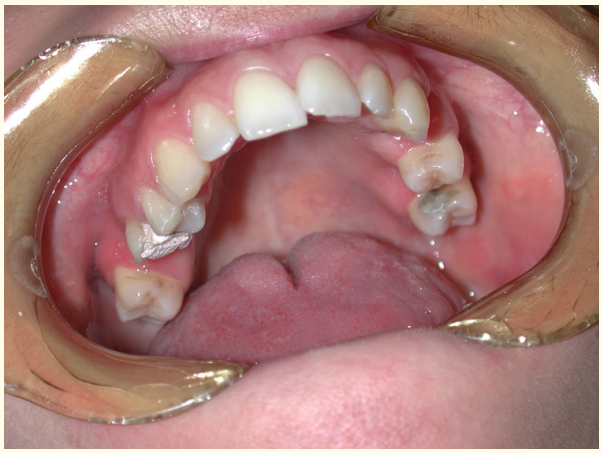

Figure 2

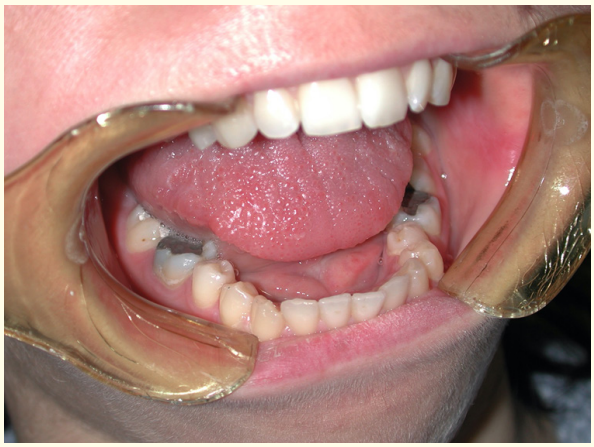

Figure 3: Fissured tongue.

The panoramic x-ray (Figure 4) and adherent, small radiograph (Figure 5 and 6) revealed:

- **Tooth 15:** Endodontically treated, incomplete obturation of the root canal.
- **Tooth 46:** Endodontically treated, incomplete obturation of the distal and mesial root canals.
- **Tooth 48:** Dens invaginatus, tooth tilted mesially, with a deep bony pocket.
- Dentinomas in teeth 17, 27, 37.

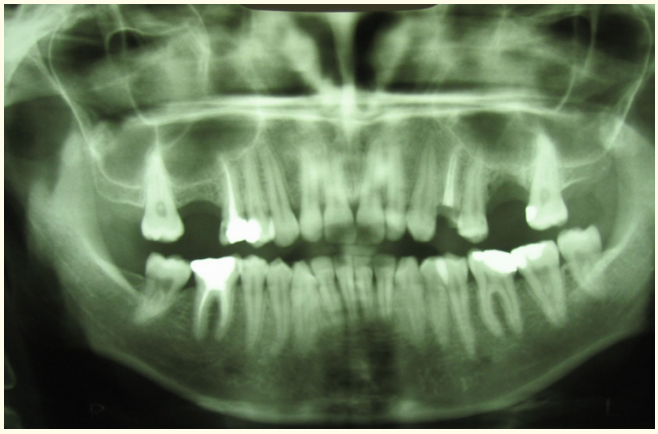

Figure 4: Panoramic x-ray.

- Tooth 15 endodontically treated in the past (incomplete obturation of the root canal)
- Tooth 46 endodontically treated in the past (incomplete obturation of the distal and mesial root canals)
- Tooth 48: dens invaginatus, tooth tilted towards the front, forming a deep bony pocket on the mesial side

dentinomas in teeth 17, 27, 37; dentinoma in tooth 37 presenting an atypical, low position within the root part of tooth chamber.

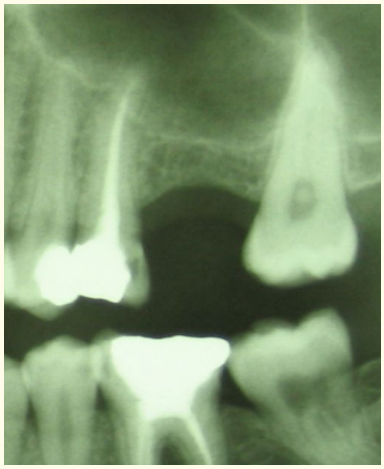

Figure 5: The x-ray demonstrates.

- Visible dentinoma in tooth chamber of tooth 17
- Dens invaginatus, tooth 48
- Incomplete obturation of the root canals of tooth 46.

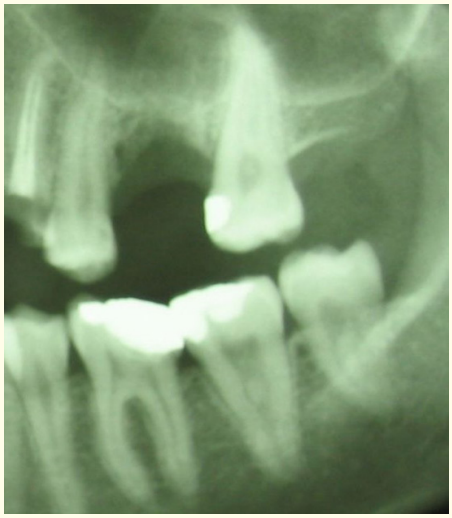

Figure 6

- Visible dentinoma in tooth chamber of tooth 27
- Denitnoma in the root canals of tooth 37.

In addition, periapical x-rays of teeth 15 and 46 were taken, and an ETO test (skin test to detect active foci of infection) was performed. A positive (+) ETO test result was obtained in the area of tooth 24 (fresh post-extraction wound) and in the area of teeth 46, 47 (tooth 46 - after previous root canal treatment). The vitality test of tooth 47 with ethyl chloride yielded an inconclusive result (+/-), but the dentin drilling test indicated that this tooth was vital (Figure 6).

Moreover, a biopsy of the lip was taken for histopathological examination. The histological picture revealed the presence of edematous connective tissue lining, dilated thin-walled blood vessels and sparse perivascular inflammatory infiltrates composed of lymphocytes, histiocytes and plasma cells, in addition to single foci with epithelial multinucleated giant cells.

Based on the clinical and histological picture, the diagnosis of incomplete presentation of Melkersson-Rosenthal syndrome was made.

The following treatment plan was established

- Endodontic retreatment of teeth 15 and 46.
- Replacement of amalgam fillings with composite fillings.
- Treatment of carious lesions.
- Restoration of missing teeth in the upper arch.

Therapy began with the revision of root canal treatment of teeth 15 and 46. The incompletely obturated root canals were negotiated, chemically and mechanically prepared, and then obturated using the lateral gutta-percha condensation method, with AH-Plus as a sealant (Figure 7,8). During the endodontic treatment of tooth 46, after the negotiation of root canals, a significantly increased swelling of the lower lip developed on the right side, and persisted until the day the treatment was completed (Figure 9). Carious lesions were also prepared and restored with composite materials, and existing amalgam fillings were replaced with composite restorations.

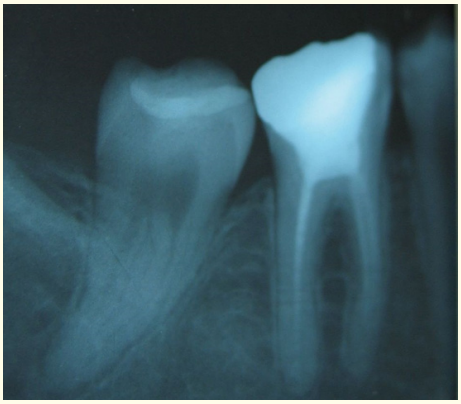

Figure 7: X-ray picture of tooth 46 before endodontic retreatment.

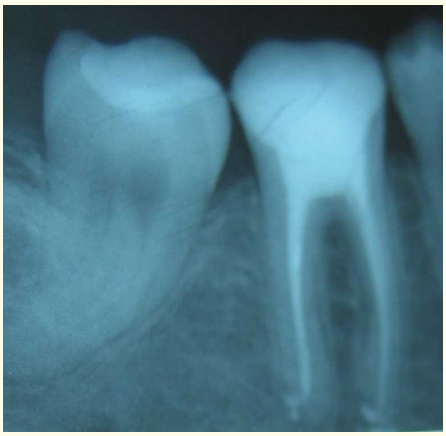

Figure 8: X-ray picture of tooth 46 after endodontic retreatment.

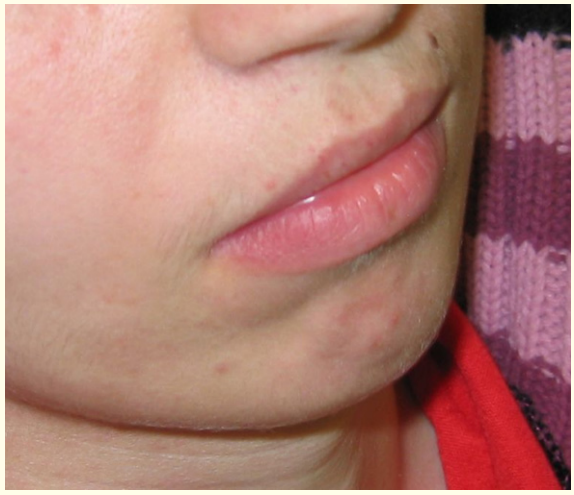

Figure 9: After the root canals of tooth 46 were negotiated, a significant swelling of the lower lip developed on the right side, lasting longer than usual. There has been no swelling of the lip within a year from the day of root canal obturation of tooth 46.

The dental treatment was completed with an upper partial denture to restore the missing teeth, which is planned to be replaced with fixed prosthetic restorations in the future (Figure 10). After the completion of dental treatment, the ETO test was performed again. The test result was negative, confirming the absence of active foci of infection in the oral cavity. Since the successful revision of a root canal treatment of tooth 46, no swelling of the lower lip has been observed.

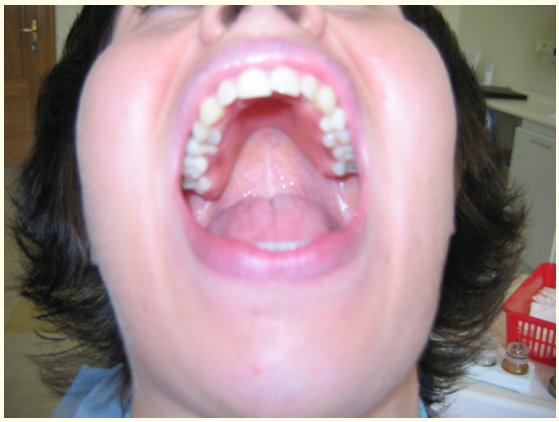

Figure 10: Picture taken one year after completion of treatment, with a removable partial upper denture, revealing also the outline of the upper and lower lip.

With more than a year of follow-up of the patient, it can be concluded that the etiologic factor of Melkersson-Rosenthal syndrome was a dentoalveolar infection focus.

Discussion

Melkersson described in 1928 a case of recurrent swelling of the lips presenting together with facial nerve palsy on the same side of the face. Three years later, in 1931, Rosenthal included fissured tongue as part of this syndrome. Lüscher distinguished a separate disease entity characterized by these symptoms and called it Melkersson-Rosenthal syndrome. In 50% of cases, it affects people around the age of 20, occurs regardless of race and gender, and its etiology is not well understood. The full-blown syndrome is rarely observed, oligosymptomatic forms with one or two characteristic symptoms are more common.

A consistent symptom of Melkersson-Rosenthal syndrome is a soft, painless swelling of the lip, usually upper, less often lower lip. The clinical picture of full-blown Melkersson-Rosenthal syndrome includes: cheilitis granulomatosa, paralysis nervi facialis: 40-50% of the cases; lingua plicata: 20-40% of the cases. Its etiology is not conclusively understood. The background is hereditary, there are abnormalities in the vascular system (such as changes in vascular wall permeability, vasomotor abnormalities), there are also causative relationships of the syndrome to changes in the nervous system, and infectious and allergic factors can be present too. Treatment includes multidisciplinary approach: dermatological, ENT, dental, neurological, and surgical. Treatment is basically symptomatic and relatively ineffective, including anti-allergic and anti-inflammatory drugs (antibiotics, corticosteroids), elimination of dental inflammatory agents, as well as surgical interventions.

Conclusion

The one-year observation allows us to conclude that the etiological factor of Merkelsson-Rosenthal syndrome was an infectious agent, originating from the root canals of tooth 46, since after the obturation of the root canals of this tooth, the clinical symptoms in the form of swelling of the lower lip regressed.

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