

Review Article

Lower Lip Oedema - Melkersson-Rosenthal Syndrome or Cheilitis Granulomatosa

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Abstract

In the intervening years 1928 and 1931 Curt Rosenthal and Ernt Melkersson described a lot of patients with triad of symptoms: recurring facial paralysis, swelling of the face and lips and scrotal tongue. Currently this relatively rare triad of symptoms has termed Melkersson-Rosenthal syndrome (MRS). In 1945 Miescher described a few cases of primary interstitial inflammation of the lips and gave them the name granulomatous macrocheilitis (GM). A lot of his patients additionally had facial nerve paralysis, and/or swelling of the face and issued tongue. At present it is very difficult to differentiate the Melkersson-Rosenthal Syndrome and granulomatous macrocheilitis. In the case report we present the study of persistent lower lip swelling with its diagnostics and we propose a therapeutic method – trimacynolone injection together with metronidazole.

Keywords: Melkersson-rosenthal syndrome; Granulomatous macrocheilitis; Oedema; Lip

Introduction

Melkersson-Rosenthal Syndrome is a disorder defined as a triad of symptoms: permanent or recurrent inflammation with swelling of lips or face, recurrent paralysis of one or both sides of the facial nerve and occurrence of fissured tongue (development of folds and furrows in the tongue – latin *lingua plicata*). In contrast, cheilitis granulomatosa (Miescher's granulomatous macrocheilitis) contains only one component from the whole triad. It is isolated recurrent swelling of the lips or lip. Cheilitis granulomatosa can be part of the Melkersson-Rosenthal Syndrome or could be a separate disease entity. The onset of MRS and GM can occur at any age, however, in most cases patients are in their second or third decade of life.

Case Presentation

A 30-year-old male patient presented with persistent, painful lower lip oedema since two years (Figure 1). There was no history of applied irritants, local trauma or atopy. The patient also suffered from seasonal hay fever. Family history was without an additional burden. He stated that he had been hospitalized 3 times for this reason and he was treated with ciprofloxacin, clindamycin, hydrocortisone, prednisone, clemastine, feksofenadine orally in different schemes. He was also on a diet free from cinnamon and benzoate. On physical examination, he presented symmetrical swelling and redness of the lower lip. Painful

fissure in the middle of the lip and mucous membrane of the lower lip. Mouth, nose and throat presented with no changes. Neither facial nerve palsy nor fissured tongue or lymph node involvement was present. Cardiopulmonary, neurological, musculoskeletal, and abdominal examinations were otherwise normal. The results of laboratory blood tests were without major changes. WBC 9.91 K/ μ L, RBC 4.68 M/ μ L, HGB 14.6 g/Dl, HCT 41.5%, PLT 236 K/ μ L, OB 2 mm/h, CRP <0.4 mg/dl, Fe 61 μ g/dl, IgA 301 mg/dl, IgE 27IU/ml, ATG >500 U/ml, Wit. B12 367 pg/ml, folic acid 8,87 ng/ml, ACE 24 U/L. The lip biopsy showed: glandular tissue and connective tissue with minor inflammatory infiltrates, oedema and single amyloid-like masses. The treatment choice was Triamcynolone (Kenalog) 40 mg/ml - injection of 1ml in lower lip. Injections took place once a week for five weeks. In addition, the patient took metronidazole 2 mg x 500 mg every day for two months [1].

Discussion

Only 25% of patients worldwide present Melkersson-Rosenthal syndrome with the complete triad of symptoms [2]. In 18% to 70% of cases the disease is manifested by the presence of only one symptom from the entire triad [3]. The most common symptom is facial oedema, including swelling of the upper or lower lip or both at the same time. It occurs in 75% to 100% of cases [2,4,5]. This symptom can be classified as a separate disease entity – cheilitis granulomatosa. Thickened, wrinkled, sometimes hard overgrown tongue with features

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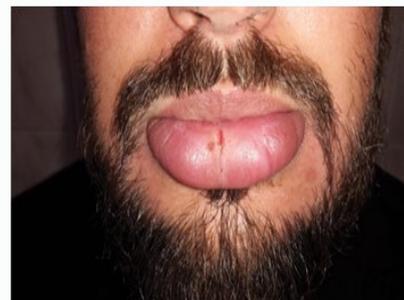


Figure 1: Patient before treatment.

of degeneration is the least typical symptom of CG [6]. The third symptom of the triad is facial nerve paralysis. Other cranial nerves may also be involved. Granulomatous cheilitis clinically presents with lip swelling that may initially be episodic, but often prolongs and persists long term. Over time, the lip swelling may become permanent. The swelling of the lips is painless and is not preceded with any prodromal symptoms. They can crack, causing pain. Lip biopsy in the early period reveals unspecific changes like swelling of connective tissue stroma, scarce perivascular lymphocytic infiltrates. With the duration of the disease, fibrous growth of connective tissue is noticed, with dense and pleomorphic infiltration of inflammatory cells, non-caseated granulomas composed of epithelial cells and giant Langerhans type cells, clusters of lymphocytes, plasma cells and histiocytes around the vessels. Regarding histopathological changes, according to Zimmer in a study of 42 MRS patients, only 46% (19/42) had granulomatous changes; 36% (15/42) had nonspecific inflammation, 11% (5/42) had incidental findings, and 7% (3/42) showed no histopathologic abnormalities [4]. At present, neither the etiopathogenesis nor the cause of both of syndromes has been clearly explained. A multifactorial origin of the disease is assumed with a significant contribution of infectious and proinflammatory factors, allergic factors, genetic predispositions and immunological defects. The discoverers of the Melkersson-Rosenthal syndrome present the vascular nerve dysfunction as a cause of vascular unblocking and tissue swelling. Dysregulation of the vegetative system and disorders in the lymphatic system should also be considered. In the literature, we can find that allergy tests showed a high index of sensitivity to cinnamon and benzoates in patients with orofacial granulomatosis [7]. In our case, a diet free of cinnamon and benzoate did not bring any results. The patient was treated with the Triamcinolone and Metronidazole treatment regimen as described above. The results of treatment were satisfactory - we achieved reduction of lip swelling, and complete healing of the fissure. One year follow-up was without recurrence (Figure 2). Triamcynolone is a synthetic glucocorticosteroid with anti-inflammatory, anti-swelling, anti-viscous, antipruritic and anti-allergic properties. It reduces the accumulation of leukocytes and their adhesion to the endothelium, inhibits the phagocytosis and the breakdown of lysosomes, reduces the number of lymphocytes, eosinophils, monocytes, blocks IgE-dependent secretion of histamine and leukotrienes. It inhibits the synthesis and release of cytokines: interferon γ , interleukins: IL-1, IL-2, IL-3, IL-6, TNF- α , GM-CSF. By inhibiting the activity of phospholipase A2 through lipocortin, it prevents the release of arachidonic acid and, consequently, the synthesis of inflammation mediators. Metronidazole is a chemotherapeutic agent from the group of nitroimidazole derivatives. It shows protocidal and bactericidal action against anaerobic microorganisms. The mechanism of action consists in blocking DNA biosynthesis after transformation of the drug into the active form in the anaerobic bacteria cell and protozoan; drug transformation occurs through its reduction to acetamide and N- (2-hydroxyethyl) -subalic acid. Antimicrobial and antiprotozoal spectrum: anaerobic bacilli from the group of *Bacteroides fragilis* and other, anaerobic Gram-positive (*Clostridium difficile*, *Clostridium perfringens*), anaerobic gram-positive cocci (*Peptococcus* spp., *Peptostreptococcus* spp.) and Gram-negative (*Veillonella* spp.), *Gardnerella vaginalis*, *Trichomonas vaginalis*, *Entamoeba histolytica*, and *Giardia lamblia*. The drug undergoes transformation in the liver by oxidation and conjugation with glucuronic acid. The main metabolite, 2-hydroxymetronidazole, also has antibacterial and antiprotozoal activity. The drug penetrates well into most tissues and organs.

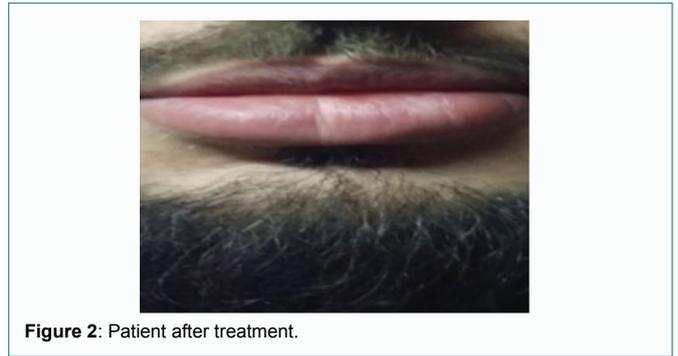


Figure 2: Patient after treatment.

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