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Case Report

A monosymptomatic Melkersson-Rosenthal Syndrome in an 8 years old boy

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Abstract. Melkersson-Rosenthal Syndrome (MRS) is a systemic neuro-mucocutaneous granulomatous disease, characterized in its classical form by a triad of recurrent facial nerve paralysis, swelling of the lips and lingua plicata. However, this classical triad is rarely present, while the monosymptomatic or oligosymptomatic forms are more frequent. The presence of two or one of the manifestations mentioned above, with granulomatous cheilitis in the biopsy, is sufficient to make the diagnosis of monosymptomatic or oligosymptomatic form of MRS. This syndrome is very rare in childhood, instead, it is more frequent in young adults between the second and third decades of life. We present the case of an 8 years old boy who was brought to us because of a non painful swelling of the upper lip, associated with gingival hypertrophy, that had persisted for more than two months. Given the negative results of the hemato-chemical and instrumental assessments, we performed an upper lip biopsy whose histological study showed granulomatous cheilitis. We diagnosed this case as a monosymptomatic MRS and administered an intralesional steroid therapy using triamcinolone, with complete recovery. (www.actabiomedica.it)

Key words: Melkersson-Rosenthal Syndrome, granulomatous cheilitis, triamcinolone

Introduction

Melkersson syndrome was described in 1928 as peripheral facial palsy and swelling of the lips. Rosenthal, in 1930, included the presence of a fissured tongue, completing the triad which defines the syndrome. Its classical form is characterized by a triad of recurrent paralysis of the facial nerve, swelling of one or both lips, and lingua plicata (also defined as "scrotal tongue" or "fissured tongue") (1). This syndrome is very rare in childhood, instead, it is more frequent in young adults between the second and the third decades of life (2). In literature, just about 30 cases have been described in pediatric age (1). The classical triad is not common (18-70% of cases), instead, the oligosymptomatic or monosymptomatic forms, with an incomplete expression of the symptoms cited above, are more frequent (1-6). The presence of two or one of the manifestations mentioned above, with granulomatous cheilitis in the biopsy, is sufficient to make the diagnosis of oligosymptomatic or monosymptomatic form of MRS (2, 4, 6, 7).

Case Report

We present the case of an 8 years old boy who was brought to us because of a non painful swelling of the upper lip, associated with gingival hypertrophy, that had persisted for more than two months. His pediatrician had administered oral antibiotics to him (Amoxicillina + Clavulanic acid) for 8 days. This the-

rapy had later on been substituted by oral Rifampicin associated with intramuscular Ceftriaxone for 5 days, without improvement of the symptoms. It emerged that this boy had been admitted to our day service a few weeks before and that on that occasion oral antihistamines and steroids had been administered for a few days without any particular benefits. At anamnesis, no allergic diseases, trauma, or past injuries were found. We were told that until a month before, the symptoms showed a recurrent-remittent pattern. Physical examination showed a non painful, swollen and erythematous upper lip, gingival hypertrophy of the upper arch with no signs of bleeding, moderate latero-cervical and lower mandibular lymphadenomegaly. The other physical signs were within the normal range for his age.

We then decided to admit the boy in the Infectious Diseases Ward of our department. During his hospitalization we carried out some laboratory tests such as: hemogram, erythrocyte sedimentation rate, coagulogram, complement components (C3, C4, C1 inhibitor), TORCH, antibodies against streptococcus, Epstein-Barr virus and Borrelia, antinuclear antibodies, immune complexes, protein electrophoresis and rheumatoid factor. Furthermore, we carried out other investigations such as prick tests for food and inhalants, echography of the upper lip and radiography of the thorax. All these tests resulted in the normal ranges and were of poor diagnostic significance. Together with our colleagues of the department of Maxillofacial surgery, we decided to perform a biopsy of the upper lip mucosa whose anatomopathologic study revealed intense inflammatory infiltration of the chorion showing dissemination of numerous non necrotic granulomas with giant Langhans' cells.

Given the anamnesis, the clinical evidence, the anatomopathologic study and the negative laboratory tests, we diagnosed this case as a monosymptomatic MRS.

We administered a steroid therapy, infiltrating triamcinolone into the swelling (10 mg/ml as first dose and 40 mg/ml as second dose one week later), with complete recovery of the symptoms. After one month from the end of this therapy, the child appeared in good clinical condition without any signs of the disease.

Discussion

Melkersson-Rosenthal Syndrome (MRS) is a systemic neuro-mucocutaneous granulomatous disease, characterized in its classical form by a triad of recurrent facial nerve paralysis, swelling of the lips and lingua plicata. The presence of non necrotic granulomas at the orofacial region explain why MRS is placed in the same group of granulomatous diseases such as sarcoidosis and Crohn's disease (2, 6).

Generally, the first and most common manifestation of MRS (75% of the cases) is a non painful swelling of the upper lip, with increase in consistency and without pruritus. The lower lip is less frequently involved (6, 7). The first episode of labial edema often resolves within a period of a few hours or a few days, raising the problem of differential diagnosis with angioedema. Subsequent episodes of edema appear at more irregular intervals and may become persistent (2, 6). The interested lip may present fissures in the central part (central cheilitis), at the corners of the mouth (angular cheilitis/ angular stomatitis) or in other sites (7).

Other than the lips, the disease can involve the oral cavity, upper airways, gums, tongue, palate, pharynx and larynx, and these may present erythema, erosions, ulcerations or small pustules (6, 8, 9). The buccal mucosa may swell, folding itself to give a "cobblestone" aspect (8). Some authors affirm that these manifestations precede those at the orofacial region by many weeks (8, 9).

The second sign of the triad characterizing MRS is represented by facial nerve paralysis (30-35% of cases) (10). Although this paralysis is initially intermittent, it may later on become permanent. It may be unilateral, bilateral, partial or complete. This paralysis is due to granulomatous infiltration of the nerve and its sheath or to its compression by tissue edema as the nerve passes through the facial canal within the temporal bone (7, 8).

The third sign of MRS is the presence of a fissured tongue or "lingua plicata". It is observed in 20-70% of adult cases (2, 6), whereas in pediatric age this symptom is present in only 30% of the cases (2). It can be associated with a burning sensation and dysgeusia (it affects 2/3 of the anterior part of the tongue). Resolution is spontaneous in about 10% of the cases (2,

7). However, lingua plicata has been described as a common anomaly in the general population, making it less significant in the diagnosis of MRS (6).

Among the secondary symptoms of MRS (present in more than 80% of the cases), those deriving from the involvement of other cranial nerves (olfactorius, vestibulocochlearis, glossopharyngeus, hypoglossus and trigeminus) are more frequently found, and include neuralgia, tinnitus, vertigo, sudden deafness, hyperacusis, anosmia, hyperesthesia and paresthesia (6, 10). Other minor symptoms can be of neurovegetative origin such as abnormal lacrimation, profused sweating, hemicrania, hyper- or hyposalivation, blepharospasm, nausea, vomiting, facial tics, tetanic spasm, and paresthesia at the extremes of the limbs (7, 10).

The etiology of MRS remains today unknown. Some authors have suggested a genetic predisposition (dominant autosomal transmission), others have associated the syndrome with an allergic reaction to cobalt or to some food additives such as monosodium glutamate or with lymphogranulomatosis, paradental infections, tonsillitis, adenoid hypertrophy, Herpes simplex virus infections and other bacterial or viral infections. However, there is no scientific evidence that the origin of this disease could be of infective, allergic or hereditary nature (2). At present it is believed that many factors join up to determine a change in the neurovegetative activity at the diencephalic level with consequent edema at the orofacial region (10).

The clinical and histological aspects of granulomatous cheilitis observed in MRS are not significantly different from those of patients who present oral cavity localization of diseases such as sarcoidosis and Crohn's disease. Some authors affirm that patients with granulomatous cheilitis are more predisposed to develop Crohn's disease (11). The relationship between these diseases has not been definitely clarified, so it is advisable to perform invasive diagnostic techniques (radiography and/or endoscopy) only in those patients who show respiratory or gastro-enteric manifestations associated with oral lesions (6).

As long as the etiology of MRS is unknown, treatment of granulomatous cheilitis remains symptomatic. A great number of therapeutic schemes employ topical, intralesional, or systemic steroids (1-3, 5-9), with symptom regression in 50-80% and recurrence in 60-75% of the cases (1). Patients with a moderate form of granulomatous cheilitis show more benefit from the administration of topical triamcinolone acetonide or clobetasol. In patients with more pronounced cheilitis, up to 1 mL of triamcinolone acetonide (from 10 mg/mL to 40 mg/mL) is injected in both sides of the affected lip. Anaesthesia at the level of the mental nerve can increase the patient's compliance. The duration of treatment has not been standardized; some authors suggest an intralesional injection of triamcinolone every two weeks, then once a week when the clinical response becomes stable, others prefer intralesional injection once a month for a period of three months (6, 9).

Surgery (cheiloplasty) is reserved for patients whose cheilitis does not respond to steroid therapy or who present a reasonable face deformation. In order to prevent recurrence of the disease, intralesional injections of triamcinolone 0,1% (at first every two weeks and later every month) are necessary for a period of 2 to 6 months after the operation (6, 12).

Due to the side effects, a long term systemic steroid therapy (prednisolone 1-1,5 mg/kg/day) is advisable only in patients with important granulomatous infiltrations (2, 6).

Other therapeutic schemes include: clofazimine, metronidazole, penicillin, erythromycin, sulfasalazine, dapsone, ketotifene and hydroxichloroquine sulphate (13).

Conclusions

MRS should be taken into consideration in every patient with recurrent or persistent swelling of the upper lip. To make the diagnosis, a biopsy of the swelling showing granulomatous cheilitis is of fundamental importance. Therapy is only symptomatic and recurrences are frequent. Given it's relationship with sarcoidosis and Crohn's disease, it is very important to make a careful anamnesis in order to differentiate between these diseases.

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