CASE REPORT
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Facial Palsy in a Child with a History of Cheilitis Granulomatosa: Melkersson–Rosenthal Syndrome

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ABSTRACT

Melkersson–Rosenthal syndrome is a rare neuromucocutaneous granulomatous syndrome of unknown etiology characterized by a classical triad of relapsing orofacial edema, recurrent peripheral facial palsy, and lingua plicata. However, the classical triad is seen in only a minority of the cases. The majority of patients present with mono- or oligosymptomatic forms of the disease. Childhood onset of Melkersson–Rosenthal syndrome is extremely rare, and only a few cases have been described in the literature. This paper reports the case of an 8-year-old girl with cheilitis granulomatosa. Two years after the initial presentation, she presented with a unilateral peripheral facial palsy and a diagnosis of Melkersson–Rosenthal syndrome was established. The aim of this paper is to raise awareness among otolaryngologists of this condition in children presenting with orofacial swelling and/or peripheral facial palsy. Since symptoms do not always occur simultaneously, diagnosis often requires repeated follow-ups. Early recognition and a multidisciplinary approach to this condition are crucial to minimize recurrences and prevent orofacial dysfunction and its associated implications for the child's psychosocial well-being.

Keywords: Melkersson–Rosenthal syndrome, cheilitis granulomatosa, facial palsy, lingua plicata, child

Introduction

Melkersson–Rosenthal syndrome (MRS) is a rare neuromucocutaneus granulomatous syndrome characterized by a classic triad of relapsing orofacial edema, recurrent peripheral facial palsy, and lingua plicata.[1-5] However, this unknown syndrome is often diagnosed late, as only a third of affected individuals exhibit this triad.[1,4] Cheilitis granulomatosa (CG), the recurrent edema of 1 or both lips, is considered the most common monosymptomatic form of MRS.[1-4] To date, the pathogenesis of MRS remains unclear: genetic factors as well as chronic infectious diseases, allergic reactions, and alterations in autoimmune functions are presumed as etiological factors.[1,4-6] Melkersson–Rosenthal syndrome frequently occurs between the second and third decade of life and the pediatric onset of the disease is extremely rare.[1,3,4,6] We present a child with MRS and discuss the clinical presentation, the diagnostic assessment as well as therapeutic options in children.

Case Presentation

An 8-year-old girl presented with a history of recurrent painless edema of the upper lip and tongue. Apart from eczema as a younger child, there was no remarkable medical history. Upon physical examination, a fissured tongue and painless edema of both the upper lip and tongue were noticed and she was unable to obtain complete lip closure. There was no facial paralysis or urticarial rash. Routine blood tests including allergic (tryptase, total and allergen-specific immunoglobulin E) and immunologic (C4, C1 esterase inhibitor) workup were all within normal limits. A gene panel for hereditary angioedema did not reveal a pathogenic disease-causing variant. Given the risk of acute airway obstruction, the child was admitted to the hospital and treated with intravenous administration of tranexamic acid 250 mg during the acute phase of swelling and cetirizine orally 5 mg twice daily for a month. This treatment resulted in a favorable clinical course with gradual decrease of the edema.

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A follow-up 1 month after discharge from the hospital revealed a persistent swollen and fissured upper lip. Additional laboratory tests to rule out rare immunological problems revealed normal serum levels of immunoglobulin G (IgG), immunoglobulin M, immunoglobulin A (IgA), thyroid-stimulating hormone, free thyroxine, haptoglobin, and alpha-2-macroglobulin. No abnormalities consistent with sarcoidosis were found on chest x-ray. Fecal calprotectin to detect Crohn's disease (CD) was within normal values. Based on the clinical features, a diagnosis of CG was suspected, which was confirmed by lip biopsy. Histopathology revealed a perivascular lymphocytic infiltrate and multiple granulomas composed of epithelioid histiocytic cells and multinuclear giant cells (Figure 1). At that time, the parents declined any treatment.

Because the girl also had complaints of recurrent vomiting, abdominal pain, and mild constipation, further investigation for underlying gastrointestinal disease was performed. Abdominal ultrasound showed no abnormalities. However, there was an increase in anti-tissue transglutaminase IgA (anti-TTG IgA) to 694 U/mL, as well as positive anti-endomysial antibodies IgA (1/160) and IgG (1/320). Based on this clear positive serology combined with subjective symptoms, a diagnosis of celiac disease was established. A gluten-free diet was started and anti-TTG IgA values dropped back to normal values.

The lip edema persisted after several months, and a treatment with metronidazole 400 mg 3 times a day was started. After 6 weeks, there was a significant decrease in swelling, but the patient developed abdominal discomfort and therefore the medication was tapered off. During this tapering, about 2.5 years after the onset of facial swelling, the girl presented with right-sided hemifacial edema and subsequent right peripheral facial palsy (House–Brackmann grade 4). Hearing was normal and magnetic resonance imaging of the posterior fossa showed normal findings. A complete autoimmunity panel was normal, except for antinuclear antibody positivity (1/80). Serological tests revealed previous varicella zoster infection (IgG 2221 mIU/mL). *Borrelia* serology was negative. Oral corticosteroids (2 mg/kg/day) were administered to treat the facial palsy. After initial improvement, there was a second recurrence of facial palsy with facial edema. At the last clinical visit, facial nerve function was completely normal. Recently, topical tacrolimus 0.03% was started once a day in combination with azithromycin 250 mg 3 times a week, with slight improvement in upper lip edema. Written informed consent was obtained from the patient and her parents to report this case.

Main Points

- The classical triad of Melkersson–Rosenthal syndrome (MRS) is seen only in a minority of the cases, and most patients present with nonsimultaneous mono- or oligosymptomatic forms.
- Common etiologies of orofacial swelling in children should first be ruled out.
- Granulomatous diseases like Crohn's disease and sarcoidosis may mimic MRS and should be excluded by appropriate diagnostic tests.
- Early recognition and multidisciplinary evaluation are important to minimize relapses and prevent orofacial dysfunction, and its associated implications for the young child's psychosocial well-being.

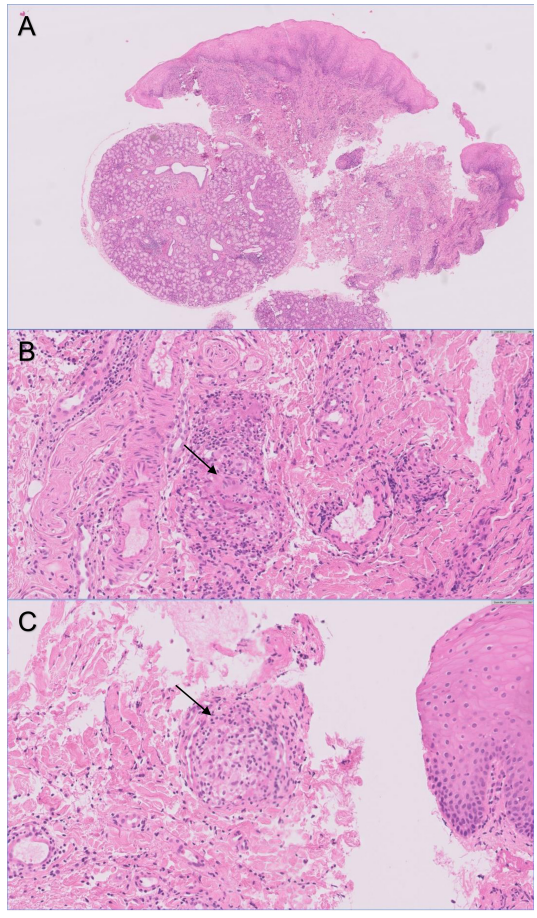

Figure 1. A-C. Histopathological specimen. (A) Histopathology revealed a perivascular lymphocytic infiltrate and multiple granulomas. (B) Giant cell (arrow). (C) Granuloma composed of epithelioid histiocytic cells (arrow).

Discussion

Since the first description of MRS in 1928, a collection of historically evolved terms, e.g., CG, orofacial granulomatosis (OFG), and MRS, have been used concurrently and have been frequently reported as the same entity.[1] To date, the etiology of MRS remains controversial. Infectious agents such as *Mycobacterium tuberculosis*, as well as autoimmune diseases like CD, sarcoidosis, and Hashimoto's thyroiditis have been considered as etiological factors in children.[6-11] The co-occurrence of MRS and celiac disease, as in our case, was described only once in literature.[2] Since MRS is a clinical syndrome, oligosymptomatic or complete forms do not require additional histological evidence.[4] Diagnosis is often of exclusion, and clinicians should rule out other etiologies of orofacial swelling, including trauma, infection, and allergic or hereditary angioedema. Congenital disorders or neural infections causing facial palsy should be excluded. Imaging is helpful to exclude trauma or neoplasms.[4] Since granulomatous diseases like CD and sarcoidosis mimic MRS, or both may be part of the same inflammatory disease according to some authors,[5,7,8] abnormalities of intestines, lungs, and lymph nodes should be detected.[7,10,11]

Most children are between 7 and 12 years old at the time of diagnosis and two-thirds of them present with mono- or oligosymptomatic forms.[4] A systematic review of pediatric OFG found a higher prevalence in boys and the mean age of onset was 11.1 years.[7] However, some authors found a female preponderance before 18 years of age.[4] As reported in adults, orofacial edema is the most frequent symptom (54.3%), followed by facial palsy (52.6%) and fissured tongue (48.3%).[4] Unlike in adults, edema usually follows facial palsy in children.[6] It mimics angioedema but is more persistent, unresponsive to antihistamines and can lead to tissue fibrosis.[4] Compared with Bell's palsy, facial palsy in MRS is usually recurrent, with worse recovery and gradual formation of fibrosis.[1,4,6] This not only results in physical sequelae but also has important implications for the child's psychosocial well-being. A recent study evaluating the long-term outcomes of pediatric facial palsy using both a patient questionnaire and clinical assessment found that self-reported outcomes differed from physician assessment, indicating that many pediatric patients suffer from subjective invisible residual symptoms impacting on their quality of life. Synkinesias were most commonly reported, followed by socially or esthetically disturbing sequelae.[12]

To date, no standardized treatment has been described for both adult and pediatric patients. Systemic corticosteroids (1-1.5 mg/kg/day) tapered over 3-6 weeks are usually the initial choice.[1,4] However, noncorticosteroid anti-inflammatory agents are safer, especially for young patients who may require long-term treatment.[13] Swagata et al[14] proposed the use of metronidazole in monotherapy in children with CG, a treatment without long-term side effects. Local triamcinolone injections provide a good alternative, and combination approaches with anti-inflammatory agents (doxycycline, minocycline, colchicine, dapsone, and sulfapyridine) successfully reduced orofacial edema in children.[13] Moreover, the combined use of oral corticosteroids with minocycline, the use of intravenous immunoglobulins, or the use of thalidomide was successful in pediatric cases.[1,3,4,8] Our patient benefited from metronidazole treatment but developed abdominal discomfort. As a second-line treatment, azithromycin was preferred to minocycline, given the risk of tooth discoloration when minocycline is used in childhood. In our patient, facial nerve function improved after treatment with oral corticosteroids. Total facial nerve decompression was found to be effective in preventing further recurrence in adults[15] and might be considered in children with severe facial dysfunction and intolerance to medical treatment.

Informed Consent: Written informed consent was obtained from the patient and her parents to report this case.

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