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MRS Chronicles: Navigating the Intricacies of Melkersson-Rosenthal Syndrome

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Abstract

Melkersson-Rosenthal Syndrome is an uncommon condition characterized by orofacial edema, facial nerve palsy, and tongue furrowing. The etiology of this condition is uncertain. Corticosteroids, such as intralesional triamcinolone acetonide, are the principal therapy choices for orofacial edema, offering only symptomatic relief. In circumstances when triamcinolone acetonide is not accessible, intralesional betamethasone and oral doxycycline can be used. This thorough review article seeks to improve understanding of Melkersson-Rosenthal syndrome among healthcare professionals, researchers, and those afflicted by the illness. It addresses the many management options used in the treatment of this unusual condition, focusing on the difficulties in diagnosis and management.

Keywords: Facial Palsy, Facial Edema, Lip Edema, Orofacial Granulomatosis, Recurrent Facial Palsy, Fissured Tongue, Lingua Plicata

Introduction

Melkersson-Rosenthal syndrome (MRS) is a rare neurological condition with an estimated frequency of 0.08% in the general population. It characterized by triad of recurrent facial paralysis (usually affecting the seventh cranial nerve), orofacial edema, and a fissured tongue. However, oligosymptomatic or monosymptomatic versions of this syndrome outweigh those with the typical triad, which affects around one-fourth or less of individuals [1, 2]. Ernst Gustaf Melkersson originally characterized the disease in 1928 in a 35-year-old female with orofacial edema and facial paralysis [3]. In 1931, Rosenthal described the association between facial paralysis and fissured tongue [4]. Symptoms often appear between the ages of 25 and 40 (range 1-69), with a female preponderance (sex ratio of 2:1). MRS is uncommon in children, with only 30 instances reported. Onset in children often occurs between the ages of 7 and 12, with the youngest youngster documented at 22 months. The diagnosis is typically delayed, with a median period between 4 and 9 years. [2, 4, 5, 6, 7]

The purpose of this article is enhancing understanding of this rare neurological illness among healthcare professionals, researchers, and those afflicted by the syndrome. It also aims to emphasize obstacles in diagnosis and management, address novel medications and research possibilities, and encourage a comprehensive approach to care for patients with Merkelson Rosenthal Syndrome.

Clinical Manifestation

The diagnosis of MRS can be challenging, especially when there is only facial paralysis or eyelid edema present. It is critical to identify MRS from other illnesses with similar symptoms, such as orbital malignancies and allergy disorders. Recurrent facial nerve palsies in childhood should raise the possibility of MRS. Facial paralysis is frequently the initial clinical sign and may precede oro-facial edema. Fissured tongue, also known as lingua plicata, is a common condition that may run in families. Other neurological and non-neurological symptoms of MRS include migraines, headaches, dizziness, tinnitus, deafness, facial paresthesias, and uveitis. MRS edema is non-pitting and can occur in a variety of bodily areas. Failure to resolve edema might cause fibrosis and irreversible deformities. Prompt diagnosis and adequate care are critical for reducing complications and improving overall outcomes in MRS patients [7, 8, 9, 10].

Etiopathogenesis

The cause of Merkelson Rosenthal Syndrome (MRS) is unknown. HSV1 infections, hereditary granulomatous disorders, mycobacterial infections (such as tuberculosis and leprosy), chronic infections, Down's syndrome, psoriasis, thyroiditis, multiple sclerosis, keratitis, Wegener's granulomatous, diabetes mellitus, sarcoidosis, ulcerative colitis, and allergic disorders have all been linked to the etiopathogenesis of this rare pediatric disorder [2, 5, 11, 12].

Respiratory infections, particularly influenza, have been linked to MRS relapses. Mutations that cause UNC-93B deficiency have also been found, which can predispose people to HSV-1 infection. This impairment preferentially reduces immunity to HSV-1 but not to other species [2, 13]. Some instances of MRS have been associated with herpes-like lesions during the outset of facial edema. In addition, mutations in the FATP1 gene, responsible for fatty acid transport protein, have been detected in one family, while autosomal dominant transmission has been reported in another family over four generations [11].

Sinusitis, candida infection, face erythema, IgA nephropathy, vitiligo, thyroid hormonal anomalies, and lacunar strokes are examples of rare MRS complications [14]. MRS, cheilitis granulomatosa, granulomatous cheilitis, and mono symptomatic MRS are used interchangeably in different publications since there are no clear-cut etiologies for MRS [15].

It's worth mentioning that inflammatory bowel illnesses like Crohn's disease can cause oral symptoms such as lip swelling with fissures, mucositis, gingivitis, glossitis, and a cobblestone appearance of the oral mucosa [16]. These signs may occasionally appear in MRS and might add to diagnostic uncertainty. As a result, investigations are primarily concerned with ruling out systemic underlying causes.

Diagnosis

A thorough assessment and investigation are essential to establish the diagnosis and rule out other possible reasons in individuals with suspected Melkersson-Rosenthal Syndrome (MRS). A complete physical examination, including checking for otitis media, assessing visual acuity, monitoring hearing function, and reviewing swollen nerves, should be part of the first assessment. A variety of studies may be recommended to help with the diagnosis and to look into underlying disease. These can include broad tests like blood glucose levels, full blood counts, and erythrocyte sedimentation rate. Additionally, liver and renal function tests might offer information about the patient's overall health state. Imaging techniques, such as CT scans of the head and MRIs of the brain, can aid in identifying structural abnormalities or ruling out secondary illnesses. Chest X-rays may also be used to look for any accompanying respiratory abnormalities.

Angiotensin Converting Enzyme (ACE) levels and Anti-Nuclear Antibody (ANA) tests can be used to detect probable autoimmune involvement. Anti-Neutrophilic Cytoplasmic Antibody (ANCA) tests might also be considered. Specific investigations may be required dependent on the patient's clinical presentation. Thyroid function tests, for example, can detect thyroid problems, although specialist testing such as a slit lamp examination for uveitis, brainstem evoked audiometry, visual evoked potentials, and facial nerve conduction studies can provide further insights. In some cases, additional investigations may be considered. These may include TB assessments, karyotyping for Down's syndrome, HLA testing for ulcerative colitis and Crohn's disease, C1 inhibitor deficiency testing for hereditary angioneurotic edema, and, if necessary, next-generation sequencing for genetic analysis [1, 2, 5, 14]

It is crucial to note that the selection of investigations may differ depending on specific patient features and the judgment of healthcare providers. As a result, talking with a healthcare practitioner or specialist is critical in determining which investigations are most suited for each patient.

Treatment

The majority of MRS signs and symptoms tend to resolve without the need for therapy, and there is no established course of care. However if left untreated episodes may become more frequent and continue longer.

Treatment options for MRS may include:

Corticosteroids:

Corticosteroids have traditionally been the cornerstone of therapy. Oral corticosteroids are frequently taken for one week before being reduced over the course of two weeks. Severe instances have required high-dose pulse methylprednisolone. Corticosteroid treatment has been reported to relieve symptoms in 50-80% of patients while reducing relapses by 60-75% [5].

Intralesional Triamcinolone Acetonide (TA):

Intralesional triamcinolone acetonide (TA) combined with lignocaine can be used to treat local edema caused by Melkersson-Rosenthal Syndrome. Studies have indicated that injecting TA (1-1.5 mL of 10-20 mg/mL solution) on four sides of each lip, with additional injections in the cheek and nasolabial folds, can considerably reduce edema severity and recurrence. If TA is not accessible, intralesional betamethasone and oral doxycycline might be administered instead. Intralesional TA is more effective for cheilitis granulomatosa without systemic illness. Corticosteroid-antibiotic combos, such as minocycline and roxithromycin, have also shown anti-inflammatory activity. Oral corticosteroids are advised for those who have facial paralysis as well as orofacial edema. Intralesional injections are recommended for isolated oro-facial edema or patients that do not respond to oral corticosteroids [2, 5, 17, 18].

Other Immunosuppressants:

Melkersson-Rosenthal Syndrome (MRS) with systemic involvement has been treated with immunosuppressants such as methotrexate, thalidomide, intravenous immunoglobulins, clofazimine, dapsone, anti-TNF medication (such as infliximab), anti-histaminic medicines, and hydroxychloroquine. These drugs have showed promise in treating MRS and related ailments such as collagen vascular diseases and granulomatous disorders. Adalimumab has been beneficial in treating patients with MRS, type 2 diabetes, and psoriasis following previous therapeutic failures, and infliximab has been useful in treating tuberculoid-like granulomas and steroid-refractory lip edema. In a study of 14 individuals with oro-facial granulomatosis, both infliximab and adalimumab showed 70% short-term response rates, with adalimumab showing efficacy for patients who did not react to infliximab. Anti-TNF therapy has been proposed as a viable therapeutic option for MRS in patients with oral sulcus involvement, intestinal Crohn's disease, and high C-reactive protein [2, 5, 19, 20, 21].

Ancillary Treatment:

Vitamins such as thiamine, niacin, riboflavin, pyridoxine, ascorbic acid, and vitamin E have been used with corticosteroids. Other therapies with uncertain effectiveness include a benzoate-free diet, a cinnamon-free diet, and acyclovir. Fumaric acid esters, which are used to treat psoriasis, have also been found to help in orofacial granulomatosis [2, 5, 22].

Surgical Management:

Recurrent facial palsies may require surgical treatment. The time of the procedure is undetermined. The middle cranial fossa method can be used to decompress the facial nerves completely. Standard mastoidectomy is performed, with the facial nerve decompressed from the internal auditory meatus to the geniculate ganglion. In one such trial, none of the patients had a return of facial palsy, unlike the individuals who were treated medically.Almost 90% of individuals who underwent surgery recovered to a near-normal state. Another surgical option is to perform subtotal nerve decompression from the stylomastoid foramen to the geniculate ganglion. This method has a modest risk of conductive hearing loss.

Lip surgeries can also be performed to treat chronic lip edema. In one example, using Conway's method, the mucosa dorsal to vermillion was removed en-block. A portion of the orbicularis muscle and some edematous tissue were also resected.Helium laser

ablation is an alternative to cheiloplasty. Both of these operations may produce feeling loss in the afflicted lip, but they have no effect on disease recurrence [2, 5, 23, 24, 25].

Conclusion

Melkersson-Rosenthal Syndrome (MRS) is an uncommon neurological condition marked by recurring facial paralysis, orofacial edema, and a fissured tongue. While the actual origin is unknown, several variables, including infections, genetic predisposition, and autoimmune pathways, have been linked. MRS diagnosis can be difficult because to its overlapping characteristics with other illnesses, demanding a thorough assessment and suitable study. Corticosteroids, intralesional triamcinolone acetonide, immunosuppressants, and auxiliary therapies like vitamins are also alternatives for treating MRS. Surgical procedures may be explored for some symptoms. Early detection and a multidisciplinary approach are essential for effective treatment. Further research is required to better understand the underlying processes and create specific treatments for MRS.

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