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Melkersson–Rosenthal Syndrome

Melkersson-Rosenthal Syndrome (MRS), also referred to as orofacial granulomatosis, is a rare, chronic neurological disorder that is characterized by a triad of symptoms: recurrent orofacial edema (facial swelling), facial paralysis, and fissured (furrowed) tongue. While these symptoms are indicative of MRS, at least two components of the triad must be present for a clinical diagnosis. The disease typically manifests during young adulthood, with episodes of disease flaring intermittently, often recurring over days to months.

Despite its clinical recognition, the exact etiology of MRS remains unclear, though it may be linked to genetic predisposition, hypersensitivity reactions, or viral infections. Furthermore, the condition is often considered in association with other granulomatous diseases, such as sarcoidosis and Crohn's disease, where granuloma formation plays a pivotal role.

Pathophysiology and Etiology

The precise cause of MRS is not well understood, though several hypotheses have been proposed. Some evidence suggests that genetic factors may play a role, as certain cases of MRS occur in families, indicating a potential hereditary component. Additionally, MRS may be triggered by hypersensitivity reactions or viral infections, though these associations are not definitively established. As a granulomatous disease, MRS shares pathophysiological features with other conditions like sarcoidosis and Crohn's disease, which also involve granuloma formation. These diseases are characterized by the accumulation of inflammatory cells, particularly macrophages, which lead to the formation of granulomas. In some cases, MRS may precede the diagnosis of these conditions, suggesting a possible link in pathogenesis.

Clinical Features

The hallmark symptoms of MRS include recurrent episodes of orofacial edema, facial paralysis, and furrowed tongue. These manifestations can vary in severity and may evolve over time.

1. **Orofacial Edema (Facial Swelling)**: The characteristic swelling in MRS typically affects the lips (cheilitis granulomatosis), with the upper lip being more commonly involved than the lower lip. The swelling may be acute, resolving in hours to days during the initial episodes, but it can become more persistent or severe in subsequent flare-ups, sometimes leading to permanent scarring. This symptom often appears as the first clinical sign and can be misdiagnosed as an allergic reaction. In some cases, swelling may extend to the area around the mouth and eyes. Persistent lip swelling, especially when accompanied by other features like facial palsy, is strongly suggestive of MRS.

2. **Furrowed Tongue (Scrotal Tongue or Lingua Plicata)**: Furrowed tongue, a key symptom of MRS, is characterized by deep grooves or fissures on the tongue's dorsal surface. This condition can be present from birth and is typically non-painful. However, tongue fissuring may lead to complications such as local infections, enlargement of the tongue, loss of taste buds, and sensations of itching or burning.
3. **Facial Palsy**: Facial paralysis, which may be unilateral or bilateral, often occurs after the first few episodes of swelling. This symptom may affect the facial muscles controlled by the facial nerve (cranial nerve VII). Recurrent episodes of facial palsy occur in approximately 10% of patients, and the severity tends to increase with disease progression. Other cranial nerves may also become involved, leading to further neurological impairments, including difficulties with swallowing or speech.
4. **Neurological and Systemic Symptoms**: In addition to facial palsy, individuals with MRS may experience a variety of neurological symptoms, including migraines, dizziness, tinnitus, and hearing loss. Visual disturbances have also been reported. Systemic manifestations can include uveitis (inflammation of the eye), as well as gastrointestinal involvement, notably diverticulitis, which may be suggestive of underlying Crohn's disease.

Diagnosis

The diagnosis of MRS is primarily clinical, based on the presence of at least two of the characteristic symptoms (facial swelling, facial palsy, and furrowed tongue). Given the rarity of the condition, it is often misdiagnosed or overlooked, especially in the early stages when symptoms are subtle. Additional diagnostic evaluations, including histopathological examination, can help confirm the diagnosis by revealing granulomatous inflammation in affected tissues. The association with other granulomatous diseases, such as sarcoidosis and Crohn's disease, should also be considered, and appropriate tests for these conditions should be performed when necessary.

Treatment Strategies

Treatment for MRS is aimed at managing symptoms, reducing inflammation, and preventing complications. Given the chronic and episodic nature of the disease, a combination of medical and surgical interventions may be required.

- ***Symptomatic Treatment****:*
  - ***Intralesional Steroids***: Inflammation and swelling can often be controlled with intralesional steroid injections, which reduce the granulomatous inflammation associated with MRS.
  - ***Oral Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)****:* NSAIDs, such as ibuprofen, may help reduce inflammation and manage pain associated with facial swelling and other inflammatory symptoms.

- ***Antihistamines***: These may be useful in managing allergic-type reactions or in alleviating itching and burning sensations associated with furrowed tongue and facial swelling.

➢ ***Systemic Therapies****:*
- ***Methotrexate***: Methotrexate, an immunosuppressive agent, has been used to manage refractory MRS. It works by inhibiting the activity of T-cells and suppressing the immune response that contributes to granuloma formation.
- ***TNF-alpha Inhibitors***: Tumor necrosis factor (TNF) alpha inhibitors, such as infliximab and adalimumab, are biologic agents that can be effective in controlling inflammation in granulomatous diseases, including MRS.
- ***Antibiotics***: In cases where secondary bacterial infections are suspected (e.g., infections related to the fissured tongue), antibiotics may be prescribed.

➢ ***Surgical Treatment****:*
- ***Surgical Decompression****:* For severe cases of facial paralysis, surgery may be indicated to relieve pressure on the facial nerves. This is especially considered when conservative treatments are ineffective in controlling nerve damage or when neurological impairment becomes debilitating.

Prognosis and Disease Progression

The progression of MRS varies among individuals. While some may experience only mild or intermittent episodes, others may develop chronic symptoms that progressively worsen. The development of permanent facial paralysis or other neurological complications is a concern in severe cases. Long-term management focuses on minimizing flare-ups, managing symptoms, and addressing any complications, such as secondary infections or systemic involvement.

Conclusion

Melkersson-Rosenthal Syndrome is a rare, chronic condition that presents with a distinct triad of symptoms: orofacial edema, facial paralysis, and furrowed tongue. While the cause of the syndrome remains unclear, it is suspected to have a genetic basis and may be linked to other granulomatous diseases. Early diagnosis and intervention are crucial for managing symptoms and preventing complications. Treatment is primarily symptomatic, with the use of intralesional steroids, NSAIDs, and biologics, alongside surgical interventions when necessary. Ongoing research into the pathophysiology and treatment of MRS is needed to optimize care and improve patient outcomes.

References

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