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Review paper

Longitudinally Extensive Transverse Myelitis: Diagnostic Pitfalls and Treatment Strategies

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ABSTRACT

Relapsing transverse myelitis (TM) is a rare but potentially debilitating neurological condition characterized by inflammation of the spinal cord, often associated with neuromyelitis optica spectrum disorders (NMOSD). TM can present with motor, sensory, and autonomic dysfunction, and when it recurs, it raises significant concerns regarding underlying chronic demyelinating diseases. Diagnosing and managing this condition, particularly in the absence of specific antibodies like NMO-IgG or MOG, remains a challenge. This article explores the pathophysiology, diagnostic criteria, and treatment options for relapsing transverse myelitis, emphasizing the importance of early detection and aggressive management to prevent permanent disability.

1. Introduction

Transverse myelitis (TM) is an inflammatory disorder of the spinal cord that can result in substantial motor, sensory, and autonomic impairment. It typically manifests with a sensory level, weakness, and bladder or bowel dysfunction. The condition can be idiopathic or linked to underlying diseases, such as multiple sclerosis (MS) or neuromyelitis optica spectrum disorder (NMOSD).

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Relapsing forms of TM, particularly those involving longitudinally extensive lesions spanning three or more vertebral segments, are strongly associated with NMOSD. These relapses, if untreated, can lead to cumulative spinal cord damage and irreversible disability. Although antibodies like NMO-IgG and MOG are valuable diagnostic markers, seronegative cases complicate diagnosis, underscoring the need for clinicians to rely on clinical presentation and imaging.

2. Pathophysiology of Relapsing Transverse Myelitis

The pathogenesis of TM, especially in the context of NMOSD, involves autoimmune-mediated inflammation targeting the spinal cord. In NMOSD, the immune

system produces antibodies against aquaporin-4 (AQP4), a protein critical for maintaining water homeostasis in the central nervous system (CNS). These AQP4 antibodies, known as NMO-IgG, lead to demyelination and necrosis of the spinal cord and optic nerves, causing the characteristic symptoms of NMOSD.

However, not all patients with NMOSD test positive for NMO-IgG antibodies. Approximately 20-30% of NMOSD patients are seronegative for NMO-IgG, and some of these individuals may test positive for MOG (myelin oligodendrocyte glycoprotein) antibodies. In seronegative cases, the exact mechanism of spinal cord inflammation is less clear, but it is likely mediated by other autoantibodies or immune pathways. Regardless of serological findings, the extensive damage caused by the immune system's attack on the spinal cord leads to the characteristic longitudinally extensive transverse myelitis (LETM) seen in NMOSD.

3. Diagnostic Challenges

Diagnosing relapsing TM, particularly in the context of NMOSD, can be challenging, especially when specific antibodies like NMO-IgG or MOG are absent. In such cases, clinicians must rely on clinical and radiological evidence. TM is often identified by the sudden onset of weakness, sensory disturbances, and bladder dysfunction, accompanied by a sensory level on neurological examination.

Imaging plays a crucial role in the diagnosis of TM. Magnetic resonance imaging (MRI) of the spine is the gold standard for visualizing spinal cord lesions. In NMOSD-associated TM, MRI typically reveals longitudinally extensive lesions that span three or more vertebral segments. These lesions are a hallmark of NMOSD and help distinguish it from other demyelinating diseases such as multiple sclerosis, where spinal cord lesions tend to be smaller and more localized.

In addition to imaging, cerebrospinal fluid (CSF) analysis can provide important diagnostic clues. While oligoclonal bands are often present in MS, they are typically absent in NMOSD. Instead, the presence of inflammatory markers such as elevated protein levels and pleocytosis may indicate spinal cord inflammation.

4. Management of Relapsing Transverse Myelitis

The management of relapsing TM requires a comprehensive approach that addresses both acute episodes and long-term prevention. Acute relapses are typically treated with high-dose corticosteroids, which act to reduce inflammation and promote recovery. Intravenous methylprednisolone is commonly used, and in cases where patients do not respond adequately to steroids, plasma exchange (PLEX) can be employed. PLEX is particularly effective in severe cases of TM, as it removes circulating antibodies that contribute to the inflammatory process.

Once the acute episode is managed, the focus shifts to preventing further relapses. Long-term immunosuppressive therapy is essential for patients with NMOSD to reduce the risk of recurrent attacks. Commonly used immunosuppressive agents include azathioprine, mycophenolate mofetil, and rituximab. Rituximab, in particular, has been shown to be highly effective in reducing relapses by depleting B cells, which play a central role in antibody production and immune-mediated inflammation.

Despite aggressive treatment, the prognosis for patients with relapsing TM remains uncertain. Each relapse can cause cumulative damage to the spinal cord, leading to permanent deficits in motor, sensory, and autonomic function. Therefore, early diagnosis and prompt initiation of treatment are critical for improving long-term outcomes.

5. Prognosis and Long-Term Implications

The long-term prognosis for patients with relapsing TM, especially those associated with NMOSD, depends on the frequency and severity of relapses, as well as the effectiveness of immunosuppressive therapy. Patients who experience multiple relapses are at high risk for permanent disability, as each episode of inflammation can result in irreversible damage to the spinal cord.

In addition to physical disability, relapsing TM can also have a significant impact on a patient's quality of life. Chronic pain, spasticity, and bladder or bowel dysfunction are common sequelae of spinal cord injury and can severely affect daily functioning. Moreover, the psychological toll of living with a chronic, relapsing condition can lead to anxiety, depression, and social isolation.

Early intervention with immunosuppressive therapy is crucial to prevent future relapses and minimize the risk of long-term disability. Patients with NMOSD should be closely monitored for signs of relapse, and treatment should be adjusted as needed to maintain disease control. While there is no cure for NMOSD, advances in immunosuppressive therapy have significantly improved outcomes for patients with relapsing TM.

6. Conclusion

Relapsing transverse myelitis, particularly in the context of NMOSD, poses significant diagnostic and therapeutic challenges. The relapsing nature of TM, combined with the potential for extensive spinal cord damage, necessitates early recognition and aggressive treatment to prevent long-term disability. Clinicians should maintain a high index of suspicion for NMOSD in patients presenting with recurrent episodes of TM, even when serological tests for NMO-IgG and MOG antibodies are negative.

The use of corticosteroids and plasma exchange during acute relapses, followed by long-term immunosuppressive therapy, is the cornerstone of treatment for relapsing TM. By preventing future relapses and limiting the extent of spinal cord damage, these treatments can help improve the prognosis and quality of life for patients with NMOSD.

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