Chapter 11
Oligodendrogliopathy in Multiple Sclerosis

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ABSTRACT

Multiple sclerosis (MS) is a complex autoimmune disease of the central nervous system (CNS), which is characterized by demyelination and neurodegeneration. Oligodendrocytes have an essential role in maintaining the integrity of myelin, the protective sheath that surrounds nerve fibers and is indispensable for efficient signal transmission. Nevertheless, in multiple sclerosis, oligodendrocytes become dysfunctional, leading to myelin deterioration and axonal degeneration. Recent research suggests that metabolic changes, including mitochondrial dysfunction and alterations in glucose and lipid metabolism, contribute significantly to the pathogenesis of MS. Mitochondrial dysfunction is observed in both immune cells and CNS oligodendrocytes of MS patients. Impaired mitochondrial function leads to energy deficits, affecting crucial processes such as impulse transmission and axonal transport, ultimately contributing to neurodegeneration. Understanding the complex relationship between these mechanisms is crucial to the development of an effective treatment for MS.

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INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune disease wich is characterized by demyelination of nerve fibers in the central nervous system. Oligodendrocytes, specialized glial cells are responsible for the production and maintenance of myelin, have an essential role in the pathogenesis of multiple sclerosis. Often referred to as oligodendrogliopathy, this phenomenon involves the destruction of normal oligodendrocyte function following an inappropriate attack by the immune system. The ensuing inflammatory response leads to myelin degradation, resulting in altered nerve signal transmission and a wide range of neurological symptoms.

The complex interaction between immune cells, oligodendrocytes and myelin in MS is the subject of ongoing research. Studies have elucidated the mechanisms by which immune cells infiltrate central nervous system and trigger an inflammatory cascade, ultimately targeting oligodendrocytes and their myelin sheaths. As oligodendrogliopathy progresses, areas of demyelination give rise to characteristic lesions and scar tissue formation, contributing to the clinical heterogeneity observed in multiple sclerosis patients.

MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a chronic and autoimmune disease of the central nervous system (CNS), manifested by inflammation, demyelinization and extensive focal lesions in the white and gray matter, and axonal loss (Lassmann et al., 2018). The prevalence of the disease in developed and developing countries is increasing exponentially, and generally occurs in young adults (Dobson R., et al., 2019). Moreover, women appear to be two to three times more likely to be affected by the disease, due to an earlier but less progressive phenotype than men (Harbo et al., 2013).

The current classification of MS includes four major phases: clinically isolated syndrome, relapsing-remitting phase (RRMS), secondary progressive phase (SPMS) and primary progressive phase (PPMS). Nevertheless, there is considerable overlap between these phases, and the transitions between them remain unclear (Dimitriou et al., 2023). RRMS, which affects around 80% of patients, is characterised by inflammation, demyelination and intermittent episodes of neurological dysfunction. Over time, untreated patients may progress to the MS phase due to continued disease deterioration and fewer clinical relapses. Conversely, around 10% of patients present with a PPMS phenotype from the outset, without prior clinical relapse. This progression may be reflected in increasing physical disability, cognitive impairment or other neurological symptoms. A recent finding, called "progression independent of relapse activity" (PIRA), has been observed in some people with multiple sclerosis, where the disease progresses without the acute relapses typical of the relapsing-remitting phase. PIRA appears to be related to chronic inflammatory tissue damage involving substantial early white matter atrophy (Cagol A., et al., 2022).

Histologically, focal lesions were found in the white and gray matter, comprising the cortex, basal ganglia, brainstem and spinal cord. Blood-brain barrier (BBB) disruption, axonal death and demyelinating lesions result in significant progressive neurodegeneration. Oligodendrocyte precursor cells and oligodendrocytes are largely affected by this disease (Stys P. K., et al., 2019). As demyelination spreads through tissues, microglia and inflammatory cells are recruited to remove myelin debris and combat the hostile environment. Two types of microglia are present in the brains of people with MS: pro-inflammatory microglia and anti-inflammatory microglia (Garg N., et al., 2015).