Main Submission

Not so liberating after all: Multiple Sclerosis disease and treatments

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Myelination of neuronal axons is essential for both the normal and rapid electrical conduction along an axon. Multiple Sclerosis (MS) is an autoimmune disorder characterized by the gradual loss of the myelin sheath, eventually resulting in loss of neuronal control. Immune cells typically have limited access to the CNS, but in MS, these cells are able to target myelin and cause inflammation, demyelination of axons and subsequent neurological impairment.[1] Initial onset of MS involves oscillations between remission and relapse, progressing to its chronic state with irreversible damage and permanent disability. In remission, for unknown reasons, the activity of the immune system decreases and the demyelinated axons are remyelinated by endogenous pools of stem cells.[1] As MS progresses into the chronic form, remyelination no longer occurs and the neuronal damage continues to accumulate, eventually leading to paralysis and death.[2]

While the cause(s) of the autoimmune reactivity to myelin is still unknown, it has been linked to genetic and environmental factors. For example, MS is more common in higher latitudes, possibly because of vitamin D deficiency.[3] Due to the complexity of MS, current treatments tend to target specific aspects of the pathology – such as inflammation or remyelination – as opposed to prevention or reversal of the autoimmune response. Most current drug treatments modulate immune system activity, which aim to prevent new lesions and limit further demyelination.[1] Ironically, suppression of the immune system as the only form of treatment may actually be detrimental. For example, inflammation and the subsequent activity of macrophages and microglia are needed to clean up cellular debris. They also release signals important to the initiation of remyelination, therefore playing an important role in remission.[4] In chronic MS, immune suppression therapy does nothing to reverse myelin loss or protect demyelinated axons from further damage.[4] Thus there is much interest in the use of stem cell therapy to reverse the loss of this tissue and re-myelinate naked axons.

A recent controversy is the suggestion by Dr. Paolo Zamboni that MS is caused by the inhibition of drainage from the brain, termed "chronic cerebrospinal venous insufficiency."[5] Dr. Zamboni suggests that MS patients have insufficient drainage of blood from the CNS, causing a reflux action that moves blood back into the CNS via secondary blood vessels. This model further proposes that due to pressure build-up in these blood vessels, there is a resulting leakage of blood into the surrounding tissue that causes a build-up of iron and initiates the immune system's reactivity to myelin.[5]

In chronic cerebrospinal venous insufficiency (CCSVI) treatment – commonly known as liberation therapy – veins are expanded to increase blood flow away from the CNS, which is similar to the mechanism of arterial stent therapy. However, there are a several flaws to this model. CCSVI is a symptom that is often seen in men, yet MS tends to occur primarily in women.[6] There is also a lack of correlation between CCSVI and MS, where not all MS patients have CCSVI, and vice versa.[7,8] Furthermore, it is unclear as to how liberation therapy, or an increase in CNS blood drainage, can inhibit the immune system's sensitivity to myelin. Typically, once the immune system has been activated, as long as the antigen (in this case myelin) is present, the immune system will be active until levels of the antigen have decreased significantly.[9] Lastly, there is no known mechanism by which liberation therapy can result in the remyelination of the damaged CNS. Because of the media attention brought on by the idea of CCSVI, there was a significant push for clinical studies looking at liberation therapy. Clinical studies have begun in several countries, and initial results have been mixed.[7,8] However, with our current understanding of MS pathology and CCSVI, there is no clear evidence or physiological mechanism to ▶

suggest that the benefits of liberation therapy outweigh any of the significant associated risks. These risks include stent migration, blood clots within the brain and subsequently stroke.[8,10]

Despite public focus on liberation therapy as a potential cure for MS, mounting evidence suggests that CCSVI is not correlated with MS, and is unlikely to be effective as a form of treatment.[7,8] Given that immune suppressant therapies can potentially be harmful, current and future research on MS treatment should focus on cell-based therapies, in conjunction with immune modulation to reverse the effects of MS. It is hoped that with a better understanding of the immune system and its activity in the CNS, MS can be detected and prevented. ■

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