DOES CHRONIC VENOUS INSUFFICIENCY PLAY A ROLE IN MS PATHOGENESIS? "NO"

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Recent studies suggested that venous insufficiency (CCSVI) may be causally related to the etiology of multiple sclerosis (MS). Patterns of venous obstruction were also associated with clinical disease phenotypes. Using percutaneous transluminal angioplasty (PTA) and stenting, one group of investigators demonstrated that vascular hypoplasia can be successfully treated. There was also a significant benefit with regard to numerous clinical outcomes in patients with MS who underwent PTA.

Based in these observations, the following hypotheses have been stated: (1) Blocked extracranial veins causes cerebral venous reflux in patients with MS. (2) A stasis of venous blood flow, or a reversal of flow, or a lack of laminar flow results in iron overload in pervascular tissue and initiates an inflammatory cascade within the central nervous system.

While results from these open-label uncontrolled trial is compelling at first glance, there are significant concerns with regard to their biological plausibility. First, Published data on the effects of iron-overload does not support its pathogenic role in autoimmunity. Also, chronic venous insufficiency has not been associated with inflammatory disorders in other parts tissues or organs. Importantly, the observations on CCSVI also do not explain other epidemiological findings, namely the latitudinal gradient of MS, or the preponderance of female patients with MS. It also does not explain some of the clinical or paraclinical disease activity associated with this disorder: (1) How does a fixed anatomical defect result in a relapsing-remitting disease course in most patients? (2) Why is there a decrease in disease activity during pregnancy? (3) Why is there a decrease in gadolinium-enhancing (Gd^{+}) lesions in the brain on magnetic resonance imaging during progressive forms of MS, when the sequelae of venous reflux should be amplified? (4) How does CCSVI explain spinal cord disease? (5) How does the presence of CCSVI explain the beneficial response of many patients to currently approved immunomodulatory and immunosuppressive pharmacotherapies?

Some of these concerns should be addressed in blinded, multi-center randomized trials.