VENOUS OBSTRUCTION IS OF PRIMARY IMPORTANCE IN MS PATHOGENESIS – COMMENTS

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Chronic cerebrospinal venous insufficiency (CCSVI) is a recently defined syndrome by Zamboni, characterized by flow blockages in the internal jugular and/or azygous veins (IJVs-AZ) with opening of venous collaterals and insufficient drainage from brain. The syndrome is thought to be strongly associated with multiple sclerosis. The arguments for the key role of this syndrome in MS pathogenesis are the following: MS is venoconcetric in nature, CCSVI causes disruption of blood-brain-barrier, perivenal iron deposits trigger immunological response and MS plaque formation. There are some findings supported the hypothesis: refluxes and stenoses of extra and intracranial veins in ultrasonography and magnetic resonance venography, the sings of hypoperfusion and presence of iron deposits in magnetic resonance of the brain in MS patients and good preliminary results of percutaneous transluminal angioplasty of the veins in remitting-relapsing multiple sclerosis (in open, not randomized clinical trial). But there is many weak points of the theory: ultrasound criteria of Zamboni are not validated and Zamboni group ultrasound results in MS patients are not replicated by independent group of researchers, there are many pitfalls in invasive venography assessment and therefore it can be overestimation of venous obstructions in MS patients, in magnetic resonance venography and flow quantification there are no significant differences in the extracranial venous system of MS patients and healthy controls.

There is also no difference in ultrasound venous malformation frequency in patients with clinically isolated syndrome in compare with controls, there is no increase in cerebrofluid ferritin level in MS patients, hypoperfusion in MS may be a consequence of disease pathogenesis, not a cause, perivenous inflammation is present in many autoimmune diseases, without venous obstruction, and up to now there is no scientific proof of efficacy of any endovascular treatment in MS. Many other questions arise concerning the Zamboni hypothesis: how fixed defect (venous obstruction) can produce relapsing-remitting MS? Why activity of MS decreases in pregnancy? Why is a decrease in gadolinium-enhancing (Gd+) lesions in the brain on magnetic resonance imaging during progressive forms of MS, when the sequelae of CCSVI should be amplified? How does presence of CCSVI explain the positive response of MS to immunomodulatory and immunosupressive therapies?

Therefore the relation of venous changes to the pathophysiology of MS may not be as simple as initially described. The hypothesis of CCSVI in MS should be investigated in controlled, well designed, randomized multicenter trials. Criteria of diagnosis should be validated. And

it is too early to treat MS patients with endovascular angioplasty in routine basis, outside randomised controlled trials.