Blood Disorders & Transfusion

Caprio and Mancini, J Blood Disord Transfus 2016, 7:6
DOI: 10.4172/2155-9864.1000370

Letter to the Editor OMICS International

Vascular Disease in Multiple Sclerosis: A Real Thing?

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Received date: Oct 05, 2016, **Accepted date:** Oct 10, 2016, **Publication date:** Oct 14, 2016

In recent years, great interest has been addressed to the association between vascular abnormalities and Multiple Sclerosis (MS) [1-8]. Many studies have shown that patients with MS have an increased cardiovascular risk and increased mortality related to stroke and cardiovascular disease compared to general population [9-13]. In addition, MS patients who had more than one cardiovascular risk factor at diagnosis were more likely to develop disabilities [2,14,15].

Some authors have recently demonstrated the existence of the cerebral perfusion abnormalities in MS patients [16]. The breakdown of the blood-brain barrier is a constant characteristic of MS focal lesions and is demonstrated by MR imaging [17,18]. Chronic lesions in MS patients, studied by Perfusion-weighted MRI, showed reduced perfusion, in contrast with enhancing lesions that showed increased perfusion. The presence of ischemic central focal areas, suggests that ischemia plays an important role in the development of some focal lesions in multiple sclerosis [19,20].

Law et al. [21] demonstrated a reduction in cerebral blood flow and a prolonged transit time in the periventricular regions of normal appearing white matter (NAWM) in MS patients than in controls. Other studies showed hypoperfusion in different regions (NAWM, and deep GM) independently of clinical MS form [22,23]. These changes in cerebral perfusion were correlated with clinical disability and neuropsychological impairment [24].

Moreover, many authors have studied the possible association between abnormal venous drainage and MS and have shown that multiple sclerosis is often associated with hemodynamic abnormalities and vascular changes [25-32].

Recently Zamboni introduced the concept of chronic cerebrospinal venous insufficiency (CCSVI) as a vascular condition characterized by anomalies of the main extra-cranial cerebrospinal venous outflow routes that interfere with normal venous outflow in patients with multiple sclerosis. This condition could cause an increase in iron vein deposit resulting in the characteristic inflammation of tissues of the MS [30,33-34]. However the studies that used Echo-color Doppler for the detection of CCSVI demonstrate too high variability of results. Therefore ultrasound is not a good screening methodology and further studies are needed to determine techniques that can measure venous cerebral outflow and are less operator-dependent and more objective.

Macro and micro circulation alterations can cause changes in the endothelial cells, resulting in immune-mediated reactions and inflammatory response. The autoimmune inflammation can lead to iron deposition and leukocyte infiltration. Furthermore the consequent production of vascular mediators by the immune system cells and endothelial activation and neovascularization can cause changes in the microcirculation [35-38]. This multiple vascular risk factors together with inflammatory factors, through interactions with neuronal cells and components of myelin, could lead to increased permeability of the blood brain barrier and neurovascular uncoupling up to neuronal damage. However, it is yet to be determined if the vascular damage is the primary causal factor of neurological disease, or secondary to inflammation-autoimmunity.

The frequent association between MS and vascular diseases suggests that vascular changes, might contribute to neuronal or degenerative dysfunction in patients with MS. However, the results in the literature are often discordant both as regards the association between vascular and brain damage in neurological diseases, both for the correlation between vascular disease and disability. Several studies are mostly "case-control" and there are no multi population studies.

In conclusion, more studies are needed to verify the existence of a real correlation between vascular damage and degenerative and demyelinating neurological diseases.

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