

Chronic cerebrospinal venous insufficiency

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Chronic cerebrospinal venous insufficiency (CCSVI) syndrome has been described only recently.¹ It is characterized by stenosis of the internal jugular and/or azygous veins with opening of collaterals and insufficient cerebrospinal venous drainage.^{1, 2}

Abnormal stenosing lesions have been demonstrated by means of gold standard catheter venography.¹ As far as the origin is concerned, they resemble truncular malformations well known and described in other venous segments; CCSVI malformations are currently inserted in the Consensus Document of the UIP on Venous Malformations.^{3, 4}

CCSVI entity rises a strong interest among vascular experts, vascular technicians, interventional radiologists and vascular surgeons because of promising results of endovascular treatment, quite recently described in two pilot studies.^{5, 6} For the strong association found between CCSVI and multiple sclerosis (MS), the most common disease causing disabilities in young people, there is an increasing interest in the neurological and neuroradiological community as well.^{1, 2, 7} Interestingly, in 1937 Putman⁸ proceeded to study the effect of obstructed venous flow in the cerebral veins of dogs. These animals developed a number of abnormalities many of them similar to encephalitis or multiple sclerosis. In this issue of *International Angiology*, Ashton Embry proposes to integrate the pathophysiologic and molecular consequences of impaired venous drainage of the brain into the current autoimmune model of MS.⁹

Brain pathophysiology is significantly modified by the presence of extracranial venous obstruction.

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Cerebrospinal fluid dynamics is the mirror of CCSVI, since reabsorption is of course hampered at the level of the dural sinus in consequence of the slight but significant increase of venous pressure.⁹ Redistribution of cerebrospinal fluid and brain volume in the skull is associated with the hemodynamic severity of CCSVI.^{10, 11}

The vascular community is familiar with the increased iron deposition in the distal part of the legs causing skin pigmentation as a consequence of chronic venous insufficiency.¹² This issue of *International Angiology* includes two papers by US authors on the higher iron levels in the basal ganglia of patients affected by CCSVI and MS, the most distal territory drained by the parenchymal veins.^{13, 14} A role for CCSVI in MS is consistent not only with the well known perivenular distribution of MS lesions, but also with recent studies that have found a central vein in the long axis of inflammatory MS lesions using ultra-high field magnetic resonance imaging (MRI) and abnormally high levels of redox active metals, particularly iron, identified with a MRI technique called susceptibility-weighted imaging. This is a new and sophisticated MRI technique developed by Mark Haacke in Detroit, capturing the interest of the neuroradiologists in this new field. It seems that CCSVI will determine some changes in the MRI assessment of MS, in order to identify aspects related to venous function.

This issue presents also some papers on the symptomatology, neurophysiology and topography of plaque distribution related to the association of CCSVI with MS by Malagoni, Plasmati and Bartolomei.¹⁵⁻¹⁷

Duplex scanning is the perfect tool for screening for CCSVI. It provides information on the prevalence of CCSVI at different geographical regions and among populations with different

genetic backgrounds. For instance, the prevalence ranges between 56% and 100%, indicating that CCSVI is one of the major risk factors for the development of MS.^{1, 18-20}

The reliability of Duplex also challenges MR venography, showing a better diagnostic accuracy.²¹ Such surprising result is explained by the nature of venous obstruction. In the majority of cases there are septa, flaps, inverted, fixed, malformed valves, that cannot be crossed by venous flow despite the activation of the respiratory pump and/or changes in patient posture. Indeed, the subject investigated for CCSVI cannot be of course diagnosed by means of MR venography because 1) cannot be performed under respiration and rapid change in posture; 2) intraluminal defects disturbing venous flow cannot be seen 3) the azygous vein cannot be properly investigated because of heart movements. Finally, the application of vascular ultrasonography in this field appears reproducible, but due to the operator dependency of this cost effective diagnostic technique, specific training is needed.²²

This issue of International Angiology is providing a comprehensive update on CCSVI, publishing peer review articles coming from several teams that have been the first to investigate such a new, controversial, and fascinating interdisciplinary vascular disease.

References

- Zamboni P, Galeotti R, Menegatti E, Malagoni AM, Tacconi G, Dall'Ara S *et al.* Chronic cerebrospinal venous insufficiency in patients with multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2009;80:392-9.
- Singh AV, Zamboni P. Anomalous venous blood flow and iron deposition in multiple sclerosis. *J Cereb Blood Flow Metab* 2009;29:1867-78.
- Lee BB, Bergan JB, Gloviczki P, Laredo J, Loose DA, Mattassi R *et al.* Diagnosis and treatment of venous malformations. A Consensus Document of the International Union of Phlebology. *Int Angiol* 2009;28:434-51.
- Lee BB, Lardo J, Neville R. Embryological background of truncular venous malformation in the extracranial venous pathways as the cause of chronic cerebrospinal venous insufficiency. *Int Angiol* 2010 [In press].
- Zamboni P, Galeotti R, Menegatti E, Malagoni AM, Giancesini S, Bartolomei I *et al.* A prospective open-label study of endovascular treatment of chronic cerebrospinal venous insufficiency. *J Vasc Surg* 2009;50:1348-58.
- Zamboni P, Galeotti R, Weinstock-Guttman B *et al.* Endovascular treatment for chronic cerebrospinal venous insufficiency in multiple sclerosis. A longitudinal pilot study. Abstract presented at the 22nd Annual Meeting American Venous Forum, Amelia Island, FL, USA; 2010 February 10-13.
- Khan O, Filippi M, Freedman M, Barkof F, Dore-Duffy P, Lassman H *et al.* Chronic cerebrospinal venous insufficiency and multiple sclerosis. *Ann Neurol Early View* (Internet). [cited 2010 March 9]. Available from: <http://www3.interscience.wiley.com/cgi-bin/fulltext/123283159/PDFSTART>
- Putnam JJ. Studies in multiple sclerosis: encephalitis and sclerotic plaques produced by venular obstruction. *Archives of Neurology and Psychiatry* 1935;33:929-40.
- Embry AF. Integrating CCSVI and CNS Autoimmunity in a Disease Model for MS. *Int Angiol* 2010;2
- Zamboni P, Menegatti E, Weinstock-Guttman B, Schirda C, Cox JL, Malagoni AM *et al.* The severity of chronic cerebrospinal venous insufficiency in patients with multiple sclerosis is related to altered cerebrospinal fluid dynamics. *Functional Neurology* 2009;24:133-8.
- Zamboni P, Menegatti E, Weinstock-Guttman B *et al.* CSF Dynamics And Brain Volume In Multiple Sclerosis Are Associated With Extracranial Venous Flow Anomalies: A Pilot Study. *Int Angiol* 2010;2:
- Bergan JJ, Schmid-Schonbein GW, Smith PD, Nicolaidis AN, Boisseau MR, Eklof B. Chronic venous disease. *N Engl J Med* 2006;355:488-98.
- Haacke EM, Garbern J, Miao Y *et al.* Iron stores and Cerebral Veins in MS Studied by Susceptibility Weighted Imaging (SWI). *Int Angiol* 2010;2
- Zivadinov R, Schirda C, Dwyer MG *et al.* Chronic cerebrospinal venous insufficiency and iron deposition on susceptibility weighted imaging in patients with multiple sclerosis: a pilot case-control study. *Int Angiol* 2010;2:
- Malagoni AM, Galeotti R, Menegatti E *et al.* Is Chronic Fatigue The Symptom Of Venous Insufficiency Associated With Multiple Sclerosis? A Longitudinal Pilot Study. *Int Angiol* 2010;2:
- Plasmati R, Pastorelli F, Fini N *et al.* Chronic cerebrospinal venous insufficiency: report of transcranial magnetic stimulation follow-up study in a patient with multiple sclerosis. *Int Angiol* 2010;2:
- Bartolomei I, Salvi F, Galeotti R *et al.* Hemodynamic patterns of chronic cerebrospinal venous insufficiency in multiple sclerosis. Correlation with symptoms at onset and clinical course. *Int Angiol* 2010;2:
- University of Buffalo. First blinded study of venous insufficiency prevalence in MS shows promising results. Press release. February 10, 2010. [cited 2010 March 9]. Available at: <http://www.buffalo.edu/news/10937>
- Simka M, Kostecki J, Zaniewski M *et al.* Extracranial Doppler sonographic signs of chronic cerebrospinal venous insufficiency in the patients with multiple sclerosis. *Int Angiol* 2010;2:
- Ma'moon HA, Rousan LA. Internal jugular vein morphology and haemodynamics byb-mode and colour doppler sonography in patients with multiple sclerosis. *Int Angiol* 2010;2:
- Menegatti E, Genova V, Tessari M *et al.* The reproducibility of colour doppler in chronic cerebrospinal venous insufficiency associated with multiple sclerosis. *Int Angiol* 2010;2:
- Hojnacki D, Zamboni P, Lopez-Soriano A *et al.* Use of neck magnetic resonance venography, Doppler sonography and selective venography for diagnosis of chronic cerebrospinal venous insufficiency. A pilot study in multiple sclerosis patients and healthy controls. *Int Angiol* 2010;2:

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