C. ALLEGRA - P.L. ANTIGNANI

Proceedings of the 21st EUROCHAP - IUA European Chapter Congress of the International Union of Angiology

Rome, Italy
(September 28 - October 1, 2013)

EDIZIONI MINERVA MEDICA

C. ALLEGRA - P.L. ANTIGNANI

Proceedings of the

21st EUROCHAP - IUA European Chapter Congress of the International Union of Angiology

Rome, Italy
September 28 - October 1 2013

EDIZIONI MINERVA MEDICA
TURIN 2013

Incidence of anatomical compressions of the internal jugular veins with full block of their flow in patients with chronic cerebro-spinal venous insufficiency and multiple sclerosis

S. Mandolesi [1], E. Manconi [2], T. Niglio [3], A. D'Alessandro [4], A. Orsini [5], D. Mandolesi [6], F. Fedele [1]
[1]Department of Cardio-vascular and Respiratory Sciences, Sapienza University, Rome, Italy
[2]Department of Cardiovascular and Neurological Sciences, University of Cagliari, Italy
[3]Istituto Superiore di Sanità
[4]Ospedale "Masselli-Mascia", San Severo (FG), Italy
[5]Gioia Hospital, Sora (FR), Italy
[6]Medicina del lavoro Sapienza, Rome, Italy

Aim

Multiple sclerosis (MS), the most common neurological disorder in young adults, is traditionally considered to have autoimmune determinants.[1] The multistep mechanism of the disease involves inflammation, demyelination, and neuro-degeneration of the central nervous system.[1-3] Interestingly, from the time of the first histological description by Charcot, MS plaques are known to be venocentric.[2, 4] Both magnetic resonance imaging (MRI) venography [5-9] and post-mortem studies show a central vein oriented on the long axis of the inflammatory lesion.
In addition, as in several neurodegenerative disorders, the brain and spinal cord of MS patients contain abnormally high levels of redox-active metals, particularly iron,[10] documented by advanced MRI [1, 12] and enhanced histo-chemical methods.[13, 14]
There are several diagnostic tools to identify the different MS types.[1, 2, 18-20] Magnetic resonance imaging (MRI) of the brain and spine shows areas of demyelination (lesions or plaques) in the absence or in the presence of gadolinium.[21, 22] Analysis of cerebrospinal fluid may provide evidence of chronic inflammation of the central nervous system by showing oligo-clonal bands of IgG,[23] while evoked potentials study putative demyelination of the optic and sensory nerves.[24] A clear demonstration of a topographic correspondence between Multiple Sclerosis plaques and the cerebral venous system has been shown by magnetic resonance venography (MRV) [7, 25] and post-mortem studies.[26]
Such new nosological vascular pattern, defined as chronic cerebrospinal venous insufficiency (CCSVI), is strongly associated with MS.[27] CCSVI is characterized by multiple stenosis/obstructions affecting the principal extra-cranial outflow pathways of the cerebrospinal venous system, the internal jugular veins (IJVs) and the azygos vein (AZY), distributed in four main hemodynamic patterns.[29] Furthermore, CCSVI determines significant changes in cerebral venous hemodynamic, with a very high incidence of reflux in both intra- and extra-cranial venous segments as well as loss of the postural regulation of cerebral venous outflow.[29-32] Recently, Zamboni suggested five echo-color-Doppler (ECD) venous criteria that characterize this syndrome.[35] The presence of two of them is enough to diagnose CCSVI.
We created a software to collect morphological venous anomalies and hemodynamic ECD data named Morphological Hemodynamic Map (www.mem-net.it, Figure 1). WE designed an algorithm for data analysis of patients with CCSVI, following Zamboni's ultrasound criteria.[27-31-35] First we identified in CCSVI patients , by using such hemodynamic morphological map (MEM-net), the compression syndrome of IJVs (Mandolesi *et al*. 2011). This study provides the hemodynamic basis for an more appropriate assessment of our new CCSVI classification.

Methods

We investigated from 2010 by echo-color-Doppler (ECD) 789 patients with CCSVI and MS (490 females, 299 males), mean age 45.4. We found 728 positive and 61 negative for CCSVI. Morphological and hemodynamic ECD data were recorded by a computerized MEM-net maps , and they were analyzed by MEM-net Clinical Analysis programs (Table I). Furthermore, the patients were divided into two groups, the first one with intravenous anomalies and the second one with extrinsic vein compression according to our classification of IJVs Compression Classification shown below.

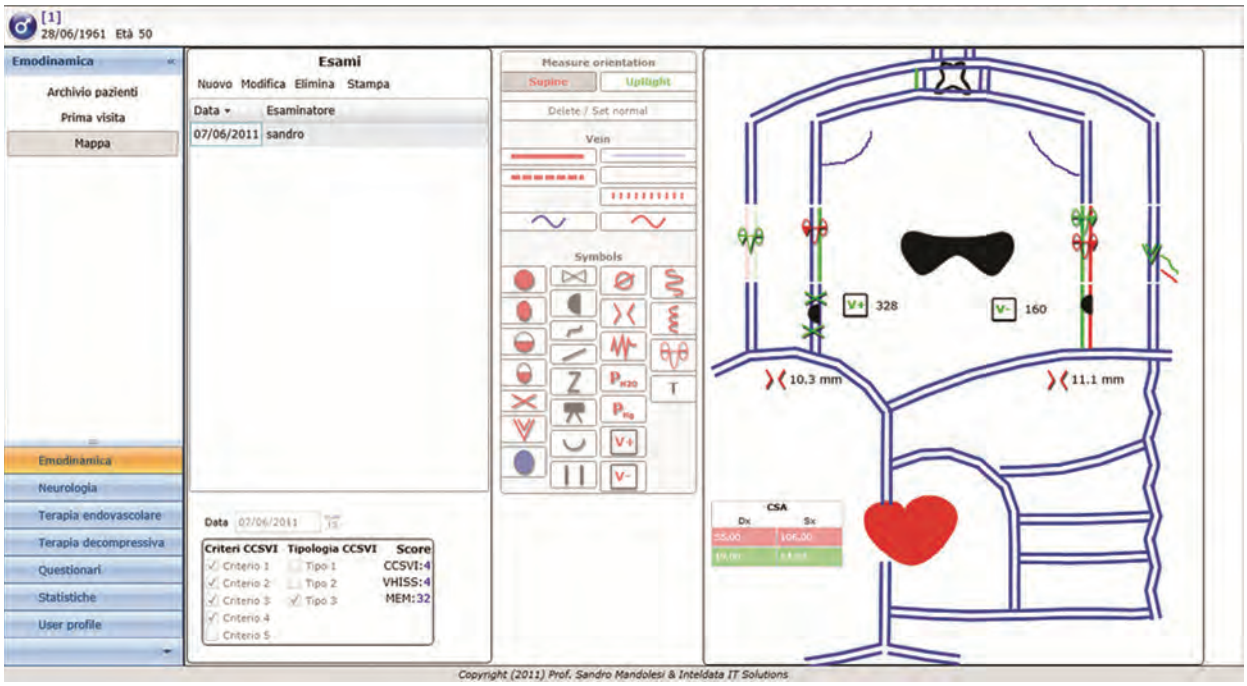

Figure 1. – Morphological Hemodynamic Map (MEM) scheme representing pattern of ECD venous cerebrospinal drainage, CCSVI types, hemodynamic severity score and patient data.

Echo-color Doppler (ECD) assessment of cerebral venous hemodynamics

The patients underwent a non-invasive study of cerebral venous return. A combined trans-cranial and extra-cranial ECD provided valid measures of venous hemodynamic (VH) parameters enabling an assessment of CCSVI cerebral venous return. The subjects were investigated in both supine and standing positions (0° and 90°) in consideration of the postural effect on the main route of cerebral outflow. We focused on the detection of three anomalous VH patterns affecting cerebral venous return according to the Zamboni's criteria and our CCSVI types Classification.[27-31]

Beside the Zamboni's criteria our population was studied using new hemodynamic patterns to complete the evaluation of the cerebro-spinal venous drainage: the venous compression of the IJVs and/or VVs not visible in supine and/or standing posture. We define venous compression as a normal vein not visible with ultrasound, because collapsed, which may expand with neck position changes and/or Valsalva maneuver such a vein presents a block of blood flow. In all our ECD assessments we performed the following ECD dynamic tests: neck movements, on right, on left rotation and anterior/ posterior intrusion of the neck; Valsalva's maneuver, performed by moderately forceful attempted exhalation against a closed airway, usually done by closing one's mouth and pinching one's nose shut.

According to these new hemodynamic parameters, we classified our patient population in three different CCSVI types. Block and/or stenosis and/or reflux of the IJVs and DCVs as Type-1; compression of the IJV and/or VV not visible as Type-2. The mixed form composed by patients with block and/or stenosis of IJVs and/or reflux of the IJVs and DCVs and compression of the IJVs and/or VVs not visible as Type-3. These parameters were used to draw up our algorithm.

Our center designed and developed for the first time the Morphological Hemodynamic Map (MEM) of the CCSVI. The MEM is made by a scheme reproducing the intracranial and extra-cranial venous circulation. The operator can insert in a few seconds different symbols to define the aforementioned hemodynamic conditions and also venous anomalies including hypoplasic veins, veins with stiffness of walls (not compliant), septum, membrane, web, annulus, twist and valve stiffness. The collected ECD data were analyzed by MEM-net software (www.mem-net.it), which includes the data analysis algorithm.

We utilized morphological and hemodynamic symbols of Consensus Conference of National Epidemiological CCSVI Observatory February 2013 (Table I).

According to Consensus Conference we subdivided the vein compression in two type : white and black compression. The compression is defined white when the vein is completely compressed and we can not detect any flow by ECD. The compression is defined

Table I. – Symbols and terminology to be used in reporting on map EchoColorDoppler examination of the veins draining the brain (Consensus Conference of National Epidemiologic CCSVI Observatory -2013).

	Symbol	Description	MEM Score
	Calcification	Endo or extra vascular	0
	Full block	When the block involve one or more segments with caliber equal or greater than the previous level or the following level	2
	Empty block	When the block involve one or more segments with caliber much lesser than the previous level or the following level	2
	Emi Full block	When the time of the drainage flow detected by Pulsed Doppler is longer than the stop flow on one or more segments with caliber equal or greater than the previous level or the following level	1
	Emi empty block	When the time of the drainage flow detected by the Pulsed Doppler is longer than the stop flow on one or more segments of size much smaller than the previous level or the following level	1
	Morphological stenosis	Organic stenosis <3 mm^2	2
	Stenosis Hemodynamics	Flow velocity >150 cm/s	2
	Membrane	Hyperechoic area endovascular	1
	Septum	Abnormal valve leaflet	1
	Thickening	Valvular thickening	1
	Twist	Twisting of the vessel	1
	Vicarious	Flow vicarious >45 cm/s on vertebrals (V2) in clino and > 60 cm/s in orto - >100 cm/s on the Internal jugulars (J2) both in clino and ortostatic position	1
	Ectasia	Vessel diameter more than 20 mm	1
	Confluence	Thickening of the confluence of jugular to subclavian	1
	Thickening-dyspasia	Thickening (dysplasia) of the vessel wall	1
	Thrombosis	Thrombosed segment	2
	Recanalization	Recanalization with parietal residues	1
	White compression	The compression is defined white when the vein is completely compressed and we cannot detect any flow	2 x each white
	Frontal		
	Right lateral		
	Left lateral		
	Back protusion		
	Black compression	The compression is defined black when the caliber of the vessel is less than 6 mm^2 and shows a flow	1 x each black

	Frontal
	Right lateral
	Left lateral
	Antero protusion

In the upright position the symbol is green. Compressions can be detected through the head in the front and/or side position right and / or left lateral position

	Vase accessory	Collateral vessel visible but with physiological flow	1
	Net	reticular image into vessel lumen	0
	Reflux	Reverse, retrograde, anti physiological flow > 0.8 s	2
	Emi-Reflux	Bidirectional flow	1
	Hypoplasia	Vase with diameter of less than 6mm	2
	Ipovisibile	EDC hypo- visible flow with PRF 0.7	1
	Invisible	ECD not visible flow with PRF 0.7	2
	Vessel accessory pathological supine and Ortho	Collateral vessel with reverse, retrograde, anti physiological flow	2
D	double channel	EDC anechoic area	2
Functional stenosis	Equivalent to hemodynamic stenosis	Presence of morphological abnormalities and reflux or two-way flow or block on the same vein	2

SYMBOLS FOR MEASURES

	Caliber	Size in mmq
	Pressure	Measurement of pressure in mmHg
	Pressure	Measurement of pressure in cmH_2O
	Velocity	Measurement of velocity in cm / s
	Valsalva+	Valsalva Test positive
	Valsalva-	Valsalva Test negative
	Diameter	Measurement in mm

ADDITIONAL SYMBOLS

	Free text
	Thyroidectomy
	Nodules

RESPIRATORY HAEMODYNAMIC INDEX OF MANCONI

CSA in J2 inspiratory phase	Normally is reduced by at least 30% of expiratory CSA
CSA in subclavian inspiratory phase	Normally is reduced by at least 30% of expiratory CSA
Speed flow in J2 inspiratory phase	At least doubled compared to the previous inspiration speed
Speed flow in subclavian inspiratory phase	At least doubled compared to the previous inspiration

black when the caliber of the vessel is less than 6 sq. mm and shows a flow by ECD examination. Compressions can be detected through the head in the front and / or right and / or left lateral position. These types of compression can be find at different level of IJVs (J1, J2 and J3) or at V2 and V3 level of VVs were the veins are not visible by ECD.

Statistical analysis

All data were analyzed by SPSS software with a stratified data description for numeric and non-numeric variables. Statistical significance "between" and "within" groups was calculated on continuous variables by the analysis of variance (ANOVA) to test the equality of means. The Chi-square Yates corrected test was used for non-continuous variables by Statcalc and Analysis programs from Epi-Info. A p value <0.05 was considered significant, and 95% confidence intervals were also calculated.

Results

The analysis of the internal jugular veins showed: the block of the drainage by endovascular causes in 222 patients supine and in175 in the upright (54% of total). The block of the drainage by extrinsic compression in 116 patients supine and in 232 in the upright (48% of total). We found a significant increase of Internal Jugular Veins compressions on changing position from supine to orthostatic Table II.

When the patient turned the head to the right and left we found the compression of the IJVs (at J2) as shown in Table III. The complete compression of the jugular veins in the front position (48% of the sample) are equally distributed on the various segments assessed (J1-J2-J3). Bilateral compressions are present in 7% of sample Table IV. The passage from the supine to upright position shows a double increase of compressions. The homo-lateral head rotation to the investigated vessel shows a significant increase of the extrinsic compressions from 7 to 9 times compared to contralateral side rotation.

Discussion

Recently some case reports about the resection of the omohyoid muscle for the treatment of vein compression syndrome of the internal jugular veins have been published in the literature.[37, 38] This muscle crosses the deep layers on the middle part of the internal jugular veins. It lowers the hyoid bone. We think that it is not enough the simple resection of the omohyoid muscle for a decompression treatment of the internal jugular veins, but should be regarded as additional possibilities. The scalene muscle can be the cause for the compressions mainly the J1 terminal segment of the internal jugular vein. The sterno-mastoid muscle mainly interested in compressions at the level J3 of the internal jugular vein where it overlaps with the internal carotid artery and it can be pinched. The altered posture with dislocation of C1-C2 with or without associated rotation of the cervical vertebrae can act more distally:

1. tensing the middle fascia with compression of the vascular-nervous loggia of the neck;
2. blocking the discharge of the vertebral veins;
3. hindering the discharge of J3 after the jugular hole.[39]

To put a surgical indication for decompressive surgery it is necessary to identify which are the tests both with dynamic postural-ECD and during venography that allow us to identify, with sufficient certainty, which of the conditions outlined above is the cause of the vein compression syndrome.

The compression syndrome of the veins draining the brain, in our ECD data, can affect only a vessel that be bilateral. It can affect both the jugular and vertebral veins and be detectable either supine that in the standing position or in both positions. All of these variables make rather difficult to assess preoperative indication to the right decompression treatment.

Our preliminary results by manipulative treatments in patients with compressive syndromes of the internal jugular veins and/or vertebral veins associated with C1-C2 misalignment has been positive and encourages us to practice a upright TC scanner assessment of the first

Table II. – Shows the incidence of Internal Jugular Veins compressions in supine and orthostatic position at J1, J2 and J3 level.

	Right clino	Right orto	Left clino	Left orto
J3	25	65	28	80
J2	42	92	50	105
J1	16	39	7	34

Table III. – Shows the incidences of Internal Jugular Veins compressions during neck rotations.

	Right rotation	Left rotation
J2Dx	211	32
J2Sn	30	286

Table IV. – Shows the incidence of bilateral Internal Jugular Veins compressions in supine and orthostatic position.

	R+L clino+orto	R+L clino	R+L orto
J2	54		
J2		15	
J2			33

two cervical vertebrae in these patients with CCSVI. Our current effort is the identification of specific postural tests that allow us to put an right indications either physiotherapeutic that surgical in patients with venous compression syndromes of the veins draining the brain.

References

1. Compston A, Coles A. Multiple sclerosis. Lancet 2002;359: 1221-31.
2. Barnett MH, Sutton I. The pathology of multiple sclerosis: a paradigm shift. Curr Opin Neurol 2006;19:242-7.
3. Frohman EM. Multiple sclerosis - the plaque and its pathogenesis. N Engl J Med 2006;354:942-55.
4. Charcot J. Histologie de la sclerose en plaques. Gazette des Hopitaux, Paris 1868;41:554-5.
5. Kermode AG, Thompson AJ, Tofts PD *et al.* Breakdown of the blood brain barrier precedes symptoms and other MRI signs of new lesions in multiple sclerosis: pathogenetic and clinical implications. Brain 1990;113:1477-89.
6. Kidd D, Barkhof F, McConnell R *et al.* Cortical lesions in multiple sclerosis. Brain 1999;122:17-26.
7. Tan IL, van Schijndel RA, Pouwels PJ. MR venography of multiple sclerosis. Am J Neuroradiol 2000;21:1039-42.
8. Fog T. Vessel-plaque relationships and CSF and brain tissue changes in multiple sclerosis. Acta Neurol Scand 1964;40:9-15.
9. Fog T. The topography of plaques in multiple sclerosis with special reference to cerebral plaques. Acta Neurol Scand Suppl 1965;15:1-161.
10. Sayre LM, Moreira PI, Smith MA *et al.* Metal ions and oxidative protein modification in neurological disease. Ann Ist Super Sanita 2005;41:143-64.
11. Haacke EM, Cheng NYC, Michael JH *et al.* Imaging iron stores in the brain using magnetic resonance imaging. Mag Reson Imaging 2005;23:1-25.
12. Tjoia CW, Benedict RH, Weinstock-Guttman B *et al.* MRI T2 hypointensity of the dentate nucleus is related to ambulatory impairment in multiple sclerosis. J Neurol Sci 2005;234:17-24.
13. Sayre LM, Moreira PI, Smith MA *et al.* Metal ions and oxidative protein modification in neurological disease. Ann Ist Super Sanità 2005;41:143-64.
14. LeVine SM, Chakrabarty A. The role of iron in the pathogenesis of experimental allergic encephalomyelitis and multiple sclerosis. Ann N Y Acad Sci 2004;1012:252-66.
15. Reingold SC. Defining the clinical course of multiple sclerosis: results of an international survey. National Multiple Sclerosis Society (USA) Advisory Committee on Clinical Trials of New Agents in Multiple Sclerosis. Neurology 1996;46:907-11.
16. Compston A, Coles A. Multiple sclerosis. Lancet 2008;372: 1502-17.
17. Miller DH, Leary SM. Primary-progressive multiple sclerosis. Lancet Neurol 2007;6:903-12.
18. Trojano M, Paolicelli D. The differential diagnosis of multiple sclerosis: classification and clinical features of relapsing and progressive neurological symptoms. Neurol Sci 2001;22:98-102.
19. McDonald WI, Compston A, Edan G *et al.* Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the diagnosis of multiple sclerosis. Ann Neurol 2001;50:121-7.
20. Polman CH, Reingold SC, Edan G *et al.* Diagnostic criteria for multiple sclerosis: 2005 revisions to the McDonald Criteria. Ann Neurol 2005;58: 840-6.
21. Rashid W, Miller DH. Recent advances in neuroimaging of multiple sclerosis. Semin Neurol 2008;28:46-55.
22. Ge Y, Zohrabian VM, Grossman RI. Seven-Tesla magnetic resonance imaging. New vision of microvascular abnormalities in multiple sclerosis. Arch Neurol 2008;65:812-16.
23. Link H, Huang YM. Oligoclonal bands in multiple sclerosis cerebrospinal fluid: an update on methodology and clinical usefulness. J Neuroimmunol 2006;180:17-28.
24. Gronseth GS, Ashman EJ. Practice parameter: the usefulness of evoked potentials in identifying clinically silent lesions in patients with suspected multiple sclerosis (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2000;54:1720-5.
25. 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;29:127-39.
26. Geurts JJ, Bö L, Pouwels PJ *et al.* Cortical lesions in multiple sclerosis: combined postmortem MR imaging and histopathology Am J Neuroradiol 2005;26:572-7.
27. Zamboni P, Galeotti R, Menegatti E *et al.* Chronic cerebrospinal venous insufficiency in patients with multiple sclerosis. J Neurol Neurosurg Psychiatry 2009;80:392-9.
28. Zamboni P, Menegatti E. Doppler haemodynamics of vertebral venous return Curr Neurovasc Research 2008;5:260-5.
29. Zamboni P, Menegatti E, Galeotti R *et al.* The value of cerebral Doppler venous hemodynamics in the assessment of multiple sclerosis. J Neurol Sci 2009;282:21-7.
30. Zamboni P, Menegatti E, Bartolomei I *et al.* Intracranial venous hemodynamics in multiple sclerosis. Curr Neurovasc Res 2007;4:252-8.
31. Franceschi C. The unsolved puzzle of multiple sclerosis and venous function. J Neurol Neurosurg Psychiatry 2009;80:358.
32. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology 1983; 33:1444-52.
33. Zamboni P, Galeotti R, Menegatti E *et al.* A prospective open-label study of endovascular treatment of chronic cerebrospinal venous insufficiency. J Vasc Surg 2009;50:1348-58.
34. Simka M, Majewski M, Fortuna M *et al.* Internal jugular vein entrapment in a multiple sclerosis patient. Case Rep Surg 2012;2012:293568.
35. Zamboni P, Morovic S, Menegatti E *et al.* Screening for chronic cerebrospinal venous insufficiency (CCSVI) using ultrasound--recommendations for a protocol. 2011;30:571-92.
36. Mandolesi S, Ciciarello F, Marceca A *et al.* Data analysis of the chronic cerebro-spinal venous insufficiency in patients with multiple sclerosis: new disease classification. 72° Congresso Nazionale della Società Italiana di Cardiologia, Roma, 10-12 Dicembre 2011.
37. Simka M, Majewski M, Fortuna M *et al.* Internal jugular vein entrapment in a multiple sclerosis patient. Case Rep Surg 2012;2012:293568.
38. Gianesini S, Menegatti E, Mascoli F *et al.* The omohyoid muscle entrapment of the internal jugular vein. A still unclear pathogenetic mechanism. Phlebology 2013 May 16. [Epub ahead of print].
39. Seoane E, Rhoton AL Jr. Compression of the internal jugular vein by the transverse process of the atlas as the cause of cerebellar hemorrhage after supratentorial craniotomy. Surg Neurol 1999;51:500-5.