Diagnosis of CCSVI in Meniere syndrome

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PURPOSE: *The authors have evaluated by ultrasound the CCSVI in Meniere's Disease.*
MATERIALS AND METHODS: *140 patients with diagnosis of Meniere's Disease, who have had not improvement to usual therapy, underwent echo color Doppler sonografy by Zamboni's protocol for the diagnosis of CCSVI . 128 were positive.*
RESULTS: *Ultrasound diagnosis of CCSVI was performed in patients with Meniere's Disease with a positivity in 128 patients on 140 examinated (90% of cases). In healthy population the presence of CCSVI has been evident in 3% of cases.*
CONCLUSIONS: *There is a significant prevalence of CCSVI in patients with Meniere's Disease*

KEY WORDS: CCSVI, Duplex US, Menière Disease, Multiple Sclerosis

Introduction

Menière's Disease (MD) is an inner ear disease characterized by dizziness, hearing loss, tinnitus and fullness with a prevalence of 0.5/100.000 of the population [3-7]. In Scandinavian Countries the incidence is of 430 cases per million people, reaching the highest percentage in England with 1.000 cases per million people. 5000 are the patients estimated effected by the disease in Italy [7]. Although it was described in 1861 by Prospero Menière for the first time [1], at the moment a certain etiology is still unknown [3].
The diagnostic level of the disease course, when is required the autopsy findings, when possible, in which the association of symptoms and clinical signs is quite labile [5].

The MD is characterized by the triad dizziness, tinnitus and hearing loss that is often associated with a sensation of ear filling, with a clinical course of relapsing, with fluctuations in auditory (initially large and dizzy acute crisis lasting tens of minutes to hours) with a negative impact on patient's quality life, particularly during the acute vertigo [3-35]. Usually the beginning is unilateral, but over the years the disease can also affect the other ear with relapsing-remitting "pattern". Often it become bilateral, in long term follow up, happens in approximately 40% of cases, but the majority of them takes place in the first 5 years; hearing ability between a crisis and the other, is reintegrated in the early stages, but over the years gradually deteriorates, usually stabilizing at levels of moderate to severe hearing loss 3-35.
The labyrinth function also undergoes progressive deterioration, which is dominated by Tumarkin's otolithic crisis and chronic instability symptoms [25].
For the physiopathology of M.D. several hypotesis have been made, in which we do not enter: genetic predisposition[26]; autoimmunity[26]; blockage of drainage /increase of endolymphatic fluid production [27,35]; anatomical variants

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Abbreviations

CCSVI: Chronic CerebroSpinal Venous Insufficiency
MD: Meniere's Disease
MS: Multiple Sclerosis

of inner ear [31]; alteration of endocrine system (adh, aquaporine system, prolactine) [5,28,35]; viral infection [14]; allergy [29]; abnormal vascular system [25,30, 36,41,42]; trauma [32].
The alterations would define the situation of endolymphatic hydrops with symptoms that characterizes this disease. In this regard, it should be remembered that the Merchant hypothesis attaches considerable importance to the phenomena of cytotoxicity from which derives the dropsical situation: we will see how this theory can be a useful substrate for the possible alterations induced by situations of CCSVI in Menier's ear [4,5,35].
The onset is mainly between the third and fourth decade of life, the diagnosis is usually smooth [3-6], with initial differential diagnosis with neurimoma of the VIII [3]. The hearing, initially fluctuating, is a sensory; instrumental diagnosis relies on tonal and vocal audiometric examination, vestibular examination, Auditory Evoked Potentials, of vestibular evoked myogenic potentials, electrocochleography, [12] glycerol test and of inner ear CT scan to exclude situations of dehiscence of the bone capsule of the labyrinth or endolymphatic fistulas, but also to highlight possible structural alterations [42]; MRI brain focused to exclude the acoustic-facial neurinoma of VIII [3-5].
MRI during angiographic phase should rule out the presence of neurovascular conflict situations on cranial nerve VIII [3,5].
CT scan and MRI 3T show a decreased vestibular aqueduct width and length compared with test patients, which would suggest that there is a morphological modification of it [3,5].
For several years is described the possibility of hydrops demonstration by high-field MRI (3T) with gadolinium injection both e.v. and intratympanic [33,34,36]. This finding, although not yet routinely obtainable, makes it possible today to the diagnosis of MD degree in vivo, according to the 1995 AAO classification [5].
At the moment there is no definitive cure for Menière's Disease [3]. Relapsing dizziness if not controlled by medical therapy, it is treatable with conservative surgical methods, (endolymphatic sac surgery), or with chemical sublabirintectomy or intratympanic injection of gentamicin in the affected ear [34], or selective vestibular neurotomy. The predominant auditory symptoms or bilaterally active cases can be treated with intratympanic steroidotherapy [34]. Among these therapies, the gold standard in the control of vertiginous symptoms in cases of MD-sided, with success rates around 90%, it is definitive sublabirinthectomy with gentamicin, easy to perform and repeteable for several times, thanks to its poor cochlear toxicity, with the new "Titration"protocols [34].
In 2006 it was reported that patients with multiple sclerosis showed a high frequency of a modification of the veins that drain blood from the brain and the medullary apparatus, slowing down the flow and the formation of collateral circulation [2]. This condition, whose pathophysiological significance is not yet entirely clear and not accepted by everybody, has been identified with the acronym CCSVI (Chronic Cerebro Spinal Venous Insufficiency). These vascular abnormalities, slowing the venous outflow, would cause, in particular in the brain, a modification of the adhesion molecules mechanism at the endothelial barrier; this phenomenon would be due to an increased permeability of the blood-brain barrier [8,21-22]. The inflammation from it should lead the activated endothelium [45] to secrete pro-inflammatory cytokines, with secondary transformation of monocytes in antigenic elements which would cause an autoimmune action against nerve cell containing myelin [8,17,22,43,44].
Among the several methods proposed for the diagnosis of CCSVI, the most suited is the evalutation of the venous flows by Echo-Doppler, integrated with the Transcranial Doppler which also allows an assessment of the deep cerebral veins and any refluxes [9,16,-19-21]. Zamboni for this reason has established an ultrasonographyc protocol identifying 5 characteristic parameters of CCSVI [19-21]:
1. Presence of two-way flow in one or both of the internal jugular veins (IJV) and/or in the vertebral veins (VV) in both positions (supine and orthostatism) or bi-direc-

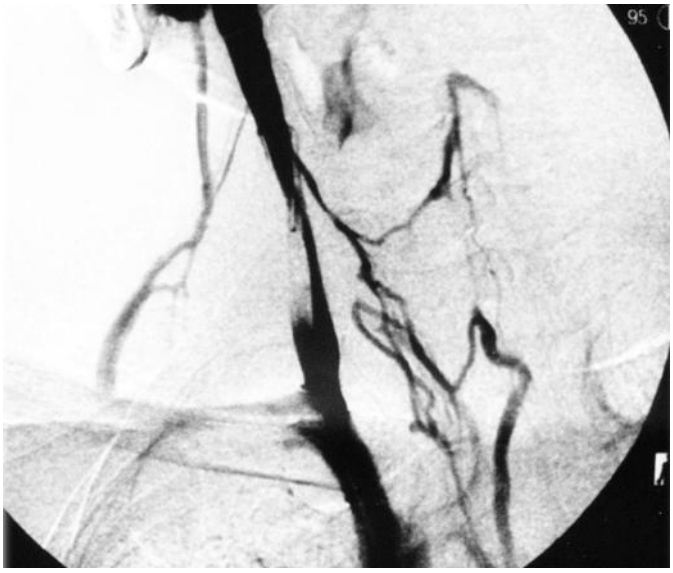

Fig. 1.

tional flow in a position with the absence of flow in the other;
2. Presence of two-way flow in the intracranial veins and breasts.
3. Visibility of intraluminal defects (flaps, septa or valvular defects) associated with hemodynamic changes (blocks, reflux or acceleration) and / or reduction of VGI in the supine position to 0.3 cm^2
4. Absence of flow in both the VGI and VV and / or absence of flow in one position and two-way flow in the other;
5. DCSA (area) of greater VGI or unchanged both 90° and 0°.

The aim of this work is to report our preliminary experience in the ultrasound diagnosis of CCSVI in patients with Menière' Disease.
At the moment there are only four works that have representatives who considered this correlation [37-40].

Materials and Methods

From April 2013 to July 2014 underwent to our observation 140 patients, 85 females, 55 Males aged 32 to 68 years with an average age of 46 aa, suffering of Meniere's disease clinically defined according to the criteria AAO 1995 [5] diagnosed in several Italian Divisions of Otolaryngology and Audiology. 80 patients suffered from monolateral and 60 from bilateral M.D. All patients had poor response to conventional treatment therapies (betahistine, cortisones, diuretics, loop diuretics osmotics, vasoactive etc..), with persistence of dizziness frequently relapsing. The enrolled patients underwent to neck and intracranial venous Echo-color-doppler examination according to Zamboni's method. The examination was performed in 100 healthy patients, not suffering from neurological disease or audiovestibular, of similar age to that of the population study.
The used device, My.Lab Vinco, was setup for the study of the venous vessels of the neck and intracranial circulation in patients with multiple sclerosis and the examination was carried out both in the position at 0° and 90°.

The used parameters were:
1. Bidirectional flow in one or both the IGV and / or the VV in both positions or bi-directional flow in one position with absence of flow in the other;
2. Bidirectional flow in the intracranial veins and sinuses;
3. Intralumuninal defects (flaps, septa or valves) associated with hemodynamic changes (blocks, reflux or acceleration) and / or reduction of the area of the IGV in the supine position to 0.3 cm /sq;
4. Absence of flow in the IGV and / or VV and / or absence of flow in one position and bidirectional flow in the other;
5. IGV DCSA increased or unchanged both at 90° to 0°

The positivity of at least two of these 5 parameters allowed the diagnosis of CCSVI.

Results

If in patients with multiple sclerosis, the incidence of CCSVI was assessed between 56% and 100% using the study protocol developed by Prof. Zamboni in patients with MD the incidence was in 45 patients (90% of cases) [9], with a presence of more severe lesions on the affected side in unilateral cases.
In patients with bilateral M.D. it has been noticed that the most affected side is the one with a history of a longer disease.
In the control population were detected abnormalities compatible with CCSVI in only three patients (3%) and none of them had diagnoses or symptoms due to a neurodegenerative disease or a Meniere's Disease.
The most detected lesions in B.Mode in the echo-Doppler have been:
– Annulus: circumferential stenosis of the entire vein;
– Septum: anomaly of the valves causing an obstruction of the outflow in the Junction of IGV with the brachiocephalic trunk;
– Membranes: In cases of parietal iperplasia with almost complete obstruction of the vessel;

Other injuries like:
– Hypoplasia: underdeveloped venous segments;
– Twist: rotation of the vein (mainly the azygos), which causes a severe stenosis of the vessel;

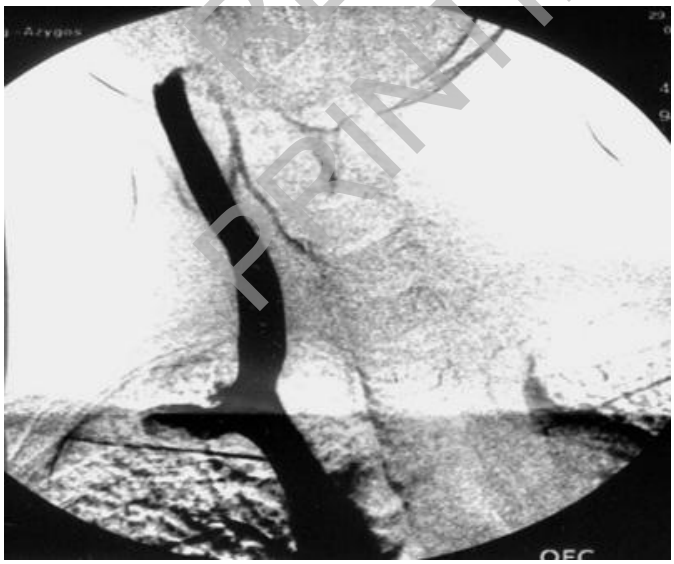

Fig. 2.

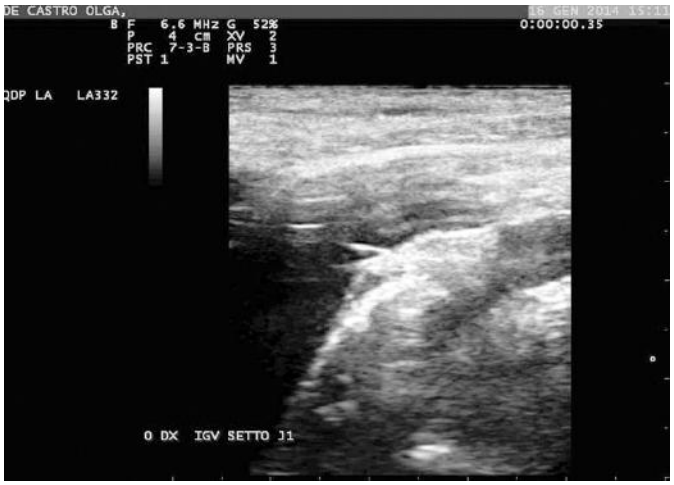

Fig. 3.

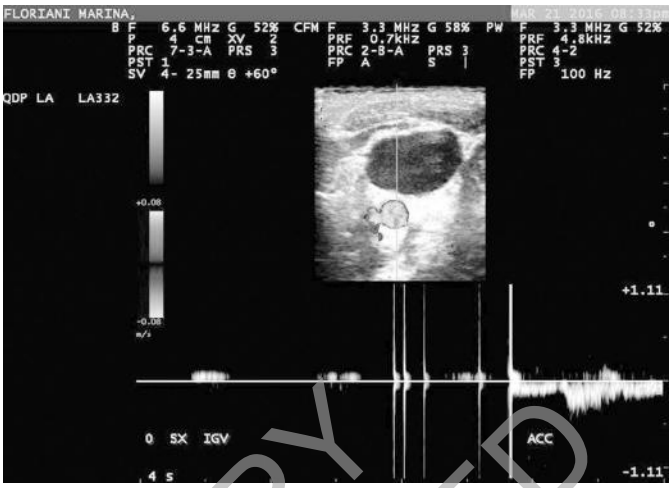

Fig. 4.

– Agenesis: complete absence of the venous segment.
Which can be observed in S.M. have not been highlighted.
The other parameters, however, were present in similar amounts to those shown in SM patients.
There were no hemodynamically significant compression of the patients studied.

Discussion

There is a high incidence of CCSVI in patients with Meniere's Disease clinically defined by a percentage unable to cast doubt on a random event in comparison with the incidence patients- control.
There is also a close correlation between the affected side and the presence of CCSVI and, in cases of bilateral disease, the side where the alterations of CCSVI are the most significant is the one where the MD first onset.
These patients presented lesions of VGI and VV malformations or stenosing similar to those characteristic of Multiple Sclerosis (CCSVI) with slowing of the cerebral venous outflow. The situation of CCSVI significantly alters the venous drainage from the brain system with a hypothetical cochlea-vestibular worsening of symptoms due to inflammatory and cytotoxic venous stasis that could arise in the inner ear.
The experience gained during this period has enabled a new ultrasonographic assessment of cerebral venous circulation so far not been performed in Meneric patients; this assessment and the identification of alterations in flow not present in normal subjects, it certainly offered a new perspective of possible pathogenetic interpretation of the disease, opening the way for a conservative treatment has so far not considered in the therapeutic strategy of Meneric Patients.

Riassunto

In questo lavoro gli autori hanno valutato la possibilità di diagnosticare l'insufficienza venosa cronica cerebro-spinale (CCSVI) nei pazienti affetti da sindrome di Meniére resistente alle terapie mediche.
Da aprile 2013 al luglio 2014 sono stati valutati 140 pazienti, 85 femmine, 55 maschi di età compresa tra 32 a 68 anni, con un'età media di 46 aa, affetti da sindrome di Meniere clinicamente definita secondo i criteri AAO 1995.
I pazienti sono stati sottoposti ad un esame eco-color-doppler delle vene del collo e dei vasi venosi intracranici secondo il metodo di Zamboni. L'esame è stato eseguito anche in 100 pazienti sani, non affetti da malattia neurologica o audiovestibolare, di età simile a quella dei pazienti arruolati nello studio.
L'incidenza della CCSVI, diagnosticata secondo il protocollo sviluppato dal Prof. Zamboni, nei pazienti con sindrome di Meniere è stata del 90%, con una presenza di lesioni più gravi sul lato interessato in casi unilaterali. Nella popolazione di controllo sono state rilevate anomalie compatibili con la CCSVI in soli tre pazienti (3%) comunque asintomatici.
Vi è un'alta incidenza di CCSVI nei pazienti con malattia di Meniere clinicamente definita, in una percentuale tale da mettere in dubbio un evento casuale, soprattutto data la bassa prevalenza nel gruppo di controllo.

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