The central vein sign for the differential diagnosis of multiple sclerosis: is it feasible in 3T MRI?

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Learning objectives

To evaluate the central vein sign (CVS) in the differential diagnosis of multiple sclerosis (MS) in 3T MRI and to present illustrative cases.
Background

Multiple Sclerosis (MS) is a chronic disease of the central nervous system (CNS) immune-mediated and demyelinating.

There is no diagnostic biomarker for MS, but MRI of the CNS can support, supplement or replace some clinical criteria to make the diagnosis.

The limited accuracy of the diagnostic criteria results in challenging cases and misdiagnosis, which are prevalent problems in MS [1,2].

The North American Imaging in Multiple Sclerosis (NAIMS) Cooperative Consensus has recently proposed, in 2016, the central vein sign (CVS) as a novel MRI biomarker to improve the accuracy and speed of multiple sclerosis diagnosis.

A substantial number of white matter lesions (WMLs) have venocentric distribution, in all MS clinical phenotypes. Eventhough the CVS is not exclusively found in MS-WMLs, evidences indicates that this sign may have the ability to accurately differentiate MS from mimicking conditions, including diseases with exacerbation, remitting periods and infectious diseases, which can mimic the MRI features [3,4].

A number of studies have shown that diseases such as Neuromyelitis optica, neurosyphilis and microangiopathic WMLs, which can present in a similar way to MS and have similar MRI scans, tend to have no (or very few) WML central veins [5-8].

Neuromyelitis optica (NMO) is the most common presentation of MS as a clinically isolated syndrome. Although NMO is a clinical diagnosis, imaging, especially magnetic resonance imaging, plays an important role in confirming the diagnosis and in contributing information to determine its prognosis. Studies on this pathology showed that only 35% of the white matter lesions were located in the vicinity of the vessels, but rarely centered on the blood vessels, of this percentage, only 9% were crossed by a central vessel, supporting the idea that the vein is a sensitive finding and magnetic resonance imaging is useful to differentiate Neuromyelitis Optical Sphygmomanometry (NMOSD) from MS [5,6].

In neurosyphilis, lesions related to the central nervous system are of immune origin. The findings of brain magnetic resonance imaging are not specific and no pathognomonic findings have been identified in the image. However, the occurrence of generalized cerebral atrophy and outbreaks of white matter signal intensity are commonly observed in these patient populations. The most frequently reported abnormalities of imaging are the middle cerebral artery and the branches of the basilar artery. There is also evidence that ischemic changes in MRI, increased mean contrast, atrophy, white matter lesions and edema may be, depending on the clinical scenario, indicative of neurosyphilis. In addition, several infarct areas in different vascular territories and at different stages of evolution
in young patients appear to be indicative of cerebral vasculitis. However, unchanged resonances are also frequently observed in patients with neurosyphilis. According to literature data, CVS is not observed in white matter lesions in patients with this isolated condition [5,6].

In cerebral vascular disease (CSVD), white matter lesions are venocentric in 45% of all lesions. This is due to the fact that CSVD affects small cerebral vessels, which may be related to numerous etiologies. Most of the time, it affects the white matter causing lesions that mimic MS lesions and may appear around a central vein. Several recent studies have consistently reported the proportion of a maximum of 45% lesions of perivenular white matter [10-14].

Many studies investigated CVS in MS, however, most of them used a 7T magnetic resonance scanner, not available in clinical practice for most services. We investigated the feasibility of evaluating this signal by 3T RM for the differential diagnosis of MS, since this scanner is widely used in radiology services and therefore plausible to be used in the evaluation of this signal in clinical practice as a tool to support the differential diagnosis and early treatment.
Findings and procedure details

According the North American Imaging in Multiple Sclerosis (NAIMS) Cooperative Consensus, structural imaging of small cerebral veins is best done using the T2*-based contrast mechanism, which exploits the magnetic properties of blood [15].

The image with a 7T scanner provides the highest sensitivity for central vein detection, however, 1.5T and 3T scanners can provide high rates (> 80%) of detection of this signal if optimized protocols are used [16, 17].

Sequences used to detect the central vein signal in the 3T magnetic resonance imaging include susceptibility-weighted images (SWI), T2*-weighted images and, more recently, an attenuated fluid inversion (FLAIR) and T2* fusion, referred to as FLAIR* [18]. This technique is suitable for the routine image of WMLs and optimizes the observation of WMLs (Figure 1).

Fig. 1: Compared to FLAIR, the FLAIR* and the SWI demonstrated the CVS more clearly. FLAIR*, in addition, better demarcated the WMLs.

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There is, however, no standardization of optimized MRI acquisitions.

In our center, we investigated the feasibility of evaluating this signal by 3T magnetic resonance for the differential diagnosis of MS using a 3T scanner to acquire the FLAIR and SWI sequences of the brain, and performed its fusion (FLAIR*) to compare the presence and distribution of CVS in white matter lesions (WMLs) in MS and mimicking conditions such as neuromyelitis, neurosyphilis and white matter lesions of cerebral vascular disease (Figure 2).
Fig. 2: When comparing white matter lesions through the FLAIR* sequence in a 3T scanner, it was shown that only multiple sclerosis showed the central vein sign in most of its lesions. In NOMSD, most of the lesions did not show this sign. In neurosyphilis and microangiopathy, the CVS was not observed.

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We selected five patients which fulfilled the revised McDonald criteria for MS that underwent MRI in a 3T scanner, image interpretation was performed on a standard picture archiving workstation.

It was included 5 patients with MS and 3 with each of the following: neurosyphilis, microangiopathy, and neuromyelitis optica spectrum disorders (NMOSD).

Using FLAIR*, the CVS was observed in a large proportion of lesions in all MS patients, it was seen in juxtacortical, periventricular and deep white matter cerebellar hemisphere, most frequently in the periventricular zone (Figure 3).

Fig. 3: Periventricular WMLs are observed, some of which present CVS. Compared to the other sequences, FLAIR* added the benefit offered by FLAIR (evidence of WMLs) to the benefit of SWI (evidence of CVS).

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Although these lesions were also visualized using the FLAIR sequence, their fusion (FLAIR*) was more accurate to evidence the WMLs and evidence the CVS, including making clear lesions not perceived in this sequence.

On the other hand, the CVS was seen in only a very small proportion of lesions in NMOSD, and in none in the other conditions (Table 1).

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<th>Table 1. Demographic and clinical features and frequency of the central vein sign (CVS) in patients with MS and three mimicking conditions.</th>
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<td><strong>Female : male ratio</strong></td>
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<td><strong>Neurological manifestations</strong></td>
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<td><strong>Frequency of the CVS</strong></td>
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Flair* has been demonstrated to be a newly technique that allows in vivo evaluation of WMLs as it was recommended in the NAIMS Cooperative consensus in 2016.
Conclusion

Recognizing the CVS image through the FLAIR* sequence on 3T magnetic resonance imaging may allow a wider use of CVS for the differential diagnosis of MS in clinical practice and is useful for the adequate diagnostic evaluation of suspected cases of MS and thus facilitating the correct differential diagnosis, taking into account clinical, laboratory and magnetic resonance images.
References


