Central vein sign evaluation by brain mri for the differential diagnosis of multiple sclerosis cases with markers of “better explanation” of the disease.

M Grammatico[1], G Carlucci[1,2],S Dallagiacoma[1], L Vuolo[3], AM Repice[2], C Mechi[2], E Magnani[2], A Barilaro[2], E Fainardi[3], L Massacesi[1,2]

[1]Department of Neurosciences, University of Florence, [2]Department of Neurology, [3]Department of Neuroradiology, Careggi University Hospital

Background

The nature of the central nervous system (CNS) white matter (WM) lesions observed in multiple sclerosis (MS) is inflammatory-demyelinating (I-D) and located around a venule, whereas WM lesions of primary small vessel disease migraine and systemic autoimmune diseases with neurological involvement are mainly ischemic and periarteriolar. By T2* MRI sequences a vein can be visualized in about 75% of the MS WM-ID lesions (the central vein, CV, sign), while in the above mentioned diseases this frequency is lower than 50%. Aim of this study is evaluation of differences in lesion pathology and pathogenic mechanisms, in MS and in MS patients with clinical, laboratory or MRi markers of “better explanation” of the diagnosis (MS-plus) not meeting the criteria of another disease.

Methods

Inclusion criteria: definite MS or MS with markers of possible “better explanation” of the diagnosis but not fulfilling the diagnostic criteria of other diseases (MS Plus). The predefined markers were clinical, serological and MRI (table 1). Each patient received one brain MRI (1.5T scanner) including volumetric T2*-EPI and FLAIR sequences after contrast injection. White matter lesions were detected on the FLAIR scans, whereas the venules and their relationships with the lesions in the SWI scans. White matter lesions were considered perivenular if an intralesional hypointense signal visible in at least two perpendicular planes was completely surrounded by hyperintense signal (Figure 1).

Results

The patients included, n= 52 (30 MS definite; 22 MS-plus). Most of the MS-plus fulfilled the MS MRI diagnostic criteria of space dissemination. The size/ location of their WM lesions were similar to that of MS. However the frequency of lesions with the CV sign was higher in MS than in the MS-plus cases: median frequency/ patient 91% (range 67-100%) vs 17.5% (range 9-83%; p< 0.0001). A CV sign frequency higher than 50% was observed in 30/30 MS patients (100%) and in 6/22 MS-plus patients (27%; p< 0.0001). In most of the MS-plus patients exceeding the 50% treshold, the frequency of the CV sign was within the range of the definite MS: 70-83% (median 74%) (Figure 2). The most frequent red flags observed in the MS-plus with low frequency of CV sign, were negative CSF exam and presence of serum autoantibodies.

Discussion

The high frequency of non perivenular WM lesions observed in most of the MS-plus suggests a non I-D underlying pathology. On the basis of the associated red flags,the main pathogenic mechanisms generating these lesions seems ischemic, probably due to primary CNS vasculitis of the small vessels. The frequency of WM lesions showing the CV sign is a useful marker for improving the accuracy of the MS diagnostic criteria.

Clinical	Laboratory	Brain MRi
Seizure history		
Severe/persistent headache	High titer autoantibodies associated to systemic autoimmune diseases (ENA; ANA; ANCA; APL)	Microbleeds
Prevaling cognitive decline	Persistently raised non specific systemic inflammation markers	Large brainstem lesions
Oral/genital aftosis Venous thrombosis	Negative CSF oligoclonal intrathecal IgG production or its normalization over time	Virchow-Robin spaces enlargement
Repeated miscarriages		Atypical contrast enhancement
Uveitis and/or rethinopathy		BWM lesions not typical for MS
Sicca syndrome Acquired artritis Acquired deafness		

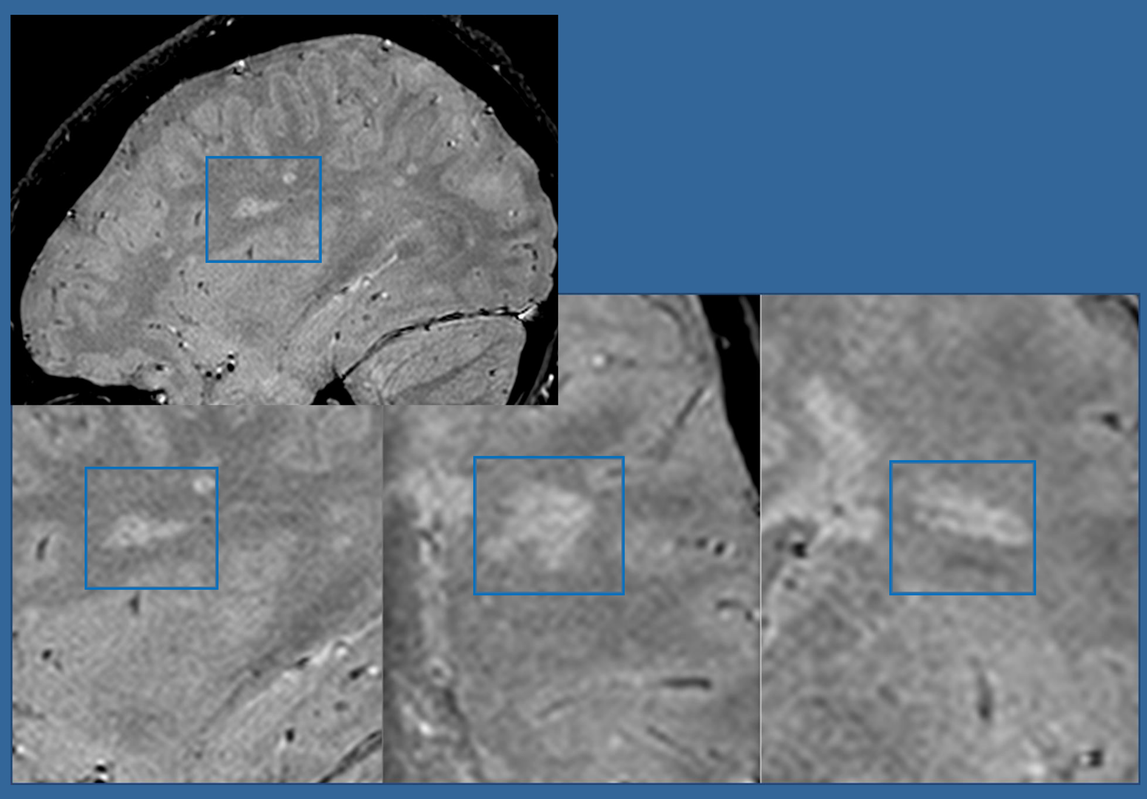

Figure 1. Perivenular lesion in a patient with Definite MS. Central vein can be viewed in the three plains as hypointense signal within the lesional hyperintensity

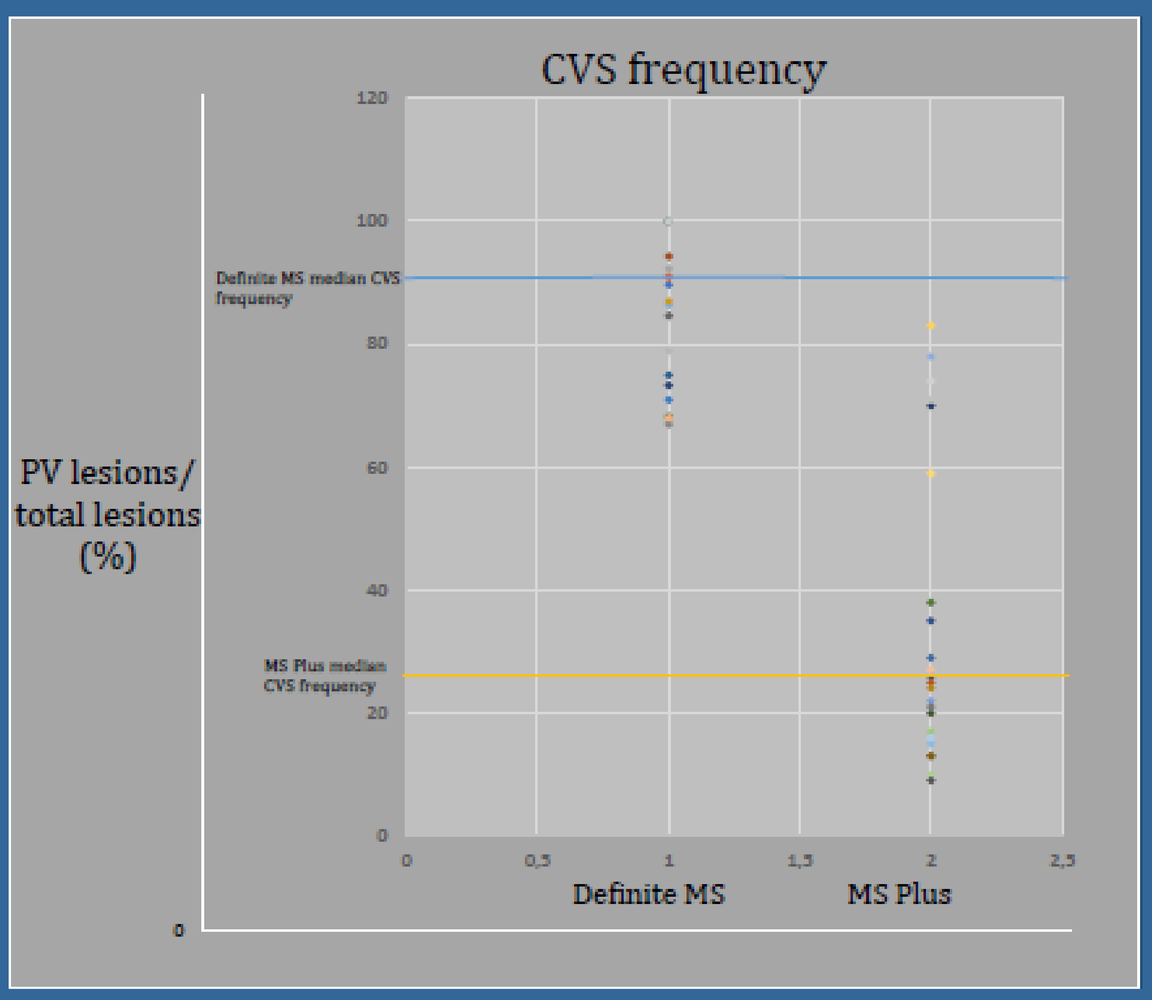

Figure 2. CVS frequency distribution in patients with Definite and Possible MS

References

- *Mistry et al. Imaging central veins in brain lesions with 3-T T2*-weighted magnetic resonance imaging differentiates multiple sclerosis from microangiopathic brain lesions. Mult Scler. 2016 Sep;22(10):1289-96*
- *Solomon et al. "Central vessel sign" on 3T FLAIR* MRI for the differentiation of multiple sclerosis from migraine. Ann Clin Transl Neurol. 2015 Dec 16;3(2):82-7*
- *Vuolo et al.. Susceptibility weighted MRI can help differentiate pathogenesis of white matter lesions in MS and CNS inflammatory vasculopathies. Abstract for EAN 2015 Congress, Berlin*