POSTER

MRI characterization of the “central vein sign” in brain white matter lesions of patients with multiple sclerosis and possible “better explantion of the diagnosis”

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Background.

The diagnosis of multiple sclerosis (MS) is currently based on highly sensitive but not equally specific MRI criteria, meaning that part of the patients receiving this diagnosis may not have MS. The frequency of an MS misdiagnosis is indeed estimated at about 5-10% of cases. This possibility is included in the diagnostic criteria in the item “unless better explanation”. Brain pathologies that can frequently mimic the clinical course and MRI features of MS in young adults are white matter (WM) ischemic lesions due to inflammatory isolated CNS small vessel diseases. However the patients with these lesions usually do not meet the diagnostic criteria of systemic autoimmune diseases and their clinical pictures are usually not severe enough to justify brain biopsy. Therefore, this criterion remains often undefined, leading to an uncertain diagnosis. However the specificity of the MS diagnosis could be improved taking advantage of one of the most specific pathological characteristics of MS, the perivenular location of the WM inflammatory lesions (the “central vein sign"), that can now be visualized in vivo by MRI (Fig.1). New but conventional MRI methods indeed, can accurately detect central veins inside WM lesions, allowing discrimination of the demyelinating lesions from those due to arteriolar chronic micro-angiopathy or to migraine (Mistry et al.; Solomon et al.; 2015). In addition recent data indicate that MRI can discriminate from MS, also WM lesions due to inflammatory/autoimmune micro-angiopathies, conditions often characterized by MS-like clinical courses in young adults (Massacesi et al. 2016).

However the “central vein sign” has never been analyzed in isolated MS-like syndromes with WM lesions fulfilling the MS diagnostic criteria, apart from the item of “unless better explanation” of the diagnosis.

Methods.

Inclusion criteria: a) age between 18 and 65 years old; Group defined MS: relapsing remitting MS defined with the McDonald’s diagnostic criteria ; Group Atypical MS: relapsing remitting MS according to McDonald’s criteria that could not fulfil the item of “unless better explanation”.

All patients had clinical, neurological and functional evaluation within one week from one MRi scan (1,5 Tesla with contrast including FLAIR and SWI images that highlights the venous blood signal down to the venule size). The images were analized out of frame. Each brain lesion was examined with the MIPAV software in the three orthogonal panes of the space. The lesions were classified as peri-venous (PV) if these had 1 or more central veins. On 1,5 Tesla MRi scans, a central vein was considered to be present if its hypo-intensity appeared in the middle of the surrounding hyper-intense lesion in at least 2 out of 3 plans.

Results

In this study a total of 26 patients were included; 16 had defined MS and 10 atypical MS. The two groups were comparable for clinical-demographic features (Table 1).

In the typical MS group, the total lesion count was 449, of which 393 were PV (87%), with a median/patient of 24 PV, (median frequency 90%; range 68-100%; mean frequency 87% ± 11; Table 2, fig 2).

In the atypical MS group, the total lesion count was 985 (of which 433 were perivenous, 44%), with a median/patient of 12 PV, (median frequency 17,5%; range 9-78%; mean frequency 33% ± 29; Table 2, Fig. 2).

The patients were then categorized according to the frequency of the PV lesions, using a threshold of 68%, that was the lowest frequency observed in the defined MS group. This categorisation identified 16/16 patients with typical MS above the threshold (100%), but only 3/10 patients with atypical MS exceed this frequency (p=0,0005; χ^2 test with Yates correction). According to these data sensibility of the test in identifying atypical MS patients resulted of 100%, with a specificity of 70%, a positive predictive value of 84%, a negative predictive value of 100%. The median frequency of PV lesion in the atypical MS showing < 67% PV lesions, was 25% (range: 9-26).

Discussion

The present study suggests that the analysis of the frequency of PV lesions is a marker for improving specificity of the current McDonald diagnostic criteria vs atypical MS cases. Indeed this marker allowed to confirm the criterion of “better explanation of the diagnosis” in 7 out 10 atypical MS patients.

This *marker* can also be rapidly translated to the clinical practice because of the 1,5 Tesla magnetic field strenght used, which is broadly available. This study provides the rational basis to others investigations that need to be prospectively planned in larger and more homogenous cohorts, in order to partially overcome the current limits of this research, that is the size of the population

Fig. 1 - The central vein sign

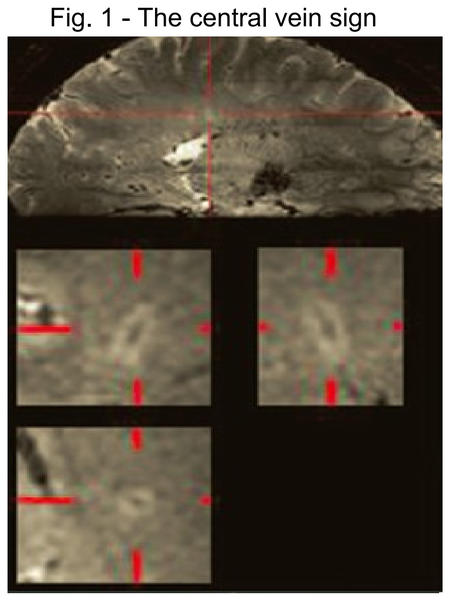


Table 1. Clinical and demographic characteristics of the population	Pz con SM (n=16)	Pz SM atipica (n=10)
ETÀ		
Media (anni) ± SD	47 ± 12	45 ± 8
Mediana (range) p = 0,58	49 (23-64)	43 (34-59)
M/F	1/16	1/10
DURATA DI MALATTIA (ANNI)		
Media ± SD	18 ± 10	16,5 ± 9
Mediana (range) p = 0,96	16 (4-33)	19,5 (1-26)
CARATTERISTICHE CLINICHE		
EDSS medio (range), p = 0,25	2,25 (0-7,5)	1,5 (0-6)
Pazienti con cefalea, n (%)	5 (29)	6 (60)
Pazienti con esiti Neurologici, n (%)	5 (29)	4 (40)
Pazienti con epilessia, n (%)	0 (0)	2 (20)
Pazienti con sintomi Psichiatrici, n (%)	5 (29)	7 (70)
Pazienti con artralgie, n (%)	2 (12)	2 (20)

Table 2- Peri-venular (PV) lesion distribution in the brain white matter

	Pazienti	Numero lesioni / paziente (n)	Numero lesioni peri-venulari (%)	
Definite MS	**Number**	**449**	**393 (87%)**	
	mean ± SD	**28 ± 15**	**24,5 ± 14**	**(87 % ± 11)**
	median, range	**26, 6-66**	**24.5, 6-57**	**(90%, 68-100)**
Atipical MS	**Number**	**985**	**433 (44%)**	
	mean + SD	**98.5 ± 91.5**	**43 ± 69**	**(33% ± 29)**
	median, range	**68.5, 10-252**	**12, 2-186**	**(17,5%, 9-78)**

Fig.2

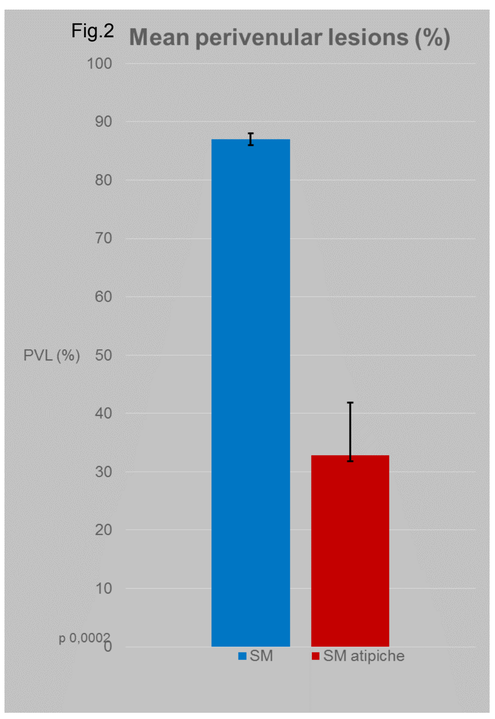


Fig. 3 – Frequency of patients with ≥ 68% peri-venular lesions (PVL)

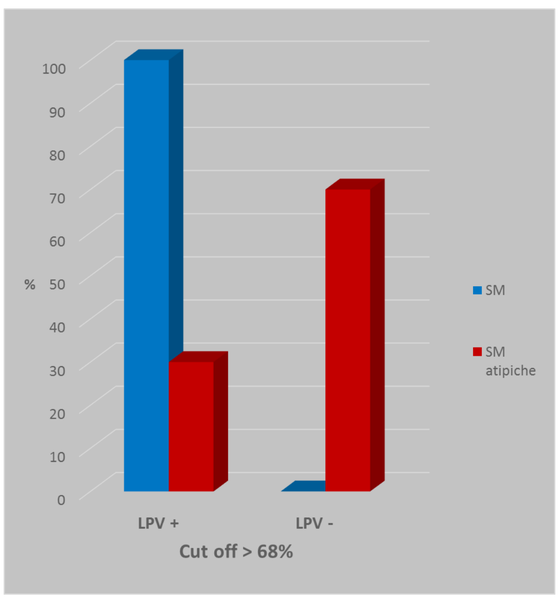
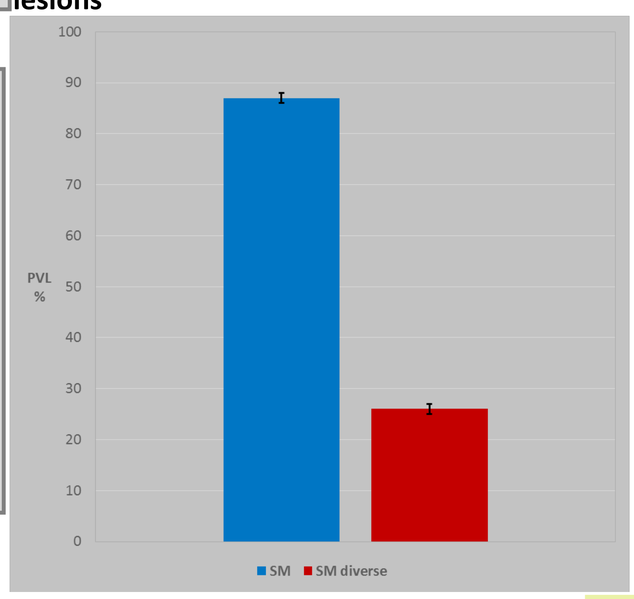


Fig. 4 – Mean perivenular lesion frequency in definite MS and in atipical MS with < 68% PV lesions



The frequency of the MS marker «central vein sign «, has the following accuracy for detecting non MS cases among definite MS and MS that fulfil the criteria of «better explanation of the diagnosis»

Sensitivity = 70% Specificity = 100%

PPV = 100% NVP= 84%

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