

NEUROCOGNITIVE ASSESSMENT OF IMMUNE-MEDIATED THROMBOTIC THROMBOCYTOPENIC PURPURA PATIENTS USING A COMPREHENSIVE TEST BATTERY IN A CROSS-SECTIONAL MRI-INTEGRATED STUDY

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Background and aims. Immune-mediated thrombotic thrombocytopenic purpura (iTTP) patients frequently report cognitive impairment during clinical remission, but magnetic resonance (MRI) findings linking cognitive impairment to cerebral small vessel disease (cSVD) MRI markers, are limited. To characterize cognitive test abnormalities in iTTP patients and evaluate their associations with MRI markers of cSVD.

Methods. Fifty-one iTTP patients in clinical remission followed at our outpatient clinic (at least 12 months after the last acute episode) underwent a standardized neuropsychological assessment covering global cognitive function, attention, logical deductive reasoning, language, memory, prefrontal function, along with brain MRI. Scores were standardized using Italian age and education adjusted norms and compared with population references using one-sample t-tests. Domain impairment was defined as at least one abnormal test per domain. cSVD was assessed both as individual MRI markers (lacunes, cerebral microbleeds [CMB], white-matter hyperintensities [WMH], and enlarged perivascular spaces [EPVS]), and as a composite total cSVD score (0-4). The association with iTTP-related variables were also explored.

Results. iTTP patients were mostly female (76%) with a median age of 58 years (Table 1). iTTP-patients showed preserved global cognition but selective deficits compared with the general population in working memory (digit Span forward and backward) and prefrontal function tests (cognitive estimates errors/bizarreness, Tower of London-accuracy). After adjustment for age and hypertension, memory impairment was associated with CMB (adjusted OR 8, 95%CI 1.5-44.1; p=0.02), and language impairment with lacunes (adjusted OR 8.7, 95%CI 1.1-70.7; p=0.04). The percentage of patients with at least 1 impaired domain increased with cSVD severity (cSVD≥2: 82% vs cSVD=1: 75% vs cSVD=0: 66%). No associations were observed between domain impairment and iTTP-related variables such as the number of relapses, time from the first acute episode, or ADAMTS13-activity levels throughout the observation time.

Conclusions. The prevalence of domain-specific deficits was higher in iTTP-patients compared with the general Italian population. CMB and lacunes were associated with memory and language impairment, whereas the composite cSVD score showed no consistent domain-specific associations, suggesting that individual cSVD markers may be more informative than total cSVD burden for neurocognitive vulnerability.

iTTP (n=51)	
Female sex, n (%)	39 (76)
Age, years, median (IQR)	58 (47 - 63)
Caucasian ethnicity, n (%)	48 (94)
Hypertension, n (%)	25 (49)
TTP-related variables	
First iTTP event, n (%)	34 (67)
Number of iTTP events, median (range)	1 (1-14)
Time to MRI from first event, years, median (IQR)	5 (2-10)
Neurological involvement at first event, n (%)	41 (80)
ADAMTS13-related variables1	
Timepoints, median (IQR)	20 (12-33)
Follow-up years, median (IQR)	5 (2-10)
Percentage of time < 20%, median (IQR)	9 (4-20)
Percentage of time 20-50%, median (IQR)	15 (2-32)
Percentage of time >50%, median (IQR)	66 (44-83)
Neuroimaging biomarkers	
Cerebral microbleeds, n (%)	16 (28)
High-grade WMH, n (%)	12 (21)
Lacunes, n (%)	9 (16)
High EPVS burden BG, n (%)	6 (11)
Total cSVD score, n (%)	
0	26 (51)
1	15 (29)
2	7 (14)
3	2 (4)
4	1 (2)
cSVD burden	
0	26 (51)
Low (1)	15 (29)
Moderate-high (2-4)	10 (20)

[1]Percent time in ADAMTS13 activity ranges was calculated using linear interpolation between consecutive measurements, summing the duration (days) spent at <20%, 20-50%, and >50%, and dividing by the total observation time up to the MRI date.

Abbreviations: BG, basal ganglia; cSVD cerebral small vessel disease; EPVS, enlarged perivascular space; IQR, interquartile range; iTTP, immune-mediated thrombotic thrombocytopenic purpura; WMH white matter hyperintensities.