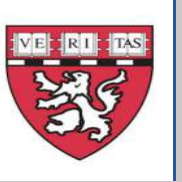


Amyloid Load and Structural Brain Alterations in Lobar Microbleed-only Patients and Cerebral Amyloid Angiopathy Related Lobar Intracerebral Hemorrhage

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Background

Cerebral Amyloid Angiopathy (CAA) is a common small vessel disease of elderly. CAA patients usually have both lobar intracerebral hemorrhage (L-ICH) and lobar microbleeds (LMB) and other MRI markers of CAA (cortical superficial siderosis [cSS], enlarged perivascular spaces [EPVS] and atrophy). CAA is also associated with increased vascular amyloid accumulation detected by Pittsburgh compound B (PiB) PET.

Lobar MBs are increasingly detected on MRI of patients without L-ICH and previous work suggested that vascular amyloid is probably the cause of these LMBs. However, the degree of CAA-related injury in these particular patients is not well known.

Aim

The aim of this study was to compare the measures of structural brain damage and amyloid load between patients who presented with lobar microbleeds on MRI but no ICH (LMB-only) and cerebral amyloid angiopathy related lobar intracerebral hemorrhage (CAA-ICH).

Methods

Definition of study groups

- L-ICH group (n=78) : CAA patients presenting with L-ICH and ≥ 1 LMB
- LBM-only group (n=37): The patients having ≥ 2 LMB without ICH at the time of presentation
- Age-matched healthy control from ADNI (N=78)

Comparison between groups

- Age, sex, vascular risk factors
- Standard MRI markers: LMB counts, the presence of cSS, EPVS counts in centrum semiovale (CSO), White matter hyperintensity (WMH) patterns
- Freesurfer based volumetric analysis : Cortical thickness (CT), White matter volume (VMV) and WMH volume, all calculated as percent of total intracranial volume
- PiB-PET measures of global amyloid deposition

Results

- Age, sex, and vascular risk factors did not differ between groups.
- WMH volume was lower in LMB-only as compared to CAA patients with L-ICH (Table)
- LMB-only patients exhibited a trend towards higher WMV as compared to CAA patients with L-ICH (Table)

	L-ICH (n=78)	LMB-only (n=37)	P
LMB count, median (IQR)	18.5 (3-69)	26 (8.5-65)	0.200
Presence of cSS, n (%)	35 (44.9%)	19 (51.4%)	0.553
EPVS-CSO count, median (IQR)	20(11-30)	18(10-23)	0.346
Multiple subcortical spots, n (%)	69 (88.5%)	33 (89.2%)	1.000
WMH volume, median (IQR)	1.45(0.55-2.04)	0.83(0.15-1.69)	0.023*
WMV, ml mean +SD	27.4 \pm 2.83	28.3 \pm 2.34	0.100
CT, mm mean +SD	2.21 \pm 0.12	2.25 \pm 0.13	0.195

White MV and GMV were significantly lower ($p < 0.001$, $p = 0.003$, respectively) in CAA-ICH patients compared to HC. WMV was significantly lower in LMB-only patients ($p = 0.001$) while GMV was not different from HC.

In patients with PiB-PET (n=38)

	L-ICH +	LMB-only	p
Global amyloid uptake	1.34 \pm 0.23	1.34 \pm 0.18	0.958
Frontal amyloid uptake	1.37 \pm 0.26	1.36 \pm 0.23	0.902
Occipital amyloid uptake	1.28 \pm 0.23	1.37 \pm 0.11	0.239

Conclusion

Similar distribution of amyloid load and hemorrhagic markers between LMB-only and CAA-ICH suggest that vascular amyloid is the predominant microangiopathy in LMB-only patients. The lower WMH volume and relatively higher GMV in LMB-only suggest that this condition represents an earlier stage of CAA, that might preferentially benefit from therapeutic interventions such as amyloid lowering.