Characterization of cerebral microbleeds and microinfarcts in patients with spontaneous intracerebral hemorrhage: a 7T MRI and histopathology study

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Background

- Spontaneous intracerebral hemorrhage (ICH) is caused by hypertensive vasculopathy (deep ICH) and cerebral amyloid angiopathy (lobar ICH in elderly patients) → insufficient simplification
- Manifestations of small vessel disease (SVD) are increasingly recognized as potential factors in understanding the underlying vascular disease, for example:
 - Cerebral microbleeds (CMB)
 - Ischemic lesions: acute (DWI) and chronic (cortical microinfarcts (CMI))
- Histopathology of MR-observed CMIs and CMBs are heterogeneous

Aim

- To gain insight in the underlying small vessel disease in patients with spontaneous ICH using a combination of post-mortem 7 tesla (7T) MRI and histopathology of focal microvascular lesions

Methods

- From the biobank of the UMC Utrecht and the Netherlands Brain Bank we selected 20 patients (12 women, 8 men) who died as a consequence of ICH (median age 77 years; 8 deep, 9 lobar, 3 infratentorial)
- From each case, we scanned three formalin-fixed coronal slices with 7T MRI using high resolution T2 and T2*-weighted sequences
- Acquired images were screened for cerebral microbleeds (CMBs) and cortical microinfarcts (CMIs)
- From each case we sampled at least one CMB and one CMI and processed the samples for histopathological analysis
- We used standard hematoxylin and eosin (H&E) stain to identify the lesions on the first sections stained adjacent sections for amyloid β , iron and fibrin to further characterize the lesions

A microbleed (red arrow) and a microinfarct (red open arrow) observed on a T2*-weighted MRI.

Results

- 7T MRI identified lesions:
 - 132 CMIs
 - 204 CMBs
- 4 cases without lesions
 - sCAA
 - Deep ICH
 - Cerebellar hemorrhage
 - Pons hemorrhage
- Sections
 - 28/72 lesions confirmed on H&E
 - 21/42 CMBs
 - 7/30 CMIs
 - 36 additional lesions
 - 18 in retrospect found on MRI
 - Lesions in retrospect not verified on MRI mostly CMIs and acute CMBs
 - 44 lesions not found

7T MRI identified lesions in non-lobar ICH patients

Case no.	Diagnosis	Sex	Age	CMBs	CMIs
1	Deep, HTN	F	49	1	5
2	Deep, possible HTN	F	44	0	1
3	Deep, HTN	M	46	23	2
4	Pons, HTN en OAC	F	75	3	0
5	Deep, HTN	F	85	3	7
6	Deep, HTN	M	81	9	1
7	Deep, HTN	F	89	8	1
8	Deep, HTN	F	89	2	0

7T MRI identified lesions in lobar ICH patients

Case no.	Diagnosis	Sex	Age	CMBs	CMIs
9	HCHWA-D	M	56	29	7
10	sCAA	M	76	40	1
11	No sCAA	F	78	3	3
12*	sCAA	M	85	1	38
13	sCAA	M	78	0	0
14	sCAA	F	83	66	8
15	sCAA	F	81	54	1
16	sCAA	F	73	1	16

CMBs = cerebral microbleeds, CMIs = cortical microinfarcts, HCHWA-D = hereditary cerebral hemorrhage with amyloidosis - Dutch type, HTN = hypertension, OAC = oral anticoagulants, sCAA = sporadic cerebral amyloid angiopathy.

Sections

H&E

Amyloid β

Iron

Fibrin

Example of a CMB in a 56 years old man with HCHWA-D

Conclusion

- CMBs and CMIs are more prevalent in lobar ICH compared to non-lobar ICH
- CMBs are histologically heterogeneous lesions and mostly not visible on MRI in the acute stage
- Around CMBs we found more leakage of iron and fibrin compared to CMIs