Dement Neurocogn Disord. 2020 Jun;19(2):74-76
https://doi.org/10.12779/dnd.2020.19.2.74
pISSN 1738-1495·eISSN 2384-0757

DND Dementia and Neurocognitive Disorder

Letter to the Editor

Amyloid Depositions and Small Vessel Disease in Patients with Cerebral Amyloid Angiopathy: a Case Series

Yun Jeong Hong, Si Baek Lee, Seong Hoon Kim, Dong Woo Ryu, Yongbang Kim, Jeong Wook Park

Department of Neurology, Uijeongbu St. Mary's Hospital, The Catholic University of Korea, Uijeongbu, Korea

Received: Jan 13, 2020
Revised: Mar 2, 2020
Accepted: Mar 31, 2020

Correspondence to
Si Baek Lee
Department of Neurology, Uijeongbu St. Mary's Hospital, The Catholic University of Korea, 271 Cheonbo-ro, Uijeongbu 11765, Korea.
E-mail: seeback@catholic.ac.kr

ORCID iDs
Yun Jeong Hong
https://orcid.org/0000-0002-4996-4981
Si Baek Lee
https://orcid.org/0000-0002-7455-1943

Conflict of Interest
The authors have no financial conflicts of interest.

Author Contributions
Conceptualization: Lee SB, Hong YJ; Methodology: Kim SH, Kim Y, Ryu DW; Supervision: Park JW; Writing - original draft: Lee SB, Hong YJ; Writing - review & editing: Lee SB, Hong YJ.

Cerebral amyloid angiopathy (CAA) is characterized by cerebrovascular amyloid depositions and amyloidosis-related vasculopathies.[1] In the elderly, CAA is a common cause of spontaneous intracerebral hemorrhage (ICH) and associated with Alzheimer's disease (AD).[2] Despite increased amyloid positron emission tomography (PET) capabilities, it is not yet well established if amyloid PET can confirm amyloid-driven vasculopathies and CAA.[1-3]

Herein, we report 5 cases that were diagnosed as probable CAA according to the modified Boston criteria. Small vessel disease, including white matter hyperintensities (WMH), lacunes, microbleeds, and cortical superficial siderosis (SS), were assessed on brain magnetic resonance imaging (MRI), and amyloid PET scans were performed. The clinical and neuroimaging findings are described below.

Case 1: an 83-year-old woman with no comorbidities visited the hospital due to cognitive decline and headache for 1–2 years. Brain MRI revealed a few old ICHs, multiple microbleeds, and SS. Two months later, she was admitted for mental changes and was diagnosed with spontaneous temporal ICH and dementia. Florbetaben PET scans showed increased amyloid depositions.

Case 2: a 76-year-old man with no comorbidities admitted due to first attack generalized seizure. Electroencephalography showed diffuse cerebral dysfunction. He showed dementia and delirium, and brain MRI revealed multiple microbleeds and SS. He was diagnosed with CAA after flutemetamol PET (positive for amyloidosis in diffuse cortex).

Case 3: a 75-year-old woman with diabetes mellitus and hypertension was admitted due to cognitive decline and gait disturbance. She was diagnosed with an acute parietal ICH. Brain MRI revealed old ICH in fronto-parietal lobes, multiple cortical microbleeds, and SS without trauma history. After florbetaben PET scans, the recurrent ICH and dementia were thought to be associated with CAA.

Case 4: a 76-year-old woman with hypertension admitted due to dysarthria and was diagnosed with an acute frontal infarction. MRI revealed extensive WMH and multiple microbleeds with lacunes in both basal ganglia, which suggested CAA. Amyloid PET scans were negative for amyloidosis, so her dementia was thought to be pure vascular dementia.

Table 1. Clinical features and neuroimaging findings

Case	Age (yr)	Sex	MMSE	CDR (SOB)	Cortical microbleed	Subcortical microbleed	SS	WMH	MTA	Lacune	Amyloid PET	APOE	Lobar ICH	Presenting symptoms
1	83	F	17	0.5 (4)	Total: 49 Temporal: 20; frontal: 7; parietal: 14; occipital: 8	0	>10	P3D3	2/2	0	Positive	2/3	Both frontal, Lt. temporal, occipital	Memory decline and headache
2	76	M	25	1 (5)	Total: 75 Temporal: 30; frontal: 5; parietal: 20; occipital: 20	0	>10	P3D3	2/2	0	Positive	NA	None	Cognitive decline and seizure
3	75	F	7	3 (18)	Total: 11 Temporal: 4; frontal: 1; parietal: 4; occipital: 2	0	>10	P3D2	1/2	9	Positive	3/3	Both frontal, right parietal	Memory decline
4	76	F	26	0.5 (3)	Total: 24 Temporal: 14; frontal: 4; parietal: 4; occipital: 2	Pons: 2; cerebellum: 2; thalamus: 2; BG: 15; frontal subcortical: 4	0	P3D3	NA	12	Negative	NA	None	Acute cerebral infarction (dysarthria)
5	63	F	6	3 (17)	Total: 82 Temporal: 30; frontal: 22; parietal: 20; occipital: 10	Pons: 7; thalamus: 14; BG: 17	0	P3D3	1/1	5	Negative	3/3	Lt. temporal lobe	Acute cerebral infarct (dizziness)

MMSE: Mini-Mental State Examination, CDR: clinical dementia rating, SOB: sum of boxes, SS: superficial siderosis, WMH: white matter hyperintensities (P and D WMH were combined; P3D3 was rated as severe WMH), MTA: medial temporal atrophy, PET: positron emission tomography, APOE: apolipoprotein, ICH: intracranial hemorrhage, BG: basal ganglia, P: periventricular, D: deep white matter, NA: not available, Lt.: left.

Case 5: a 63-year-old woman with hypertension, epilepsy, and old ICH was admitted due to dizziness and left hemiparesis. Brain MRI demonstrated acute medullary infarct, extensive WMH, and multiple microbleeds. She was diagnosed with vascular dementia, and the florbetaben PET scans were negative for amyloidosis.

Our cases showed numerous cortical microbleeds (>10) and extensive WMH on MRI. Although all cases were diagnosed as probable CAA based on clinical criteria, only three cases showed amyloidosis. They showed different clinical presentations and neuroimagings according to existence of amyloidosis (**Table 1** and **Fig. 1**). CAA patients with amyloidosis

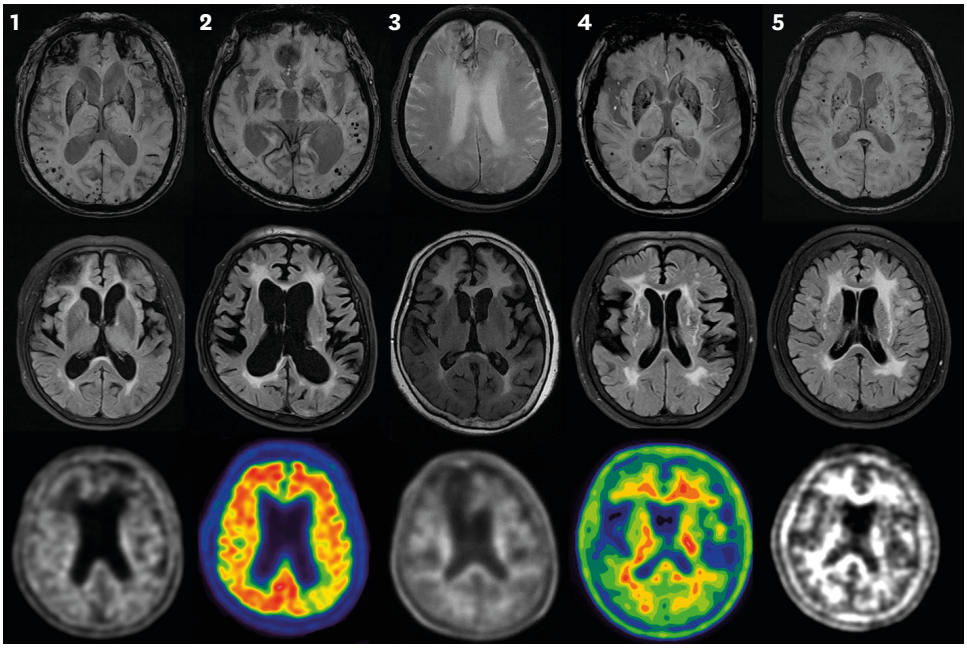

Fig. 1. Brain magnetic resonance imagings show microbleeds (upper), white matter hyperintensities and lacunes (middle), and amyloid PET findings (lower) from each case (from case 1 [left] to 5 [right]). Florbetaben PET scans in case 1, 3, and 5; flutemetamol PET scans in case 2; and florapronol PET scans in case 4.
PET: positron emission tomography.

https://doi.org/10.12779/dnd.2020.19.2.74

presented with dementia or seizure, while patients without amyloidosis, pure vascular dementia, presented with acute cerebral infarctions. Patients with amyloidosis had numerous SS and more frequent hippocampal atrophy, suggesting possibilities of combined AD-related neurodegeneration. On the other hand, the 2 patients with pure vascular dementia had many subcortical microbleeds and lacunes, which suggested poorly controlled vascular risk factors. Hence, existence of SS, subcortical microbleeds, and lacunes might be important factors to discriminate pure vascular dementia from CAA.

Considering that most patients with AD also have CAA-vasculopathies (up to 80%) because parenchymal amyloidosis plays an important role in vascular amyloid uptake,[2] establishing a diagnosis of CAA and amyloidosis has a therapeutic value, as it prompts caution regarding anticoagulation or thrombolysis.[2] In addition, physicians can predict rapid cognitive decline considering the high probability of AD.[2] Previous studies reported that vascular amyloidosis has a predilection of posterior brain regions; the disproportionately greater occipital amyloidosis may serve as a differential point between pure CAA and AD.[3] The usefulness of amyloid PET as a biomarker of CAA needs to be clarified more extensively.

The cases suggested that the vascular markers might be different between PET-positive and PET-negative patients, possibly related to different vasculopathies. Although amyloid PET is not yet included as a biomarker for CAA, patients could be divided into PET-positive CAA with high risks of AD and progressive dementia and PET-negative CAA that suggests pure vascular dementia with non or stepwise progressive dementia. MRI findings including SS, microbleeds, and lacunes might be relevant to PET-positivity.

REFERENCES

1. Baron JC, Farid K, Dolan E, Turc G, Marrapu ST, O'Brien E, et al. Diagnostic utility of amyloid PET in cerebral amyloid angiopathy-related symptomatic intracerebral hemorrhage. J Cereb Blood Flow Metab 2014;34:753-758.
PUBMED | CROSSREF
2. Charidimou A, Gang Q, Werring DJ. Sporadic cerebral amyloid angiopathy revisited: recent insights into pathophysiology and clinical spectrum. J Neurol Neurosurg Psychiatry 2012;83:124-137.
PUBMED | CROSSREF
3. Johnson KA, Gregas M, Becker JA, Kinnecom C, Salat DH, Moran EK, et al. Imaging of amyloid burden and distribution in cerebral amyloid angiopathy. Ann Neurol 2007;62:229-234.
PUBMED | CROSSREF