Clinico-Radiological Characteristics and Pathological Diagnosis of Cerebral Amyloid Angiopathy-Related Intracerebral Hemorrhage

Tadashi Doden, MD,*†‡ Hiromasa Sato, MD,* Etsuko Sasahara, MD, PhD,* Takahiro Murata, MD, PhD,§ Takehiro Yako, MD,§ Kazuo Kitazawa, MD, PhD,§ Kayoko Higuchi, MD, PhD,‖ Shigeaki Kobayashi, MD, PhD,§ and Takao Hashimoto, MD, PhD*†

Objective: We aim to clarify the clinico-radiological characteristics of cerebral amyloid angiopathy-related intracerebral hemorrhage and to investigate the efficacy of pathological diagnosis using biopsy specimens. *Method:* We retrospectively reviewed 253 consecutive patients with cortico-subcortical hemorrhage who had been admitted to Aizawa Hospital between January 2006 and July 2013. We had performed craniotomy and hematoma evacuation in 48 patients, as well as biopsy of the evacuated hematoma, cerebral parenchyma adjacent to the hematoma, or both, and they were classified according to the histological results (positive or negative for vascular amyloid deposition) and to the Boston criteria. We compared the clinico-radiological characteristics of cerebral amyloid angiopathy-related intracerebral hemorrhage. We also investigated the detection rate of cerebral amyloid angiopathy with respect to the origins of the specimens. *Results:* Pathological examination revealed that 22 subjects were positive for vascular amyloid. The number of the cerebral microbleeds located in the deep or infratentorial region was significantly larger in the negative group than in the positive group ($P < .05$). There was no significant difference in the distribution of lobar cerebral microbleeds and in the prevalence of hypertension. In the probable cerebral amyloid angiopathy-related intracerebral hemorrhage patients, the probability of having vascular amyloid detected by biopsy of both hematoma and parenchyma was 100%. Rebleeding in the postoperative periods was observed in 2 cases (9.1%) of the positive group. *Conclusions:* Our results demonstrate the importance and safety of biopsy simultaneously performed with hematoma evacuation. Deep or infratentorial microbleeds are less correlated with cerebral amyloid angiopathy-related intracerebral hemorrhage than with noncerebral amyloid angiopathy-related intracerebral hemorrhage.

From the *Department of Neurology, Aizawa Hospital, Matsumoto, Japan; †Brain Imaging Research Center, Aizawa Hospital, Matsumoto, Japan; ‡Department of Medicine (Neurology and Rheumatology), Shinshu University School of Medicine, Matsumoto, Japan; §Department of Neurosurgery, Aizawa Hospital, Matsumoto, Japan; and ‖Department of Anatomic Pathology, Aizawa Hospital, Matsumoto, Japan.

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Address correspondence to Tadashi Doden, MD, Department of Neurology, Aizawa Hospital, 2-5-1 Honjo, Matsumoto 390-8510, Japan. E-mail: aidr214@ai-hosp.or.jp.

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Introduction

Cerebral amyloid angiopathy (CAA) is caused by the accumulation of amyloid fibril on the cortical and leptomeningeal vessel walls, and it is an important cause of cerebral cortico-subcortical hemorrhage, cerebral infarction, leukoencephalopathy, cerebral vasculitis, and dementia in the elderly.[1-4] The incidence of CAA increases with age. Approximately half of elderly people (aged 60 years and older) and 74% of the individuals aged 90 years and older are affected with CAA.[4] CAA is closely related to the etiology of Alzheimer's disease (AD) and vascular dementia. CAA is commonly found with an incidence of about 80%-100% in AD.[4-6] CAA leads to multiple cortico-subcortical or lobar hemorrhages in the elderly, and it is then referred to as CAA-related intracerebral hemorrhage (CAA-ICH).[3,7] Boston criteria were established for CAA-ICH by the Boston Cerebral Amyloid Angiopathy Group, and a definite diagnosis of CAA-ICH can be formulated only by demonstrating lobar or cortico-subcortical hemorrhage and severe CAA with vasculopathy after whole histological investigation of affected brain tissue is obtained at autopsy.[8,9] Biopsy of the evacuated hematoma or cerebral cortex contributes to premortem diagnosis of probable CAA-ICH with supporting pathology; however, the positive ratio of amyloid deposition in the specimens obtained from brain biopsy or hematoma evacuation has not been investigated enough.[9-12] We retrospectively searched the patients with clinically diagnosed CAA-ICH who underwent biopsy of evacuated hematoma, cerebral parenchyma, or both, and classified them into CAA-pathology positive and negative groups, depending on the pathological results. As a prerequisite, the CAA-pathology positive group could be estimated to have a higher ratio of definite CAA-ICH and a lower ratio of hypertensive ICH than the CAA-pathology negative group. We investigated the differences of clinico-radiological characteristics in these 2 groups. We also investigated the differences of positive ratios of amyloid deposition, depending on the site of biopsy.

Methods

We retrospectively reviewed 253 consecutive patients with cortico-subcortical hemorrhage who had been admitted to Aizawa Hospital Stroke Center between January 2006 and July 2013 (Fig 1, A). We had performed craniotomy and hematoma evacuation in 48 patients, and biopsy of evacuated hematoma, cerebral parenchyma adjacent to the hematoma, or both in 44 of these 48 patients. We divided 22 CAA-pathology positive patients and 22 CAA-pathology negative patients into 3 groups, "probable CAA," "possible CAA," and "excluded," respectively, according to the Boston criteria. The origins of the biopsy specimens in probable or possible CAA patients were evacuated hematoma in 6 patients, cerebral parenchyma in 13 patients, and both in 12 patients. This study was approved by the institutional ethical committee, and written informed consents for surgical treatment and biopsy were obtained from either the patients or their families.

In clinical and radiological evaluation, the age at onset, the clinical diagnosis of CAA-ICH (possible or probable), hypertension (blood pressure ≧140/90 mmHg) before onset, antithrombotic drugs, dementia (Mini-Mental State Examination ≦23) before onset, estimated volume in hematoma, rebleeding, cerebral microbleeds (MBs), intraventricular hemorrhage (IVH), focal subarachnoid hemorrhage (SAH), cortical superficial siderosis (SS), and white matter lesions were compared between the CAA-pathology positive group and the CAA-pathology negative group. Brain computed tomography (CT) was performed in all patients, and volume in hematoma was estimated by the ABC/2 formula.[13] Brain magnetic resonance imaging (MRI) was performed in 17 of the 22 CAA-pathology positive patients and in 7 of the 9 CAA-pathology negative patients. The ratio of rebleeding was calculated for all patients except for 2 CAA-pathology positive patients with whom contact had been lost. We checked for a history of antithrombotic drugs, hypertension, and dementia based on the information from patients' families and medical records.

The MRI techniques were as follows. Standardized T2-weighted image (WI), fluid-attenuated inversion recovery, and T2* gradient-echo sequence (T2*WI) were acquired from 24 subjects using the 1.5 T MRI scanner (MAGNETOM Avanto, syngo MR VB17; Siemens, München, Germany). T2*WI was obtained using the following parameters: axial slice thickness = 5.0 mm, interslice thickness = 1.5 mm, repetition time = 737 ms, echo time = 26 ms, flip angle = 20°, and matrix size = 512 × 512 pixels.

MBs and cortical SS were evaluated in T2*WI. MBs are defined as focal areas of very low signal intensity, homogeneous round lesions with a diameter of 2-5 mm; superficial vessels and small calcification in basal ganglia or dentate nucleus were excluded.[14] Cortical SS is defined based on rims of hypointensity enveloping the surface of the cortical fissures. White matter lesions in the periventricular areas and deep or subcortical areas were graded into 4 stages, according to the method of the previous reports.[15,16] Imaging analysis was done by an

experienced neuroradiologist who had not been informed about the patients' clinical information.

For pathological investigation, all samples were stained by hematoxylin and eosin and by Congo red (Wako Pure Chemical Industries, Ltd., Osaka, Japan). Immunohistochemistry with antibody to β-amyloid (Aβ) was also performed. Aβ deposition in vascular walls was checked and CAA-pathology positive was diagnosed by circumferential deposition of Aβ. We investigated the CAA detection rate with respect to the origins of the specimens.

Statistical analysis was performed using chi-square test or Fisher exact test for categorical variates (chi-square test: white matter lesion; Fisher exact test: male sex, preoperative diagnosis, hypertension, dementia, antithrombotic drug, IVH, focal SAH, cortical SS, recurrence of hemorrhage, MBs) to compare the difference in the data between the 2 groups: the CAA-pathology positive group and the CAA-pathology negative group. Unpaired *t*-test or Mann–Whitney *U*-test was used for continuous variates (unpaired *t*-test: age, hematoma volume; Mann–Whitney *U*-test: total number of MBs in each patient, number of MBs). A two-tailed *P* value of <.05 was considered statistically significant. The statistical package (SPSS version 18.0 software, SPSS Inc., Chicago, IL, USA) was used for analyses.

Results

Characteristics of the Study Groups

The demographic characteristics of the patients are presented in Figure 1. Figure 1, B shows the clinical diagnoses of the 44 patients in the CAA-pathology positive and negative groups. Thirteen patients in the CAA-pathology negative group were excluded, according to the Boston criteria. Seven patients with probable CAA-ICH and 15 patients with possible CAA-ICH were identified in the CAA-pathology positive group. Two patients with probable CAA-ICH and 7 patients with possible CAA-ICH were identified in the CAA-pathology negative group.

Comparison of the Clinical and Radiological Features between the CAA-Pathology Positive and CAA-Pathology Negative Groups

Table 1 shows the clinico-radiological characteristics of the patients. There is no significant difference in the prevalence of hypertension and dementia between the CAA-pathology positive group and the CAA-pathology negative group. With regard to the difference in the distribution of MBs, the number of MBs located in cerebellum, brain stem, thalamus, and basal ganglia (deep or infratentorial MBs) was significantly larger in the CAA-pathology negative group than in the CAA-pathology positive group ($P < .05$).

Representative Cases

Figure 2 shows the radiological and pathological features of the 3 representative cases with CAA-pathology positive and negative. A 68-year-old woman was pathologically diagnosed with CAA-pathology positive by biopsy of evacuated hematoma. Photomicrographs of evacuated hematoma demonstrated amyloid-laden blood vessels as concomitants of the arachnoidal tissue (Fig 2, A-F).

A 60-year-old woman with multiple subcortical hemorrhages underwent cortical biopsy of the left temporal lobe. Photomicrographs of biopsied cortical and meningeal tissue demonstrated amyloid-laden blood vessels (Fig 2, G-L).

An 82-year-old woman with multiple deep or infratentorial MBs underwent biopsy of the cerebral parenchyma adjacent to the hematoma, but CAA pathology was not detected (Fig 2, M-O).

Figure 3 shows the relationship between the sites of the biopsy specimen and the CAA pathology. It reveals that the highest ratio of CAA-pathology positive was found in the patients who had undergone biopsy from both hematoma and parenchyma.

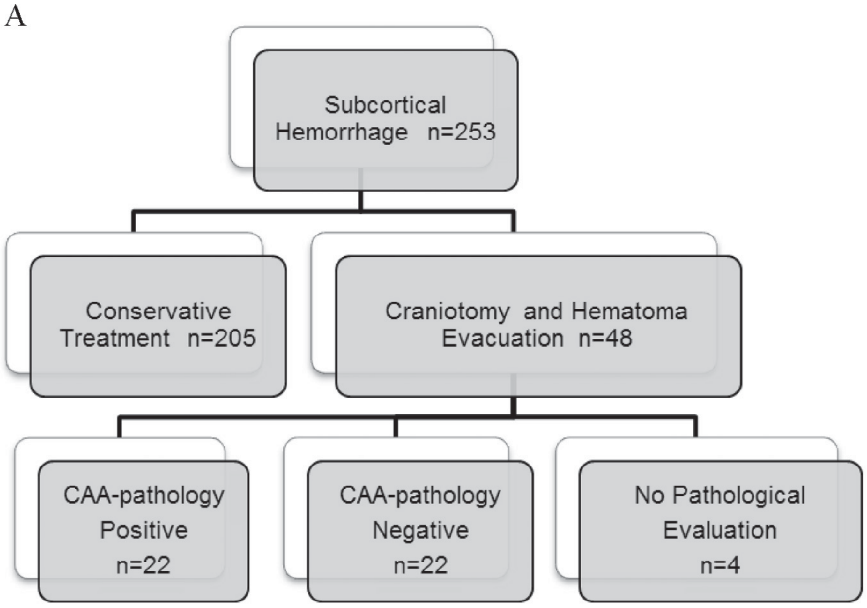
Table 2 shows the results of CAA pathology in 12 patients who underwent biopsy from both hematoma and parenchyma. Five cases showed CAA-pathology positive in both hematoma and parenchyma. On the other hand, 1 case showed CAA-pathology positive only in hematoma. The CAA detection rate was 50.0% in hematoma and 83.3% in parenchyma. One patient who underwent biopsy of the cerebral cortex and hematoma in the left parietal lobe showed CAA-pathology negative. MBs of the patient were strictly distributed within the deep or infratentorial area.

Table 3 shows the relationship between the clinical diagnosis, the kind of biopsy specimen, and the probability of definitive CAA. We defined "definitive" CAA as clinically probable or possible CAA-ICH patients with pathological proof of vascular amyloid deposition. The probability of definitive CAA in patients who underwent biopsy of hematoma or parenchyma was 60% in probable CAA patients. On the other hand, all 4 of the patients who underwent biopsy of both hematoma and parenchyma were CAA-pathology positive; thus, the probability of definitive CAA was 100%. In possible CAA patients, the probability of definitive CAA in patients who underwent biopsy of hematoma or parenchyma was 57%. Two patients were clinically diagnosed as probable CAA but pathologically diagnosed as CAA-pathology negative. The vascular structure was not included in the evacuated hematoma in 1 patient and the cerebral white matter adjacent to the bottom (deep white matter, thus, not cerebral cortex) of the hematoma cavity was biopsied in the other patient.

Rebleeding in the CAA-Pathology Positive Group

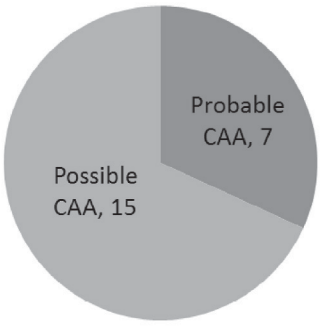
The surgery of hematoma removal was performed from 5 hours to 22 days, mean 2.8 days, after ICH onset in our series.

A



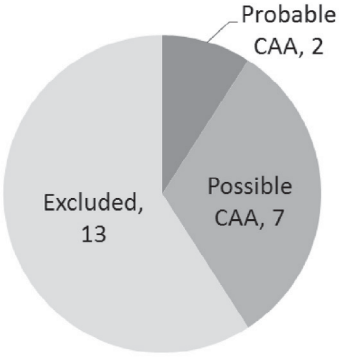
B

Clinical Diagnosis in Patients with CAA-pathology positive



n=22

Clinical Diagnosis in Patients with CAA-pathology negative



n=22

Details of Excluded Patients	
Age < 55 years	2
Cerebral infarction	2
Brain tumor	1
Head trauma	1
Sinus thrombosis	1
Arteriovenous malformation	1
Cavernous angioma	1
Thrombocytopenia	2
Coagulopathy	2
Total	n=13

Figure 1. *Demographic characteristics of the patients. (A) Classification of the subjects. (B) Clinical diagnosis in patients with CAA-pathology positive group and negative group. Abbreviation: CAA, cerebral amyloid angiopathy.*

Rebleeding in the postoperative periods was observed in 2 cases (9.1%) of the CAA-pathology positive group. These 2 cases (a 70-year-old man and an 85-year-old woman) each presented a clinically severe condition due to a large hematoma (estimated volume in the hematoma was more than 75 ml) and needed a craniotomy and hematoma evacuation as critical care. Both of them died because of rebleeding associated with the initial surgical sites in the acute or subacute postoperative periods.

Discussion

Clinico-Radiological Characteristics of CAA-ICH

Differences in the Distribution of MBs in CAA and Hypertensive Microangiopathy

There was no significant difference in the number of lobar MBs between the CAA-pathology positive group and the CAA-pathology negative group, whereas the

Table 1. *Characteristics of the patients*

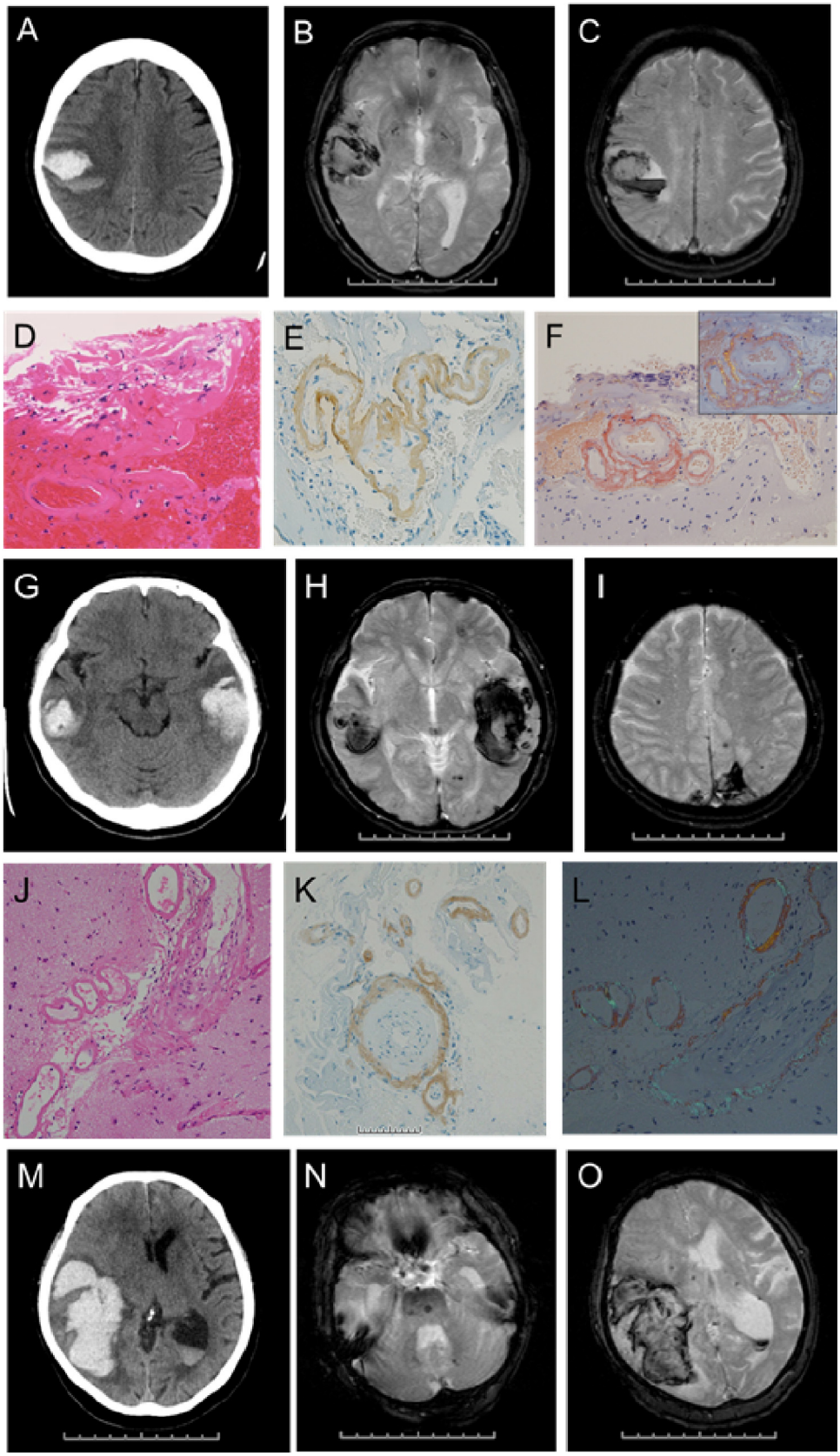
Characteristics of the patients	CAA-pathology positive n = 22		CAA-pathology negative n = 9		*P*
	n	%	n	%	
Age (years)	75.3 ± 7.7		72.8 ± 9.2		.447
Male sex	6	27.3	4	44.4	.302
Preoperative diagnosis					
Probable CAA-ICH	7	31.8	2	22.2	.472
Possible CAA-ICH	15	68.2	7	77.8	
Hypertension	12	54.5	5	55.5	.637
Dementia	5	22.7	3	33.3	.424
Antithrombotic drug	4	18.2	1	11.1	.595
Hematoma volume (ml)	69.6 ± 36.2		58.8 ± 31.5		.439
Intraventricular hemorrhage	14	63.6	4	44.4	.279
Focal subarachnoid hemorrhage	11	50	2	22.2	.154
Cortical superficial siderosis	6	35.3	0	0	.092
Recurrence of hemorrhage	7	35	0	0	.050
MBs	11	64.7	6	85.7	.306
Total number of MBs in each patient	3.06 ± 4.13		5.43 ± 3.05		.098
Number of MBs					
Frontal lobe	.94 ± 2.22		.14 ± .38		.531
Parietal lobe	1.59 ± 2.92		0		.079
Temporal lobe	.35 ± .79		.14 ± .38		.590
Occipital lobe	.47 ± 1.38		.14 ± .38		.956
Basal ganglia and thalamus	.06 ± .24		1.71 ± 1.50		.001*
Brain stem	.18 ± .53		1.57 ± 1.90		.015*
Cerebellum	0		1.71 ± 2.56		.001*
PVH grade					
0; none	0	0	0	0	.427
1; caps or lining	9	40.9	6	66.7	
2; bands	9	40.9	2	22.2	
3; irregular	4	18.2	1	11.1	
DSWMH grade					
0; none	4	18.2	1	11.1	.311
1; punctate	9	40.9	5	55.5	
2; early confluent	9	40.9	2	22.2	
3; confluent	0	0	1	11.1	

Abbreviations: CAA, cerebral amyloid angiopathy; CAA-ICH, cerebral amyloid angiopathy-related intracerebral hemorrhage; DSWMH, deep and subcortical white matter hyperintensity; MBs, cerebral microbleeds; PVH, periventricular hyperintensity.

Chi-square test, Fisher exact test, *t*-test, or Mann–Whitney *U*-test was conducted.

*$P < .05$.

Figure 2. *Brain images and photomicrographs of evacuated hematoma and cerebral cortex in three patients. The clinical diagnosis was probable CAA-ICH in the first 2 cases and possible CAA-ICH in the latter, according to the Boston criteria. (A-F) A 68-year-old woman. The CT revealed subcortical hemorrhage in the right frontal lobe (A). There were no microbleeds in the basal ganglia or thalamus, and small calcifications were identified in the bilateral globus pallidus in MRI T2*WI (B). But several cortico-subcortical microbleeds and superficial siderosis were identified in the bilateral hemispheres (C). Craniotomy and hematoma evacuation was performed and photomicrographs of the evacuated hematoma demonstrated amyloid-laden blood vessels as concomitants of the arachnoidal tissue (D; hematoxylin and eosin, original magnification 200×, E; immunohistochemistry with antibody to Aβ, F; Congo red stain, upper-right side photomicrograph is under polarized light). (G-L) A 60-year-old woman. The brain CT and MRI T2*WI image revealed acute subcortical hemorrhages in the bilateral temporal lobes and an old subcortical hematoma in the left parietal lobe. There were multiple lobar microbleeds in the bilateral hemispheres (G, H, I). Photomicrographs of biopsied cortical and meningeal tissue, demonstrating amyloid-laden blood vessels (J; hematoxylin and eosin stain, original magnification 200×, K; immunohistochemistry with antibody to Aβ, L; Congo red stain under polarized light). (M-O) An 82-year-old woman. The brain CT revealed massive hematoma in the right temporo-parietal lobe (M). T2*WI demonstrated multiple microbleeds in the brainstem, cerebellar hemisphere, and basal ganglia (N, O). The woman underwent hematoma evacuation and biopsy from the cerebral parenchyma adjacent to the hematoma cavity. CAA pathology was not detected from these specimens. Abbreviations: Aβ, β-amyloid; CAA-ICH, cerebral amyloid angiopathy-related intracerebral hemorrhage; CT, computed tomography; MRI, magnetic resonance imaging; T2*WI, T2*-weighted image.*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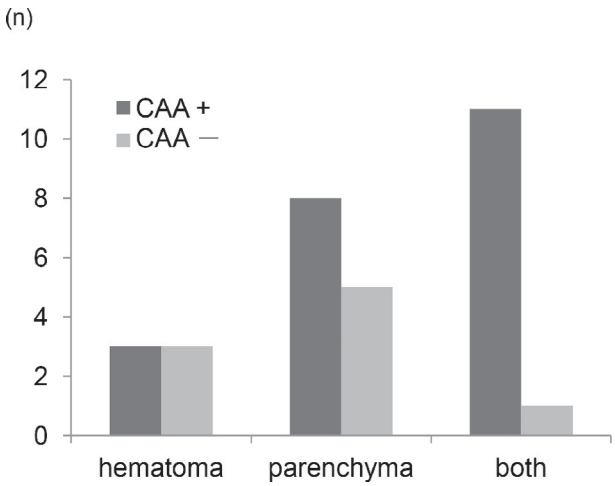

Figure 3. *Details of tissue sample obtained by biopsy and CAA pathology. The ratio of CAA-pathology positive in each kind of specimen was 50%, 61.5%, and 91.7% in hematoma, parenchyma, and both, respectively. Abbreviations: CAA, cerebral amyloid angiopathy;* ■ *CAA+;* ■ *CAA–.*

number of deep or infratentorial MBs in the CAA-pathology positive group was significantly lower than in the CAA-pathology negative group. MBs represent hemosiderin-containing macrophages which have engloped red blood cells derived from extravasation from small vessels, and they are correlated with bleeding-prone microangiopathy such as lipohyalinosis or CAA.[17] Cortico-subcortical areas are preferentially affected by MBs in accordance with the distribution of Aβ deposition in vascular walls in patients with CAA.[17-19] Deep or infratentorial MBs were positively correlated with CAA-pathology negative in the present study. A previous study suggested that deep or infratentorial MBs are relevant to cardiovascular risk factors, the presence of lacunar infarcts, white matter lesions, and underlying hypertension.[20] Deep MBs have been suggested to be relevant to subcortical small vessel disease (SVD), such as lacunar infarction or white matter lesions, but not to amyloid burden.[21] Thus, deep or infratentorial MBs strongly suggest the existence of hypertensive microangiopathy rather than CAA.

Table 2. *Results of CAA pathology in 12 patients who underwent biopsy from both hematoma and parenchyma*

Distribution of CAA pathology	
Hematoma	1
Hematoma and parenchyma	5
Parenchyma	5
Total	11*

Abbreviation: CAA, cerebral amyloid angiopathy.
*One patient with CAA-pathology negative was excluded.

Relationship between CAA-ICH and Hypertension

In our study, there is no significant difference in prevalence of the hypertension between the CAA-pathology positive group and the CAA-pathology negative group. The progression of CAA causes fibrinoid necrosis and, as a result, microaneurysm formation, secondly to focal bulging of the affected vascular wall, could be observed. These structural changes of the affected vessels are important as contributing factors in the development of CAA-ICH and are collectively called CAA-associated vasculopathy.[3] These pathological changes are also observed in patients with cerebral SVD resulting from arteriosclerotic diseases such as hypertension or diabetes mellitus.[22]

In the past, the development of CAA had not been thought to correlate with the presence of common cerebrovascular risk factors, including hypertension, diabetes mellitus, hyperlipidemia, or the severity of atherosclerosis of the cerebral arteries.[23] Thereafter, the correlation between CAA, on the one hand, and cerebral arteriosclerosis and arteriolar sclerosis, on the other, has attracted attention.[6] Recently, the correlation in the severity of SVD

Table 3. *Relationship between clinical diagnosis, kind of specimen, and probability of definitive CAA*

			Pathological diagnosis		
Clinical diagnosis	Specimen	n	CAA-pathology positive	CAA-pathology negative	Probability of definitive CAA (%)
Probable CAA	All	9	7	2	77.8
	Hematoma	1	0	1	.0
	Parenchyma	4	3	1	75.0
	Both	4	4	0	100.0
Possible CAA	All	22	15	7	68.2
	Hematoma	5	3	2	60.0
	Parenchyma	9	5	4	55.6
	Both	8	7	1	87.5
Total		31	22	9	71.0

Abbreviation: CAA, cerebral amyloid angiopathy.

and CAA was demonstrated by postmortem pathological investigation of elderly subjects.[5] As mentioned above, the prevalence of CAA in the elderly increases with age. An autopsy series reported that the prevalence of CAA over the age of 70 years was 43%, and almost half of the cases were estimated to have moderate-to-severe CAA.[3] The prevalence of hypertension also increases with the age. The prevalence of hypertension at age 50 is about 30% and 20% in the United States and Canada, respectively, and it increases to about 60% and 50% at age 70.[24] As the prevalence of CAA and hypertension increases in the elderly, it is probable that the rate of their coexistence is higher in older people. Actually, Smith et al. reported that 25% of patients with ICH had both CAA and hypertensive microangiopathy.[25] It was pointed out that the coexistence of CAA and hypertension might be a cause of the wide distribution of MBs.[17] Thus, structural degenerations of the cortical and/or leptomeningeal vessel walls such as fibrinoid necrosis or microaneurysm formation exist in patients with CAA, and high blood pressure may trigger a rupture of the vessel walls, which results in lobar hemorrhage. We cannot exclude the possibility of CAA-ICH in the diagnosis of patients with lobar hemorrhage and hypertension,[12] and it is difficult to strictly distinguish CAA-ICH from hypertensive ICH solely based on clinical and radiological findings.[26]

Focal SAH and Cortical SS in the Diagnosis of CAA

In this study, we investigated the relationship between CAA pathology and hemorrhagic lesions associated with ICH on MRI such as focal SAH or cortical SS. SAH and cortical SS tended to be observed more frequently in the CAA-pathology positive group. This result supports the hypothesis that various hemorrhagic lesions are elicited with the progression of CAA-associated vasculopathy.[27,28]

Factors That Influence the Detection of CAA Pathology

The highest ratio of CAA-pathology positive was obtained by biopsy of both hematoma and cerebral cortex in the present study. Furthermore, the biopsy of cerebral parenchyma showed a higher CAA detection rate than did the biopsy of hematoma in the 12 patients who underwent biopsy of both hematoma and cerebral parenchyma. Our results support the notion that histopathological examination of both cerebral cortex and hematoma is necessary to make a reliable diagnosis of CAA, as shown in the Boston criteria.[8,9] However, CAA distribution is characteristically patchy and segmental; it may lead to the possibility of having false-negative cases.[1,3,29]

On the other hand, several attempts using amyloid imaging, such as ^{11}C-Pittsburgh compound B positron emission tomography (^{11}C-PiB PET), have been made to detect CAA as an underlying disease in several pathological conditions such as dementia, cortical SAH, and cerebral angitis.[30-34] A positive relationship between local amyloid burden and a future risk for hemorrhage has been suggested based on the result of a longitudinal cohort study with ^{11}C-PiB PET and MRI.[31] However, the presence of vascular amyloid in the tissue sample is not perfectly specific for CAA-ICH because elderly people may incidentally present with asymptomatic vascular amyloid deposition.[3,4,11] For more definitive diagnosis of CAA-ICH, ruptured amyloid-laden blood vessels adjacent to the hematoma should be identified in postmortem study.[35]

Safety of Craniotomy and Biopsy in Patients with CAA-ICH

The rebleeding ratio after craniotomy and hematoma evacuation in patients with CAA-pathology positive is 9.1% (2 of 22 cases) in our patients, and both patients died from rebleeding. On the other hand, no apparent adverse events related to surgical interventions were observed in the other patients. Previous studies have indicated that neurosurgical procedures in patients with CAA may cause uncontrollable perioperative and postoperative hemorrhages, and they have not recommended surgical interventions.[36-38] On the other hand, the safety and effectiveness of hematoma evacuation for patients with CAA-ICH have been warranted in recent years.[39,40] Several reports have also referred to the safety of the biopsy of the cerebral cortex in patients with CAA-ICH.[41-44] Mehndiratta et al. reported that the probability of postoperative hemorrhage within the first 48 hours of surgery was 11.8% on average (the probability ranged from 0% to 22% among the previous reports), and the mortality rate was 24.4% on average (0%-75%) in patients with CAA-ICH. The patients' poor outcome in CAA-ICH with surgical intervention was estimated to be associated with poor preoperative functional status, age over 75 years, preoperative diagnosis of dementia, hematoma volume greater than 60 ml, the presence of IVH, and postoperative hemorrhage.[45]

The time to surgery after ICH onset is one of the critical factors affecting the rate of rebleeding. A previous report presented the rate of rebleeding as 12% of the patients, mostly with deep ICH, who had been treated by open craniotomy and hematoma evacuation within 12 hours.[46] Another study reported that 3.8% of the patients, mostly with putaminal or thalamic hemorrhage, had rebleeding after CT-guided stereotactic surgery; 76% had been performed later than 3 days after symptom onset.[47] The rate of rebleeding and the timing of surgery in our cases fell within the ranges of the results of these previous reports, supporting the relative safety of hematoma evacuation surgery in CAA-ICH. Early surgical treatment might have functional and survival advantage for the patients with spontaneous superficial ICH without IVH[48-50]; however, careful consideration of the indication for surgical intervention and perioperative management is still needed, especially for the patients at high risk of surgical intervention.

Limitations of This Study

This is a clinical research study that was planned and executed in a single institution, and the sample size is relatively small. Standardization of the specimens and biopsy locations were not strictly controlled; the specimens were obtained from cerebral white matter, not cerebral cortex in a few cases; and the evacuated hematoma contained no vessel. Furthermore, the distribution of CAA is patchy and segmental. Therefore, there could be false-negative cases in the CAA-pathology negative group. Postmortem examination is essential for the definite pathological diagnosis of CAA at the present time, and a large-scale comparative study that deals with clinical diagnosis based on the clinico-radiological findings, including amyloid imaging and pathological diagnosis obtained from biopsy and autopsy, is needed.

Conclusion

Deep or infratentorial MBs in T2*WI are less correlated with CAA-ICH than with non-CAA-ICH.

Hypertension may play an important role in the pathogenesis of CAA-ICH.

With regard to biopsy and pathological diagnosis of CAA-ICH performed with craniotomy and hematoma evacuation, the amyloid detection rate of biopsy of hematoma alone was low compared with the rate of biopsy of both hematoma and cerebral parenchyma. A specimen of the cerebral cortex adjacent to the hematoma should be obtained to detect CAA.

Hematoma evacuation surgery for CAA-ICH is relatively safe, but it should be carefully performed.

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