

Fluid-Blood Level and Hematoma Expansion in a Cerebral Amyloid Angiopathy-Associated Intracerebral Hematoma

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF **Ryoichi Suzuki**
ABCDEF **Tomohiro Yamasaki**
BDEF **Shinichiro Koizumi**
BDEF **Takao Nozaki**
BDEF **Hisaya Hiramatsu**
ABCDEF **Tetsuro Sameshima**
BDEF **Kenji Sugiyama**
BCDEF **Hiroki Namba**

Department of Neurosurgery, Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan

Corresponding Author: Tomohiro Yamasaki, e-mail: tyuyuyuu@yahoo.co.jp
Conflict of interest: None declared

Patient: Male, 77
Final Diagnosis: Cerebral amyloid angiopathy
Symptoms: Aphasia • hemiparesis
Medication: —
Clinical Procedure: Hematoma evacuation
Specialty: Neurosurgery

Objective: Unusual clinical course
Background: Cerebral amyloid angiopathy (CAA) results from progressive deposition of amyloid- β in the walls of cortical and leptomeningeal vessels, leading to CAA-associated intracerebral hemorrhage (ICH). Hematoma expansion is a common early complication of spontaneous ICH, and is a strong independent predictor of poor outcome. However, there are limited reports of hematoma expansion related to CAA-associated ICH. Herein, we describe a novel case of hematoma expansion with a fluid-blood level in the cystic cavity of CAA-associated ICH.

Case report: A 76-year-old male was initially diagnosed with probable CAA according to the modified Boston criteria, and presented with lobar ICH in the left frontal lobe 4 months later. Admission computed tomography scans showed an ICH including a high-density hematoma within a cystic cavity, revealing a clearly lower-density fluid component. Serial computed tomography scans showed no evidence of an expansion of the high-density clot, but obvious expansion of the fluid component containing a fluid-blood level. We recognized a bleeding site with no enhancement on preoperative magnetic resonance imaging. Left frontal craniotomy revealed a liquefied hematoma, which was removed by suction. We subsequently evacuated the blood clot extending into the left frontal sulcus, and confirmed and cauterized the bleeding site, leading to successful hemostasis.

Conclusions: We report a CAA-associated ICH case showing hematoma expansion with a fluid-blood level. Intraparenchymal fluid-blood level suggests extravasation of blood into pre-existing cystic cavities because of hematoma liquefaction. Thus, fluid-blood levels are an important finding of hematoma expansion in acute CAA-associated ICH, and early treatment should be considered.

MeSH Keywords: Cerebral Amyloid Angiopathy • Cerebral Hemorrhage • Cyst Fluid • Siderosis

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/915919>

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Background

Cerebral amyloid angiopathy (CAA) is defined as the progressive deposition of amyloid- β in the wall of cortical and leptomeningeal vessels [1]. Approximately 12% to 15% of lobar ICH in the elderly is associated with CAA [2], and detection of CAA-associated intracerebral hemorrhage (ICH) is important because it is associated with a higher risk of recurrent ICH and multifocal ICH [3]. Hematoma expansion is a common early complication of spontaneous ICH, and is a strong independent predictor of poor outcome [4]. However, there are limited reports of hematoma expansion related to CAA-associated ICH. Fluid-blood levels (FBLs) within a hematoma are occasionally seen on acute computed tomography (CT) scans of ICH associated with coagulopathy, although patients with normal coagulation parameters can also exhibit FBLs [5]. In the past report, FBLs were found in cystic cavities caused by hematoma liquefaction, and the presence of intraparenchymal FBLs suggested extravasation of blood into preexisting cystic cavities [6]. Furthermore, FBLs were reported to be related to both the presence of probable/definite CAA according to the modified Boston criteria (Table 1) and the presence of cortical superficial siderosis (cSS) [7], as well as to hematoma expansion of ICH leading to a worse outcome, and potential early treatment [5].

We report on a case of CAA-associated ICH within a cystic cavity revealing an expansion of the fluid component containing an FBL on CT and magnetic resonance imaging (MRI). A bleeding site with no enhancement was noted on preoperative MRI. A left frontal craniotomy revealed a liquefied hematoma, which was removed by suction. We subsequently evacuated the blood

clot extending into the left frontal sulcus, and confirmed and cauterized the bleeding site, leading to successful hemostasis. This report details the clinical and radiological courses of the patient, including surgical and pathological findings.

Case Report

A 76-year-old male with no history of hypertension or dementia presented with sudden onset dizziness causing nausea and vomiting, and was transferred to our hospital. Neurological examinations revealed right sensorineural hearing impairment and truncal ataxia with gait disturbance. T2-weighted (Figure 1A), T2*-weighted gradient recalled echo (T2*-GRE) (Figure 1B), and susceptibility-weighted imaging (Figure 1C) sequences on MRI showed a low signal intensity in the subarachnoid space of the bilateral widespread cerebral convexities, in the superficial layer of the brainstem, and in the cerebellum. These MRIs were indicative of superficial siderosis. However, there were no corresponding hyperdense findings on CT (Figure 1D) scans, or hyperintense signal on T1-weighted (Figure 1E) or fluid-attenuated inversion recovery images (Figure 1F). CT scans and MRIs ruled out acute hemorrhagic lesions, acute ischemic lesions, brain aneurysms, cerebral artery stenosis, arteriovenous malformations, and tumors. The patient's symptoms resolved the following day. He was diagnosed with probable CAA (Table 1) presenting as transient focal neurological episodes, and was discharged from our hospital.

Four months later, he presented with acute decreased level of consciousness with aphasia, and he was readmitted to

Table 1. Modified Boston criteria for CAA-related hemorrhage.

Definite CAA	Full postmortem examination demonstrating: <ul style="list-style-type: none"> • Lobar, cortical or corticosubcortical hemorrhage • Severe CAA with vasculopathy • Absence of another diagnostic lesion
Probable CAA with supporting pathology	Clinical date and pathologic tissue demonstrating: <ul style="list-style-type: none"> • Lobar, cortical or corticosubcortical hemorrhage • Some degree of CAA in specimen • Absence of another diagnostic lesion
Probable CAA	Clinical date and MRI or CT demonstrating: <ul style="list-style-type: none"> • Multiple hemorrhages restricted to lobar, cortical or corticosubcortical regions (cerebellar hemorrhage allowed) or • Single lobar, cortical or corticosubcortical hemorrhage and superficial siderosis • Age ≥ 55 years • Absence of other cause of hemorrhage or superficial siderosis
Possible CAA	Clinical date and MRI or CT demonstrating <ul style="list-style-type: none"> • Single lobar, cortical or corticosubcortical hemorrhage or • superficial siderosis • Age ≥ 55 years • Absence of other cause of hemorrhage or superficial siderosis

CAA – cerebral amyloid angiopathy; MRI – magnetic resonance imaging; CT – computed tomography.

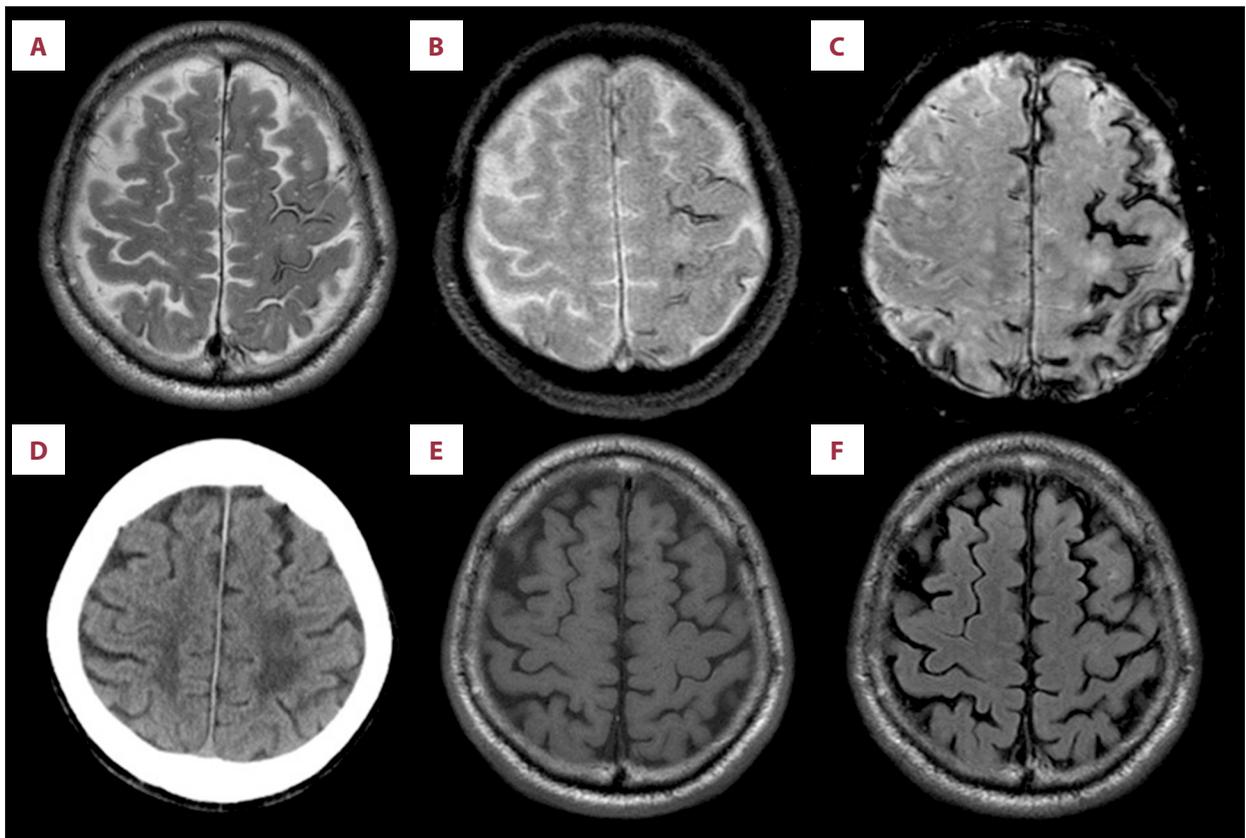


Figure 1. Initial magnetic resonance imaging (MRI) findings: T2-weighted imaging (A), T2*-weighted gradient recalled echo (T2*-GRE), (B), susceptibility-weighted imaging (SWI), and (C) sequences on MRI. There was a low signal intensity in the subarachnoid space of the bilateral widespread cerebral convexities, in the superficial layer of the brainstem, and in the cerebellum, representing superficial siderosis. There were no corresponding hyperdense findings on computed tomography (CT) scans (D), or hyperintense signals on T1-weighted (E), or fluid-attenuated inversion recovery (FLAIR) (F) images.

our hospital. His blood pressure was 101/57 mm Hg, with a regular heart rate of 80 beats per minute. Admission CT scans showed an ICH, including a high-density hematoma extending to subarachnoid space in the superficial layer (Figure 2A) which was within a cystic cavity showing a clear lower-density fluid component in the deep layer (Figure 2B) of the left frontal lobe. The volume of the ICH was 46 mL calculated by using the formula $ABC/2$ [8]. Although he underwent conservative treatment with a hemostatic agent, his consciousness gradually deteriorated and he presented with right hemiparesis. Serial CT scans obtained on Day 3 revealed no evidence of expansion of the high-density clot (Figure 2C), while there was expansion of the fluid component containing an FBL (Figure 2D). The volume of the ICH was 79 mL, indicating an increase in volume of 33 mL (42%). MRI obtained on Day 4 showed a hyperintense signal component extending into the superior frontal sulcus on T1-weighted imaging (Figure 3A), corresponding to the slightly low intensity signal on T2-weighted imaging (Figure 3B), in the superficial layer. T2*-GRE showed high intensity signal areas in the dilated low intensity signal of left superior frontal sulcus (Figure 3C). MRI in the deep

layer showed FBL (Figure 3D–3F). There was no enhancement on gadolinium-enhanced T1-weighted images.

Left frontal craniotomy was performed on Day 4 to evacuate the hematoma and identify the cause of hematoma expansion. The surface of the brain showed widespread subarachnoid hemorrhagic changes. In particular, the medial side of the superior frontal sulcus showed a blackish brown appearance, implying a large subcortical clot (Figure 4A). A dilated superior frontal sulcus was opened from the intact cortical side, and a dark red fluid hematoma was found under the blood clot. The fluid hematoma was aspirated without additional bleeding. The coagulated hematoma was evacuated after removing the cortex (Figure 4B) and identifying the bleeding source adjacent to the dilated superior frontal sulcus, which involved a tangle of vessels (Figure 4C). We then thoroughly cauterized the bleeding sites, leading to successful hemostasis.

The cortex over the subcortical hematoma was removed, and pathological examination was performed. Hematoxylin and eosin-stained sections showed homogeneous and eosinophilic

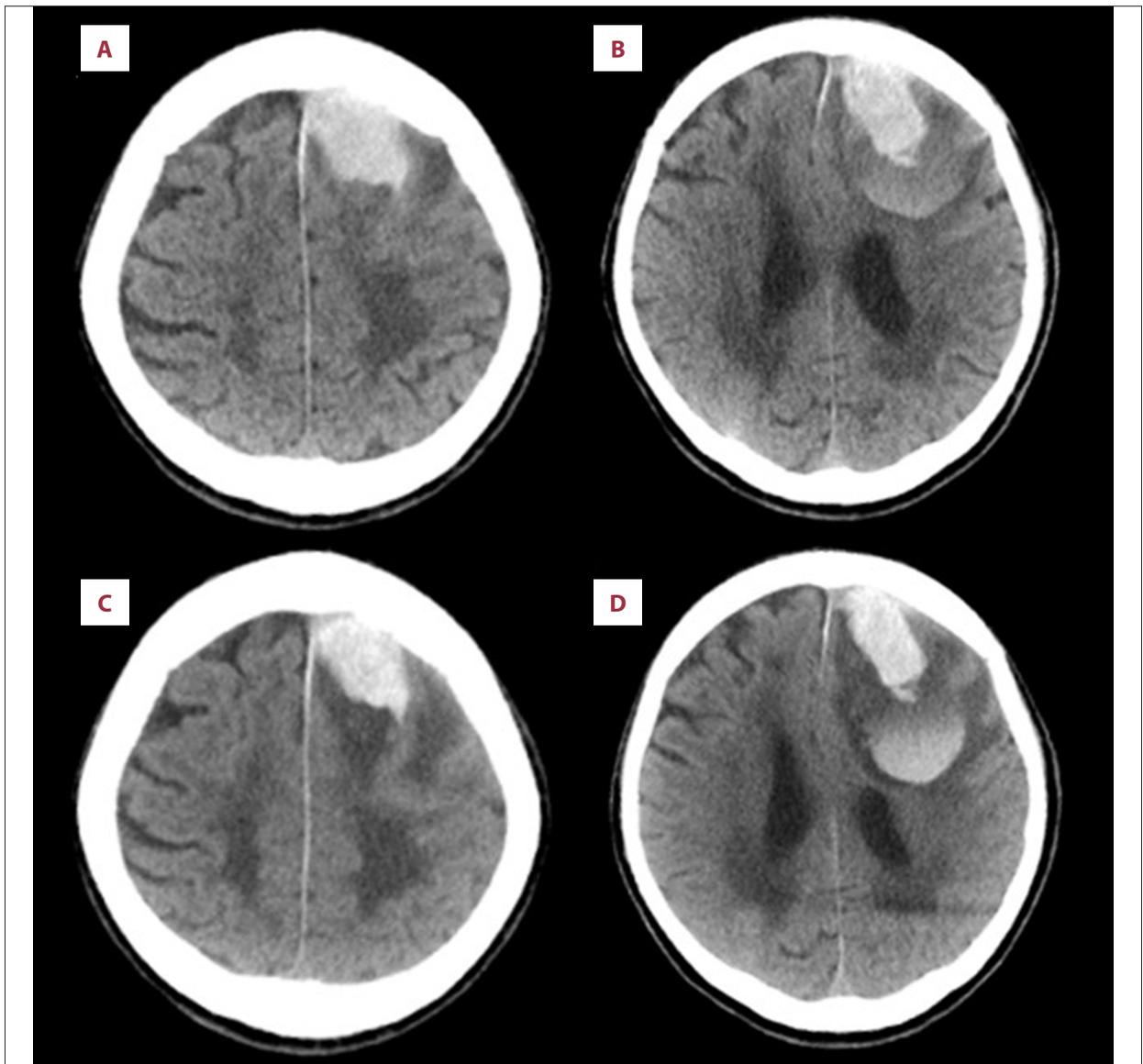


Figure 2. Admission computed tomography (CT) scans and preoperative CT scans after intracerebral hemorrhage (ICH). Admission CT scans showed an ICH including a high-density hematoma extending to the subarachnoid space in the superficial layer (A), which was within a cystic cavity showing a clear lower-density fluid component in the deep layer (B) of the left frontal lobe. Serial CT scans obtained on Day 3 revealed no evidence of expansion of the high-density clot (C), while there was an expansion of the fluid component containing a fluid-blood level (FBL) (D).

deposition in the tunica media and adventitia of the thickened cortical and leptomenigeal arterioles and small arteries (Figure 4D). Many leptomenigeal vessels had distinctive double-barreled lumina, in which a circumferential cleft was present in the tunica media. Congo red-stained sections showed a widespread typical orange-salmon color in the tunica media (Figure 4E), which was unaffected by potassium permanganate pretreatment, indicating CAA as the underlying cause of the ICH. Inflammatory cells including macrophages were present in the wall of the cyst (Figure 4F).

His postoperative course was uneventful. Follow-up CT and MRI showed no recurrence of the lesion. He underwent rehabilitation for 3 months after the operation, and was able to walk independently, but with mild aphasia.

Discussion

We described a case of CAA with cSS presenting as hematoma expansion with an FBL. Lobar ICH is the most important clinical presentation of CAA, while cSS and cerebral microbleeds

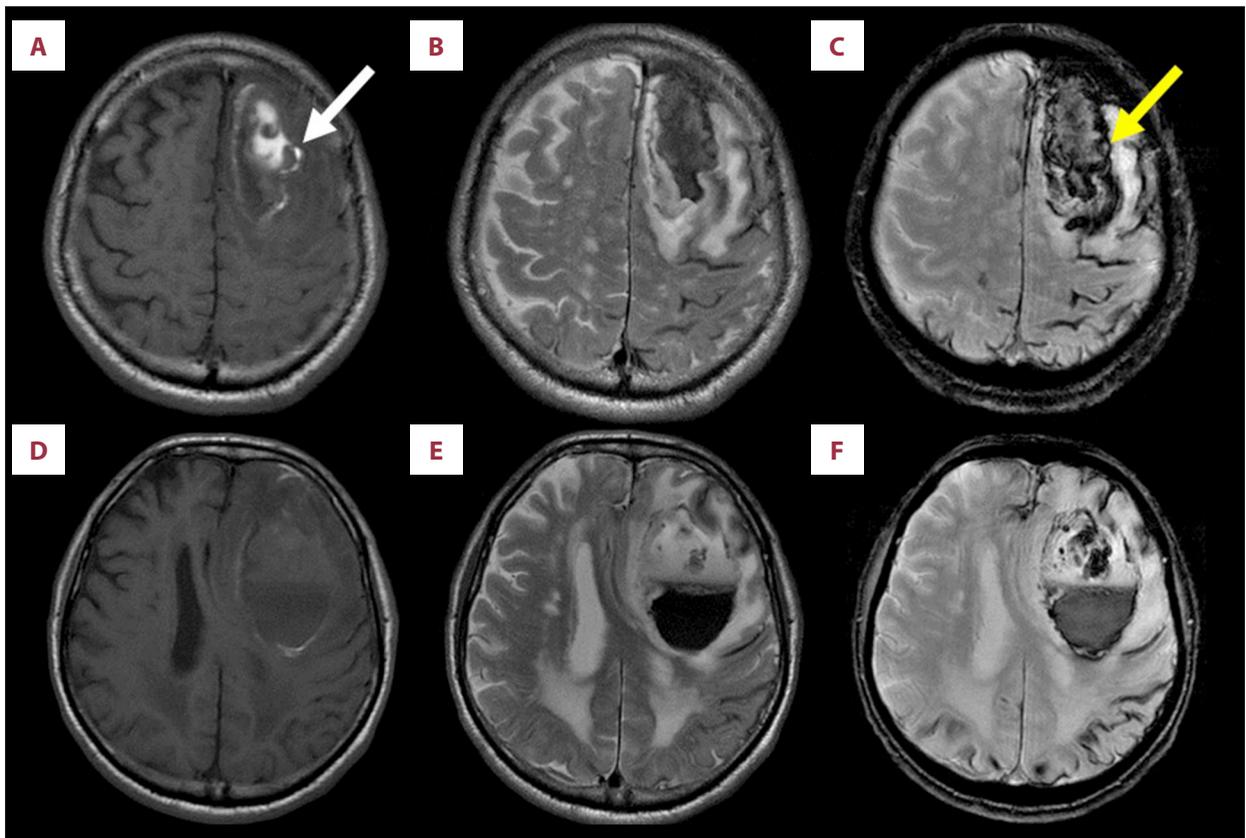


Figure 3. Preoperative magnetic resonance imaging (MRI). MRI obtained on Day 4 showed a hyperintense signal component extending into the superior frontal sulcus (white arrow) on T1-weighted imaging (A), corresponding to a slightly low intensity signal on T2-weighted imaging (B), in the superficial layer. T2*-GRE showed high intensity signal regions (yellow arrow) in the dilated low intensity signal of the left superior frontal sulcus (C). MRI in the deep layer showed an FBL (D-F).

are common CAA findings on MRI [9]. cSS has a distinct preference for the convexity of the cerebral hemispheres, reflecting linea blood-breakdown products including hemosiderin in the superficial layer of the cerebral cortex or in the sub-arachnoid space [1,9–11]. cSS was described in the modified Boston criteria for diagnosis of CAA without supporting pathological evidence from biopsy [9] and is of increasing utility as a diagnostic marker of CAA and a predictor of future ICH [12].

In acute CAA-associated ICH, the hematoma is typically surrounded by edema and necrosis with infiltration of inflammatory cells [13]. A secondary cascade of injury is produced by a combination of vasogenic edema from blood-brain barrier breakdown, mitochondrial dysfunction, and the products of hemoglobin breakdown [13]. Hemostasis is eventually achieved by activation of the coagulation cascade, along with mechanical tamponade [14]. However, in our case the CT scans obtained on Day 3 revealed an expansion of the fluid component with an FBL.

FBLs are defined as a horizontal interface between hypodense bloody serum layered ventrally above hyperdense erythrodeposition settled dorsally on CT scans [5]. FBLs are uncommon

in ICHs because there is no pre-existing fluid-filled space in which red blood cells can settle as sediment, such as for subdural and intraventricular hemorrhages. In this context, Daniels et al. and Richmond et al. reported that cystic cavities caused by hematoma liquefaction are an unusual finding in cases of arteriovenous malformation and that the presence of intraparenchymal FBLs suggests extravasation of blood into preexisting cystic cavities [6,15]. In our case, non-contrast CT scans also showed an FBL in left frontal lobe, with extension of blood into the cystic cavity from an overlying hematoma.

Previous reports have described the presence of FBLs on CT scans associated with warfarin use, tumors, or radiation-induced cystic necrosis [5,16,17]. For example, Pflieger et al. reported that FBLs within a hematoma were associated with coagulopathy and an increased risk of expansion, while 3 FBLs were seen in 185 intracerebral hemorrhages in patients with a normal prothrombin time-international normalized ratio [5]. This finding indicates that FBLs in ICH are rare in patients with normal coagulation parameters, as was found in our case [18]. Interestingly, Blacquiere et al. demonstrated that FBLs predicted hematoma expansion, as a surrogate marker for a similar phenomenon,

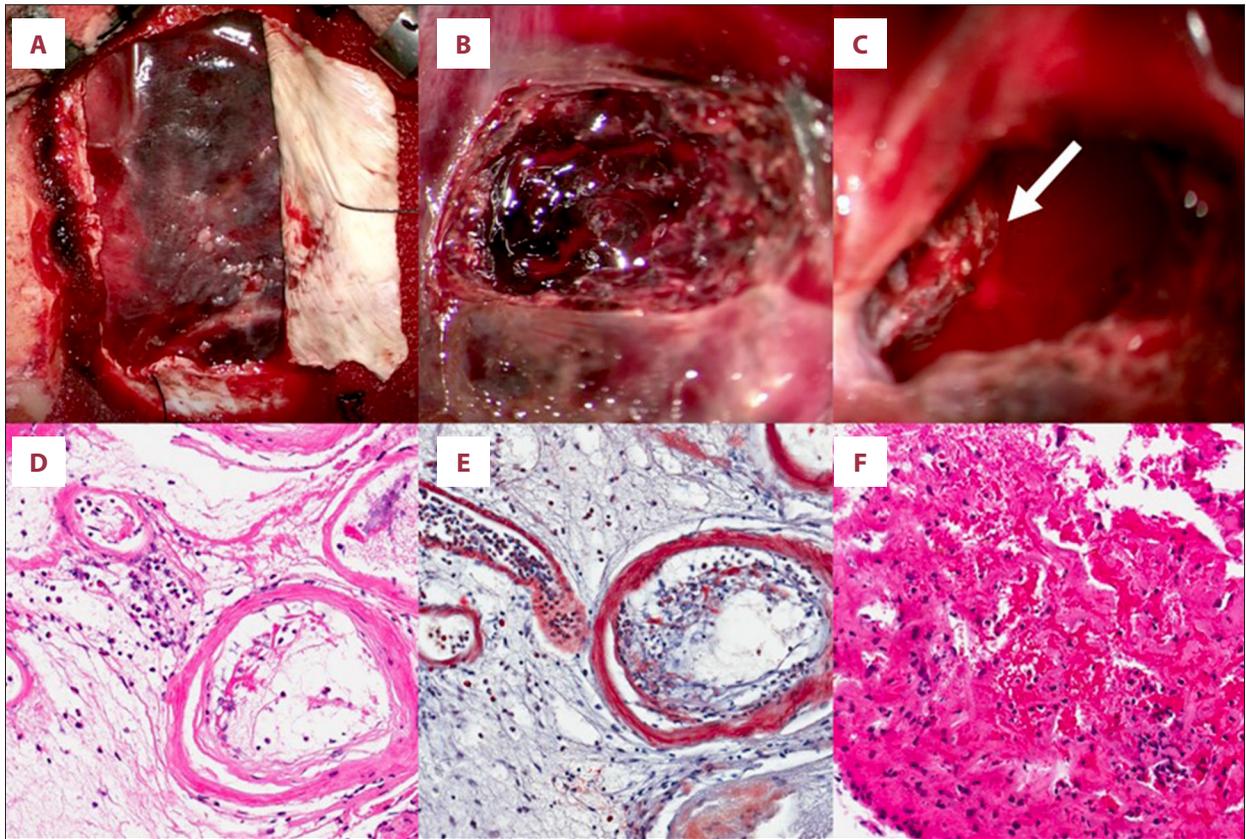


Figure 4. Operative and pathological findings. The surface of the brain showed widespread subarachnoid hemorrhagic changes. In particular, the medial side of the superior frontal sulcus showed a blackish brown appearance, implying a large subcortical clot (A). The coagulated hematoma was evacuated after removing the cortex (B), and the bleeding source was identified (white arrow) adjacent to the dilated superior frontal sulcus, which involved a tangle of vessels (C). Hematoxylin and eosin (H&E)-stained sections showed homogeneous and eosinophilic deposition in the tunica media and adventitia of the thickened cortical and leptomeningeal arterioles and small arteries (D: 100×). Many leptomeningeal vessels had distinctive double-barreled lumina, in which a circumferential cleft was present in the tunica media. Congo red-stained sections showed widespread typical orange-salmon color in the tunica media (E: 100×). Inflammatory cells including macrophages were present in the wall of the cyst (F: 100×).

as well as the spot sign, indicating ongoing and active bleeding within the hematoma when a CT angiogram is available [19]. FBLs have also been found to be related to both the presence of probable/definite CAA according to the modified Boston criteria and the presence of cSS [7]. Thus, FBLs might be an important indicator of hematoma expansion in acute CAA-associated ICH leading to worse outcomes, and early treatment may be required.

In the study of Minagawa et al., the characteristic surgical findings in patients treated by direct surgery were subarachnoid hemorrhage adjacent to the intracerebral hematoma and the existence of a tangle of vessels in the hematoma cavity. Moreover, evacuation of hematomas was relatively easy, without any difficulty in maintaining hemostasis during surgery [20], despite the requirement for coagulation hemostasis in our case. In the present case, serial CT scans revealed no evidence of expansion of the blood clot, although there was expansion of the fluid component with an FBL. Nevertheless, it remains

unclear whether coagulopathy with no laboratory evidence was related to expansion of the fluid component. Further studies in more cases are required.

Conclusions

We reported the details of a CAA-associated ICH case showing hematoma expansion presenting with FBL within the cystic cavities. Intraparenchymal FBLs suggest extravasation of blood into pre-existing cystic cavities because of hematoma liquefaction. Thus, FBLs are an important finding for hematoma expansion in acute CAA-associated ICH, and early treatment should be considered based on preoperative MRI.

Conflict of interest

None.

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