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Case Report

# A case of multiple cerebral hemorrhages followed by shower emboli ☆,☆☆

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ABSTRACT

An 87-year-old woman was admitted to our hospital (day 0) because of acute disorientation caused by multiple acute intracerebral hemorrhages. T2*-weighted magnetic resonance imaging (MRI) at admission revealed multiple subcortical old microbleeds indicative of cerebral amyloid angiopathy. Microbleeds in the right cerebellar hemisphere and acute spotty ischemia in the left cerebellum were also identified. The patient had been afebrile, and blood examinations on day 7 were within normal limits of inflammatory findings without antibiotics. On day 11, she developed a high fever and blood culture was performed. Her fever resolved within 2 days of antibiotic administration, although subsequent findings revealed her blood culture was positive for *Staphylococcus aureus*. Echocardiogram revealed bacterial vegetation in the mitral valve and moderate mitral regurgitation, with a diagnosis of infectious endocarditis (IE). Follow-up MRI demonstrated multiple spotty acute infarctions and an increased number of microbleeds. The patient may have been infected via peripheral infusions administered during the first few days after admission. However, considering the coexistence of acute hemorrhagic and ischemic lesions on MRI, as well as the acute lesions in the cerebellum, it is possible that IE was already latent on admission, and that the multiple brain hemorrhages might have been caused by IE rather than by cerebral amyloid angiopathy.



## Introduction

*Staphylococcus aureus* (*S. aureus*) is the most common cause of infectious endocarditis (IE), which can trigger embolic events with significant morbidity and mortality [1,2], although the origin of the infection is difficult to identify in 25% of cases [3]. Cerebral complications, which include cerebral ischemia, microbleeds, hemorrhages, abscesses, and microbial aneurysms, occur in 20%–70% of IE patients [1,4]. Magnetic resonance imaging (MRI) can effectively identify the cerebral complications associated with IE, with evidence of multiple old

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microbleeds in every part of the brain [4,5]. However, the coexistence of old microbleeds, chronic small infarctions, and old focal subarachnoid hemorrhages over different time periods is also a feature of cerebral amyloid angiopathy (CAA) [6]. Considering the clinical course and laboratory data, it is normally simple to distinguish between CAA and IE. However, in patients with silent progressive IE without neurological symptoms, it might be difficult to distinguish the 2 diseases using imaging findings because microbleeds and small infarctions on MRI can overlap between CAA and IE, especially in elderly.

## Case presentation

An 87-year-old woman, who had been living alone, experienced a generalized tonic seizure with right conjugate deviation for 2 minutes, and she was transferred to our hospital by ambulance. On arrival, her consciousness level was Glasgow Coma Scale (GCS) 10 (eye opening, 3; verbal response, 2; motor response, 5), and she moved her hands aimlessly without following our commands. Her blood pressure was 148/72 mmHg, heart rate was 106 beats per minute, body temperature was 36.0°C, and percutaneous oxygen saturation ($SpO_2$) was 97% under room air. She had no history of epilepsy, and had been taking antihypertensive and anti-cholesterol medications.

She was admitted to our hospital (day 0) because a head computed tomography (CT) scan showed a subcortical hemorrhage (2.5 cm in diameter) in the right frontal lobe, and spotty hemorrhagic lesions and focal superficial cortical hemorrhage in the left cerebral hemisphere (Fig. 1, CT yellow circles). On admission, her white blood cell (WBC) count was 7900 cells/μl and C-reactive protein (CRP) was 1.77 mg/dL. For differentiation from metastasis, MRI was performed (Fig. 1). T2*-weighted MRI demonstrated multiple old microbleeds and subcortical hemorrhages (T2*, white circles), while diffusion-weighted imaging (DWI) revealed spotty ischemic lesions. No abnormal vessels or aneurysms were observed on MR angiography (MRA), and no abnormal enhancements with gadolinium-dimeglumine (Gd) were identified on T1-weighted imaging (T1W). Spinal fluid examination showed a cell count of 2 cells/μL, protein of 42 mg/dL, glucose of 76 mg/dL (serum glucose 128 mg/dL), and no abnormal cells by cytology. Various tumor markers were within the normal range, which suggested no malignancy in the patient.

Levetiracetam (500 mg) and glyceol (200 mL) infusions were administered twice daily. The patient recovered to GCS 13 (E4V4M5) by the following morning, and was able to perform oral intake with assistance. Glyceol administration was discontinued after 4 days, while levetiracetam was switched to oral administration. Although mild disorientation remained with a GCS of 14 (E4V4M6), she was able to walk unassisted on day 7. Her WBC was 5600 cells/μL, while her CRP decreased to 0.52 mg/dL. Although the patient had a normal body temperature from admission, she developed a fever of 38.0°C on day 10 and 40°C on day 11, while her WBC increased to 9300 cells/μL and CRP to 23.07 mg/dL.

CT on day 11 revealed no new findings, while hemorrhages identified on admission showed evidence of absorption (Fig. 2, yellow circles). A urinary tract infection was suspected

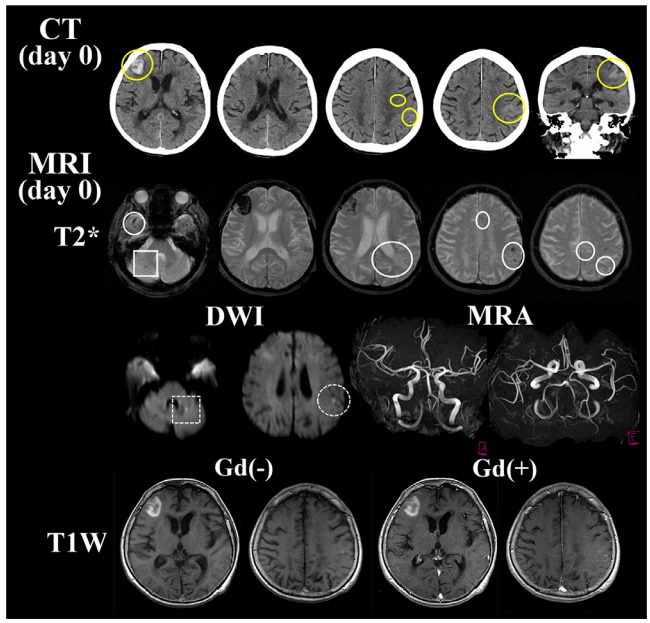


**Fig. 1 – Computed tomography (CT) and magnetic resonance imaging (MRI) at admission. CT on admission showed multiple multi-type hemorrhagic lesions (yellow circles), which included subcortical hemorrhage in the right frontal lobe, microbleeds, and superficial cortical hemorrhage in the left hemisphere. T2*-weighted MRI demonstrated multiple microbleeds (white circles) including the right cerebellar hemisphere (white square) that were not identified on CT, which were suggestive of old microbleeds. Spotty high signals (white dotted circles) including the left cerebellar hemisphere (white dotted square) were also identified on diffusion-weighted imaging (DWI), which were suggestive of acute ischemia. No vascular abnormalities were identified on magnetic resonance angiography (MRA), and there were no enhanced abnormal lesions by gadolinium-dimeglumine (Gd) on T1-weighted imaging (T1W).**

because of cloudy urine, and after urine and blood cultures were obtained, intravenous ceftriaxone sodium hydrate was initiated. The patient was free of any fever from the third day of treatment, and ceftriaxone sodium hydrate administration was continued. Her WBC had reduced to 8700 cells/μL and CRP to 7.24 mg/dL on day 15, and she still spoke well with a good appetite. On day 16, a urine culture performed on day 11 was found to be *Escherichia coli*-positive (3+). Next day, her body temperature rose to 39°C, and her WBC markedly increased to 28500 cells/μL and CRP to 10.22 mg/dL. On day 18, IE was diagnosed because the blood culture on Day 11 was reported positive (1+) for methicillin-susceptible *Staphylococcus aureus* (MSSA) and echocardiography showed 7.6 mm-sized warts in the mitral valve and marked mitral regurgitation (Fig. 2, echocardiogram). MRI revealed an increased number of microbleeds on T2*-weighted MRI (Fig. 2, white circles), and multiple spotty ischemic lesions in the cerebellum and bilateral cerebral hemispheric cortex on DWI (Fig. 2). An extremely high signal was observed in the hemorrhagic area in

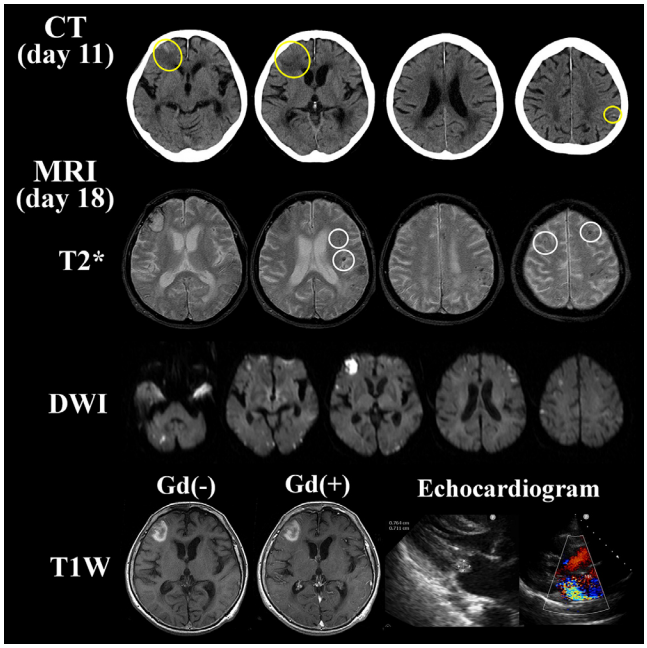


**Fig. 2 – Follow-up computed tomography (CT), magnetic resonance imaging (MRI), and echocardiogram. CT at day 11 showed that the intracerebral hemorrhages identified at admission were being absorbed. In addition to the increased number of microbleeds on T2*-weighted MRI, multiple ischemic lesions were identified in the cerebellar hemisphere and at the surface of the brain cortex on diffusion-weighted imaging (DWI). Although the right frontal lobe showed an extremely high signal on DWI, no enhancement by gadolinium-dimeglumine (Gd) was observed in the lesion, which ruled out a brain abscess. Echocardiogram illustrated a bacterial mass at the mitral valve (left) and definite mitral regurgitation (right).**

the right frontal lobe on DWI, while there was no contrast effect and a brain abscess was ruled out (Fig. 2, T1W). Although the patient was still talkative and eating well, she was transferred to a facility with cardiology and surgical facilities on day 19 of admission before she presented with serious neurological deficits or cardiac failure symptoms.

## Discussion

In the present case, CAA and IE were the 2 possible causes of cerebral hemorrhage. The cerebral hemorrhage in our patient was atypical for a normal hypertensive hemorrhage. Furthermore, MRI findings on admission showed multiple old microbleeds scattered throughout the subcortex, but without evidence of microbleeds in the basal ganglia and brainstem, which is compatible to features of CAA [6]. Multiple small infarctions are another feature identified in CAA patients [7,8]. Because of the advanced age of our patient and the fact that encephalitis and malignant disease were ruled out, it is possible that the cerebral hemorrhage was caused by CAA. Despite the absence of antibiotic treatment, it was unlikely that the MSSA bacteremia was latent from the time of admission because there were no signs of inflammation at day 7 of admission and no fever until day 9. Drug injections are also a major cause of IE [9], and it is possible that our patient was infected by MSSA via the peripheral infusion performed after admission. The bacteremia progressed silently, and high fever occurred on day 10 when MSSA bacteremia became symptomatic. Although the fever temporarily subsided with antibiotics, the bacteria attached to the mitral valve and proliferated, which resulted in an embolic stroke on day 18 of admission. The observed increase in the number of microbleeds by DWI can be explained by IE.

Despite these findings, MRI at admission also showed multiple acute intracerebral hemorrhages and multiple acute spotty infarctions. Importantly, the coexistence of multiple acute hemorrhagic and fresh ischemic lesions is a finding seen in cerebral complications due to embolism, and has not been reported in CAA. For example, Introna et al. reported 4 cases of convex subarachnoid hemorrhage and small acute ischemia, concluding that all 4 were due to embolic sources rather than CAA [10]. Our case also showed multiple microbleeds in the right cerebellar hemisphere and acute spotty ischemia in the left cerebellum (Fig. 1, T2*-weighted imaging and DWI). Microbleeds in IE are found in all regions of the brain, but with a high frequency in the cerebellum, which differs from the microbleeds seen in hypertension and CAA [5]. Although there were no clinical symptoms suggestive of IE at onset, the admission MRI findings also suggested the possibility that the patient already had IE at admission, and that the multiple cerebral hemorrhages were caused by IE, while the original microbleeds caused by CAA made a diagnosis of IE difficult.

## Patient consent

This case report was written with the permission of the patient's family, and a signature of the patient's family was obtained for written consent.

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