Recurrent cerebral microbleeds with acute stroke symptoms
A case report
Pahn Kyu Choi, MD, Ji Yeon Chung, MD, Seung Jae Lee, PhD, Hyun Goo Kang, MD PhD.*

Abstract
Rationale: Cerebral microbleeds are lesions that appear as round low signal intensity areas with a diameter of 2–5 mm on gradient echo T2-weighted sequence magnetic resonance imaging. Cerebral microbleeds are hemorrhages found in the brain parenchyma and they are caused by the extravasation of the blood. Although more patients with ischemic stroke are found to have cerebral microbleeds, only a few studies have evaluated other neurologic abnormalities outside of cognitive dysfunction due to cerebral microbleeds.

Patient Concerns: A 73-year-old female patient had only a lacunar infarction with the development of a new microbleed whenever a new neurologic symptom occurred, without the occurrence of acute ischemic stroke.

Diagnoses: A 73-year-old female patient diagnosed symptomatic cerebral microbleeds.

Interventions: Brain magnetic resonance imaging was taken within a few hours of the occurrence of a new symptom and we confirmed increased cerebral microbleeds in the ventral-posterolateral area of the thalamus, consistent with the symptoms.

Outcomes: This case study is meaningful because it proves that repeated occurrences of cerebral microbleeds in a specific area can induce acute ischemic stroke-like symptoms.

Lessons: Cerebral microbleeds have been considered to be asymptomatic lesions thus far. However, recent studies have reported the association of cerebral microbleeds with neurological symptoms including cognitive dysfunction. This study confirmed the presence of newly formed cerebral microbleeds through imaging follow-ups whenever a symptom occurred.

Abbreviations: CMB = cerebral microbleed, DWI = diffusion weighted image, GRE = gradient echo image, MRC = Medical Research Council, MRI = magnetic resonance imaging.

Keywords: cilostazol, microbleeds, MRI, recurrent, stroke

1. Introduction
Cerebral microbleeds (CMBs) are lesions that appear as round low signal intensity areas with a diameter of 2 to 5 mm on gradient echo image (GRE) T2-weighted imaging sequence magnetic resonance imaging (MRI).[1] CMBs are hemorrhages found in the brain parenchyma and they are caused by the extravasation of the blood vessel. It is believed that they exhibit a low signal intensity on GRE because of the paramagnetic effects of blood breakdown products including hemosiderin, deoxyhemoglobin, and ferritin.[2] Although more patients with ischemic stroke are found to have CMBs,[3] only a few studies have evaluated other neurologic abnormalities outside of cognitive dysfunction due to CMBs.[4] The authors present the case of a patient who had only a lacunar infarction with the creation of a new CMB whenever a new neurologic symptom occurred without the occurrence of acute ischemic stroke. Therefore, we report this case with a review of the previous literature.

2. Case report
A 73-year-old female patient visited the hospital due to left-sided hemiparesis. She did not have a family history of stroke and had been taking antihypertensive medication for the past 10 years and angina medication for the past 6 years. She had a chronic headache for past few years. She had frequent headache with nausea or vomiting on 15 days per month. A neurological examination was conducted, and left hemiparesis, paresthesia, and dysarthria were found (Fig. 1). The muscle power of the left upper and lower limbs was Medical Research Council (MRC) grade III and the brain diffusion-weighted MRI (diffusion weighted image [DWI]) showed a right lenticulostriate artery territorial infarction. Obstruction and stenosis of the main vessel were not observed. Multiple CMBs were found in the bilateral deep gray matter and pons on GRE MRI (Fig. 2A). Transthoracic echocardiography was normal. Cilostazol 50 mg twice daily was
administered for secondary prevention of stroke in consideration of the multiple CMBs. The muscle power of the patient’s left upper and lower limbs improved to MRC grade IV on the 7th day of hospitalization so she was discharged. Outpatient follow-up examination found that the muscle power of patient’s left upper and lower limbs improved to MRC grade V 1 month after discharge. However, her hypertension was not controlled. Therefore, the dose of existing hypertension medication was increased and the follow-up examination found that her blood pressure was well controlled afterward.

The patient presented with numbness in the left upper limb 6 months after discharge, and DWI and GRE brain MRI were performed. The newly taken DWI and GRE brain MRI were not different from previous images (Fig. 2B). Eight months after discharge, the patient experienced acute left hemiparesis and paresthesia with headache and she visited the emergency room within 1 hour of its onset. Neurological examination revealed that the muscle strength of the left upper and lower limbs was decreased to MRC grade IV. The blood pressure of the patient was 200/110 mmHg when she visited the emergency room and electrocardiography did not show any abnormal findings except sinus bradycardia. The blood test was normal. The recurrence of cerebral infarction was suspected so brain MRI and DWI were performed but an acute infarction was not found. However, a

---

**Figure 1.** Timeline of the patient. DWI = diffusion-weighted image, ER = emergency room, GRE = gradient echo image, Lt = left.

---

**Figure 2.** Brain images of the patient. (A) Brain MRI with acute ischemic stroke. Brain DWIs show right lenticulostriatal artery territorial infarction. Multiple microbleeds are seen in the bilateral deep gray matter (arrow) and pons on GREs. (B) The newly taken DWI and GRE brain MRI do not appear different from previous images (arrow). (C) Eight months after the previous ischemic stroke, a new microbleed was observed (arrow) in addition to previous microbleeds in the right thalamus on GRE, with the patient presenting with left hemiparesis and paresthesia. (D) Two months after the previous microbleed, a new microbleed was observed (arrow) in addition to previous microbleeds in the right thalamus on GRE, with the patient again presenting with left paresthesia. DWI = diffusion-weighted image, GRE = gradient echo image, MRI = magnetic resonance imaging.
Although Teo et al. reported a case of CMBs causing a neurological abnormality, it was not possible to know if the CMBs existed before the onset of the symptoms because there was no history of trauma or surgery. Moreover, the presence of CMBs in the brain was not confirmed by brain MRI at the time of patient hospitalization. CMBs are known as silent lesions, but recent studies have reported that CMBs are related to cognitive dysfunction. No large-scale study has shown that CMBs cause other neurological symptoms. Patient was followed up for 12 months and there was no abnormal neurological symptoms.

### Table 1

| Patient          | Age/sex | Brain MRI before stroke symptom | First attack | Second attack | Third attack | Symptom correlation with CMB lesion |
|------------------|---------|--------------------------------|--------------|---------------|--------------|-----------------------------------|
| Watanabe et al.  | 72/male | T2 weighted image: multiple lacunar infarction with brainstem | None         | T2 weighted image: no other new lesion | N/A          | +                                 |
| James et al.     | 69/male | None                            | Brain DWI: no lesion | Brain GRE: new CMB in medial lemniscus in pons | N/A          | +                                 |
|                  | 78/male | Brain GRE: no lesion            | Brain GRE: CMB in right pons | Brain GRE: CMB in right pons | N/A          | +                                 |
| Our patient      |         | Brain DWI: right LSA territorial infarction | Brain DWI: no lesion | Brain DWI: no lesion | Brain DWI: no lesion | +                                 |

CMB = cerebral microbleed, DWI = diffusion-weighted image, GRE = gradient echo image, LSA = lenticulostriate artery, N/A = not applicable, VPL = ventral-posterolateral.
caused by CMBs. On the other hand, in this case, we obtained brain MRI within a couple of hours of the occurrence of a new symptom and confirmed the increased CMBs in the ventral-posterolateral area of the thalamus, consistent with the symptoms. Moreover, the lesion correlated with the new symptoms. These are important findings, particularly the new symptoms could be the common fluctuation of residual symptoms due to the sequelae of existing cerebral ischemic stroke. However, it is noteworthy that new CMBs were observed in the area associated with the symptoms.

CMBs are hemorrhages in the brain parenchyma where hemosiderin deposits locally around the small vessel. Hypertensive arteriopathy and cerebral amyloid angiopathy are known as the main causal mechanisms of CMBs. Lobar CMBs generally occur in cerebral amyloid angiopathy and CMBs in the deep gray matter are associated with hypertensive arteriopathy.\(^{[9]}\) CMBs are also known as indicators of small vessel disease.\(^{[10]}\) In particular, CMBs are highly associated with small vessel disease when they are located in the deep gray matter or infratentorial area.\(^{[11]}\) The occurrence mechanisms of lacunar infarction and white matter change are similar to those of CMBs,\(^{[12]}\) because they are also caused by the extravasation of the blood vessel and blood components due to damage to the arterial endothelium.\(^{[13]}\) Moreover, hypertension is known as an important causal factor of lacunar infarction and white matter change, while CMBs can also be caused by hypertension.\(^{[9,13]}\) The causal mechanisms of CMBs are similar to those of small vessel disease or lacunar infarction.

It is believed that CMBs, which typically follow the path of the corticospinal tract, easily causing symptoms, even with a small lesion, or are located in areas such as the thalamus, would cause symptoms similar to an ischemic stroke. The patient in this case had CMBs in the thalamus as well as lacunar infarction. Furthermore, she had uncontrolled hypertension and experienced acute stroke symptoms and headache several times when her blood pressure was not controlled well. Whenever she experienced a symptom, new CMB lesions were observed in the thalamus. The dosage of antiplatelet was maintained continuously and the dosage of antihypertensive agent was increased during each admission. New neurological symptoms and headache were not observed in follow-up after her hypertension was controlled. Therefore, the authors suspect that uncommon symptomatic CMBs occurred due to hypertensive arteriopathy because her hypertension was not controlled well. Moreover, all neurological symptoms owing to the CMBs improved within a few days in this case. These results suggest that neurological symptoms due to CMBs could have improved rapidly as the extravasation of the small vessel hemorrhage improved, unlike the symptoms of ischemic stroke, which mostly remain because of the sequelae of cell death.

Cilostazol is known to act as an antiplatelet agent and enhance endothelial function.\(^{[14]}\) Our patient had taken cilostazol 100 mg twice a day after acute ischemic stroke throughout the outpatient follow-up. Therefore, endothelial cell stability was improved, and this may be helpful for the rapid recovery of neurological symptoms due to CMBs. However, it is impossible to generalize that CMBs cause neurological symptoms only based on the results of this case study, because it is a single case and not a large-scale prospective study. Therefore, it will be necessary to have a large-scale study of the relationship between the blood pressure control of patients with lacunar infarction and the occurrence of symptomatic CMBs in the future.

CMBs have been considered to be asymptomatic lesions thus far. However, recent studies have reported the association of CMBs with neurological symptoms including cognitive dysfunction. However, as far as the authors are aware, no study has confirmed that the number of new CMB lesions increased with the occurrence of repeated acute ischemic stroke-like symptoms based on imaging evidence. This case study is meaningful because it proves that repeated occurrences of CMBs in a specific area can induce acute ischemic stroke-like symptoms and this study confirmed the presence of newly formed CMBs through imaging follow-ups whenever a symptom occurred. The results of this study suggest that a large-scale prospective study will be needed to determine the symptom occurrence according to the location of CMBs.

**Author contributions**

**Conceptualization:** Pahn Kyu Choi, Ji Yeon Chung, Hyun Goo Kang.

**Data curation:** Hyun Goo Kang.

**Formal analysis:** Hyun Goo Kang.

**Methodology:** Pahn Kyu Choi, Ji Yeon Chung, Seung Jae Lee, Hyun Goo Kang.

**Resources:** Pahn Kyu Choi, Ji Yeon Chung.

**Supervision:** Seung Jae Lee.

**Validation:** Ji Yeon Chung, Hyun Goo Kang.

**Writing – original draft:** Pahn Kyu Choi.

**Writing – review & editing:** Ji Yeon Chung, Seung Jae Lee, Hyun Goo Kang.

Hyun Goo Kang orcid: 0000-0001-5443-3635

**References**

1. Schrag M, McAuley G, Pomakian J, et al. Correlation of hypointensities in susceptibility-weighted images to tissue histology in dementia patients with cerebral amyloid angiopathy: a postmortem MRI study. Acta Neuropathol 2010;119:291–302.

2. Kidwell CS, Saver JL, Villablanca JP, et al. Magnetic resonance imaging detection of microbleeds before thrombolysis: an emerging application. Stroke 2002;33:95–8.

3. Werring DJ, Coward LJ, Losseff NA, et al. Cerebral microbleeds are common in ischemic stroke but rare in TIA. Neurology 2005;65:1914–8.

4. Werring DJ, Frazer DW, Coward LJ, et al. Cognitie dysfunction in patients with cerebral microbleeds on T2* weighted gradient-echo MRI. Brain 2004;127:2265–75.

5. Greig CM, Chaudhary UJ, Brown MM, et al. The Microbleed Anatomical Rating Scale (MARS): reliability of a tool to map brain microbleeds. Neurology 2009;73:1759–66.

6. Hamann GF, Okada Y, Fitridge R, et al. Microvascular basal lamina antigens disappear during cerebral ischemia and reperfusion. Stroke 1995;26:2120–6.

7. Watanabe A, Kobashi T. Lateral gaze disturbance due to cerebral microbleed in the medial lemniscus in the mid-pontine region: a case report. Neuroradiology 2005;47:908–11.

8. Teo JTH, Ramadhan H, Greig CM, et al. Cerebral microbleeds cause an acute stroke syndrome? Neuror Clin Pract 2011;1:75–7.

9. Fazekas F, Kleinert R, Roob G, et al. Histopathologic analysis of foci of signal loss on gradient-echo T2* weighted MR images in patients with spontaneous intracerebral hemorrhage: evidence of microangiopathy-associated microbleeds. AJNR Am J Neuroradiol 1999;20:637–42.

10. Wardlaw JM, Smith EE, Bussel GJ, et al. Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration. Lancet Neurol 2013;12:822–38.

11. Norrving B. Evolving concept of small vessel disease through advanced imaging. J Stroke 2015;17:94–100.

12. Kato H, Izumiya M, Izumiya K, et al. Silent cerebral microbleeds on T2* weighted MRI: correlation with stroke subtype, stroke recurrence, and leukoaraisis. Stroke 2002;33:1536–40.

13. Wardlaw JM, Sanderson PA, Dennis MS, et al. Is breakdown of the blood-brain barrier responsible for lacunar stroke, leukoaraisis, and dementia? Stroke 2003;34:806–12.

14. Lee SJ, Lee JS, Choi MH, et al. Cilostazol improves endothelial function in acute cerebral ischemia patients: a double-blind placebo controlled trial with flow-mediated dilation technique. BMC Neurol 2017;17:169.