Case Report

Subsequent bilateral intracerebral hemorrhages in the putamen and thalamus: A report of four cases

Satoshi Tsutsumi, Kiyotaka Kuroda, Hiroki Sugiyama, Natsuki Sugiyama, Hideaki Ueno, Hisato Ishii

Department of Neurological Surgery, Juntendo University Urayasu Hospital, Urayasu, Japan.

E-mail: *Satoshi Tsutsumi - shotaro@juntendo-urayasu.jp; Kiyotaka Kuroda - kiyotaka.kuroda@gmail.com; Hiroki Sugiyama - hi-sugiyama@juntendo.ac.jp; Natsuki Sugiyama - natsuking0602@yahoo.co.jp; Hideaki Ueno - hideakuieno1229@gmail.com; Hisato Ishii - hisato-i@juntendo.ac.jp

INTRODUCTION

Despite the recognition of the benefits of a healthy lifestyle and the advantages of preventive medicine, spontaneous intracerebral hemorrhage (ICH) remains a dismal disease. It is estimated to develop at a mean rate of 26 out of 100,000 in the general population per year. Approximately half of ICH patients survive for 1 year, and nearly, two-fifths survive for 5 years.\(^\text{[3]}\) In Japan, the incidence of ICH declined steeply from the 1960s to the 1970s due to a reduction in hypertension and alcohol intake. However, this decline has leveled subsequently, presumably due to the increased incidence of thalamic hemorrhage in the elderly.\(^\text{[4]}\)

Simultaneous or subsequent bilateral ICHs are distinct entities that typically result in worse outcomes than solitary hemorrhages. They have been most frequently reported as bilateral
putaminal or thalamic hemorrhages. However, in them, "simultaneous" and "subsequent" cases were not separately described. Therefore, subsequent bilateral ICHs (SBICHs) in the putamen and thalamus remain unclear. Cerebral microbleeds, typically asymptomatic hemosiderin deposits found in the basal ganglia and thalamus, have been reported to show dynamic temporal changes. They are associated with large ICHs and significant volumes of white matter hyperintensities. In addition, microbleeds are thought to be associated with serum levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C).

Here, we report four cases of SBICHs that developed in the putamen and thalamus.

In this study, SBICHs were defined as a combination of asymptomatic, older hemorrhages in the unilateral putamen or thalamus, and younger hemorrhages in the contralateral counterparts that caused stroke. These hemorrhages appeared at least partially hyperdense on computed tomography (CT) and hypointense on gradient-echo T2*-weighted magnetic resonance imaging (T2*WI). In addition, microbleeds were determined to be hemorrhages smaller than 10 mm that appeared iso- or hypodense on CT, accompanied by dense hemosiderin depositions that were assessed on T2*WI.

**CASE PRESENTATION**

Between February 2017 and February 2022, 386 patients with spontaneous ICHs were admitted to the authors’ hospital. Among these patients, 4 (1.0%) were diagnosed with SBICHs. These four patients are described as follows:

**Case 1:** A 47-year-old fully dependent woman presented with the left hemiparesis on awakening in the morning. The patient had a medical history of hypertension, diabetes mellitus, and hyperuremia. However, she had not been prescribed anticoagulants or antiplatelet drugs. Initially, her blood pressure was 184/120 mmHg. Serum TC, LDL-C, and HDL-C levels were 279 mg/dl (128–219), 197 mg/dl (70–139), and 47 mg/dl (41–96), respectively. CT and T2*WI images at presentation revealed a right thalamic hemorrhage, 16 mm × 19 mm × 21 mm in maximal dimension with ventricular perforation. In addition, a small, older hematoma, 10 mm × 5 mm in size, was identified in the left thalamus. It was accompanied by a hyperdense rim on CT [Figure 1a]. Contrast-enhanced CT revealed no spot signs [Figure 1b]. On T2*WI, microbleeds were identified in the right thalamus, medulla oblongata, pons, and left temporal [Figures 1c and d]. The rim of the small hematoma found in the left thalamus appeared a hypointense rim on T2*WI [Figure 1d].

This patient was conservatively managed and eventually transferred to a rehabilitation facility with a modified Rankin scale (mRS) of 2.

**Case 2:** A 53-year-old fully dependent man presented with a disturbance in consciousness that measured nine points on the Glasgow Coma Scale. The patient's medical history was unremarkable. Anticoagulants and antiplatelet drugs had not been prescribed. Initially, this patient's blood pressure was 184/131 mmHg. Serum levels of TC, LDL-C, and HDL-C were 203 mg/dl, 123 mg/dl, and 60 mg/dl, respectively. CT and T2*WI images at presentation revealed a large left putaminal hemorrhage, 52 mm × 35 mm × 38 mm in dimension. A small and older hematoma, 5 × 5 mm in dimension, was identified in the right thalamus with perilesional brain edema. This older hematoma appeared hypointense on CT [Figure 2a]. Contrast-enhanced CT revealed no spot signs [Figure 2b]. On T2*WI, the small right thalamic hematoma appeared hypointense. In addition, microbleeds were observed in the right putamen [Figure 2c]. The patient underwent hematoma evacuation and was transferred to a rehabilitation facility with a mRS of 4.

**Case 3:** A 65-year-old fully dependent woman presented with the right hemiparesis. The patient's medical history was unremarkable.
Anticoagulants and antiplatelet drugs had not been prescribed. At presentation, her blood pressure was 168/68 mmHg. Serum levels of TC, LDL-C, and HDL-C were 201 mg/dl, 90 mg/dl, and 95 mg/dl, respectively. CT at presentation and T2*WI that were performed on posthospitalization day (PHD) 1 revealed a left putaminal hemorrhage, 20 mm × 40 mm × 35 mm in dimension. In addition, a small, older hematoma, 8 × 8 mm in dimension, was identified in the right putamen with perilesional brain edema. This older hematoma was accompanied by a hyperdense rim on CT [Figure 3a]. Contrast-enhanced CT revealed no spot signs [Figure 3b]. On T2*WI, the right putaminal hematoma was accompanied by a hypointense rim. Microbleeds were not observed [Figure 3c]. The patient was conservatively managed and transferred to a rehabilitation facility, with an mRS score of 3.

Case 4: A 75-year-old fully dependent woman presented with the right hemiparesis. The patient had a medical history of hypertension and diabetes mellitus. She had not been prescribed anticoagulants or antiplatelet drugs. Initially, her blood pressure was 186/110 mmHg. Serum levels of TC, LDL-C, and HDL-C were 245 mg/dl, 145 mg/dl, and 64 mg/dl, respectively. CT at presentation and T2*WI that were performed on PHD 8 revealed a left thalamic hemorrhage, 19 mm × 30 mm × 25 mm in dimension. In addition, small, older hematomas, 2 and 8 mm in dimension, were identified in the right thalamus and cerebellar hemisphere, respectively. These hematomas appeared hyperdense on CT and hypointense on T2*WI [Figures 4a-c]. Contrast-enhanced CT was not performed due to newly found renal dysfunction. On T2*WI, microbleeds were found in the left cerebellar hemisphere, the right thalamus, and the left temporal lobe [Figures 4c and d]. The patient was conservatively managed with spontaneous resolution of the hematomas. Eventually, she was transferred to a rehabilitation facility, with an mRS score of 4. The clinical data of these four patients are summarized in [Table 1].
DISCUSSION

In our four patients, SBICHs in the putamen and thalamus presented as a combination of asymptomatic, small ICH in the subacute phase, and contralateral ICH that occurred stroke. Initially, these patients exhibited an elevated blood pressure at mean of 180.5 ± 7.3/107.3 ± 23.8 mmHg. This suggested that hypertension may be an associated factor of the SBICHs. In addition, all the small ICHs were asymptomatic and <10 mm in diameter. They were cystic in Cases 1 and 3 and solid hematomas in Cases 2 and 4. The various consistencies may reflect dynamic temporal changes of microbleeds.[11] Three of the four patients underwent magnetic resonance imaging within 1 day after onset, suggesting that the age of hematomas was well detected on it. Furthermore, in two of the four patients, a small ICH was found to accompany perilesional brain edema, indicating a characteristic finding of microbleeds.[14] Therefore, the small and asymptomatic ICHs found in the putamen and thalamus were considered to be microbleeds in the subacute phase. On the other hand, based on the findings on neuroimages, symptomatic ICHs occurring in the contralateral putamen and thalamus were thought to develop subsequently to the small ICHs or microbleeds. This means that certain spontaneous ICHs may develop in the putamen or thalamus subsequent to subacute microbleeds occurring in their contralateral counterparts.

Microbleeds are thought to be associated with serum levels of TC, LDL-C, and HDL-C. The previous studies have suggested that a low level of TC and HDL-C may be associated with an increase of microbleeds in the deep cerebral hemisphere, while a high level of LDL-C may act as a protective factor against increased microbleeds.[11,12] None of our patients had low serum levels of TC, HDL-C, or LDL-C, potentially

Table 1: Summary of four patients.

| Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|-----------|-----------|-----------|-----------|
| Age (y.o.)| 47        | 53        | 65        | 75        |
| Gender    | Woman     | Man       | Woman     | Woman     |
| Me. his.  | HT, DM    | Unremarkable | Unremarkable | HT, DM    |
| Anti plt./coag. therapy | (-) | (-) | (-) | (-) |
| Initial BP (mmHg) | 184/120 | 184/131 | 168/68 | 186/110 |
| TC (128–219 mg/dl) | 279 | 203 | 90 | 145 |
| LDL-C (70–139 mg dl) | 197 | 123 | 95 | 64 |
| HDL-C (41–96 mg/dl) | 47 | 60 | - | - |
| Hemo. Type | rt. Th. and lt. Th. | lt. Pu. and rt. Th. | lt. Pu. and rt. Pu. | lt. Th. and rt. Th. |
| Size of sym. he. (mm) | 16×19×21 | 52×35×38 | 20×40×35 | 19×30×25 |
| Spot sign | (-) | (-) | (-) | (-) |
| Date of MRI | PHD 0 | PHD 0 | PHD 1 | PHD 8 |
| Location of microbleeds | rt. Th., med., pons, lt. tl | rt. Pu. | (-) | lt. cereb., rt. Th., lt. tl. |
| Treatment | Conservative | Surgery | Conservative | Conservative |
| mRS at Dis. | 2 | 4 | 3 | 4 |

bil: Bilateral, BP: Blood pressure, cereb: Cerebellum, coag: Coagulation, Dis: Discharge, DM: Diabetes mellitus, HDL-C: High-density lipoprotein cholesterol, he.: Hematoma, Hemo.: Hemorrhage, his.: History, HT: Hypertension, LDL-C: Low-density lipoprotein cholesterol, lt: Left, Me.: Medical: med.: Medulla oblongata, MRI: Magnetic resonance imaging, mRS: modified Rankin scale, PHD: Post hospitalization day, plt.: Platelet, Pu.: Putamen, rt: Right, TC: Total
promoted factors for the development of microbleeds. Further, accumulation of cases is required for an enhanced understanding of SBICHs.

CONCLUSION

SBICHs are rare bilateral hemorrhages that may present with asymptomatic microbleeds in the putamen or thalamus coupled with symptomatic, subsequent hemorrhages in the contralateral counterparts. The latter hemorrhage may develop during the subacute phase of microbleeds in the putamen or thalamus.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Balestrieri A, Lucatelli P, Suri HS, Montisci R, Suri JS, Wintermark M, et al. Volume of white matter hyperintensities, and cerebral micro-bleeds. J Stroke Cerebrovasc Dis 2021;30:105905.
2. Choudhary A, Goyal MK, Singh R. Simultaneous bilateral hypertensive thalamic hemorrhage: A rare event. Neurol India 2018;66:575-7.
3. Dromerick AW, Meschia JF, Kumar A, Hanlon RE. Simultaneous bilateral thalamic hemorrhages following the administration of intravenous tissue plasminogen activator. Arch Phys Med Rehabil 1997;78:92-4.
4. Gotoh S, Hata J, Nomiyama T, Hirakawa Y, Nagata M, Mukai N, et al. Trends in the incidence and survival of intracerebral hemorrhage by its location in a Japanese community. Circ J 2014;78:403-9.
5. Han JH, Jeon JP, Choi HJ, Yang JS, Kang SH, Cho YJ. Delayed consecutive contralateral thalamic hemorrhage after spontaneous thalamic hemorrhage. J Cereb Blood Flow Metab 2016;36:352-63.
6. Imai K. Bilateral simultaneous thalamic hemorrhages--case report. Neurol Med Chir (Tokyo) 2000;40:369-71.
7. Kabuto M, Kubota T, Kobayashi H, Nakagawa T, Arai Y, Kitai R. Simultaneous bilateral hypotensive intracerebral hemorrhages-two case report. Neurol Med Chir (Tokyo) 1995;35:584-6.
8. Kono K, Terada T. Simultaneous bilateral hypertensive putaminal of thalamic hemorrhage: Case report and systematic review of the literature. Turk Neurosurg 2014;24:434-7.
9. Laiwattana D, Sangsawang B, Sangsawang N. Primary multiple simultaneous intracerebral hemorrhages between 1950 and 2013: Analysis of data on age, sex and outcome. Cerebrovasc Dis Extra 2014;4:102-14.
10. Lee SH, Kim BJ, Roh JK. Silent microbleeds are associated with volume of primary intracerebral hemorrhage. Neurology 2006;66:430-2.
11. Lee SH, Lee ST, Kim BJ, Park HK, Kim CK, Jung KH, et al. Dynamic temporal change of cerebral microbleeds: Long-term follow-up MRI study. PLoS One 2011;6:e25930.
12. Li X, Zhang L, Wolfe CDA, Wang Y. Incidence and long-term survival of spontaneous intracerebral hemorrhage overtime: A systematic review and meta-analysis. Front Neurol 2022;13:819737.
13. Lin CN, Howng SL, Kwan AL. Bilateral simultaneous hypertensive intracerebral hemorrhages. Gaoxiong Yi Xue Ke Xue Za Zhi 1993;9:266-75.
14. Lin WM, Yang TY, Weng HH, Chen CF, Lee MH, Yang JT, et al. Brain microbleeds: Distribution and influence on hematoma and perihematomal edema in patients with primary intracerebral hemorrhage. Neuroradiol J 2013;26:184-90.
15. Mitaki S, Nagai A, Oguro H, Yamaguchi S. Serum lipid fractions and cerebral microbleeds in a healthy Japanese population. Cerebrovasc Dis 2017;43:186-91.
16. Perez J, Scherle C, Machado C. Subsequent bilateral thalamic haemorrhage. BMJ Case Rep 2009;2009:bcr04.2009.1734.
17. Sunada I, Nakabayashi H, Matsuoka Y, Nishimura K, Yamamoto S. Simultaneous bilateral thalamic hemorrhage: Case report. Radiat Med 1999;17:359-61.
18. Yen CP, Lin CL, Kwan AL, Lieu AS, Hwang SL, Lin CN, et al. Simultaneous multiple hypertensive intracerebral haemorrhages. Acta Neurochir (Wien) 2005;147:393-9.
19. Zhao J, Chen Z, Wang Z, Yu Q, Yang W. Simultaneous bilateral basal ganglia hemorrhage. Neurol Neurochir Pol 2016;50:275-9.

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