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Multiple simultaneous intracerebral hemorrhages: Clinical presentations and risk factors

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ABSTRACT

Objective: Multiple simultaneous intracerebral hemorrhages (MSICH) are a rare clinical entity. The mechanism and risk factors have yet to be elucidated. The purpose of this study was to clarify clinical presentations and risk factors of MSICH compared with solitary intracerebral hemorrhages (ICH).

Patients and methods: Medical records of 313 consecutive patients with ICH admitted to our institution between April 2011 and September 2014 were retrospectively reviewed. Seventeen cases of MSICH were identified, and 10 clinical and neuroimaging variables were compared between MSICH cases and solitary ICH cases using the unpaired *t*-test, chi-square test, and multiple logistic regression analysis.

Results: There were significant differences in size between larger hematomas (mean 59.2 ± 69.1 mL) and smaller hematomas (mean 1.7 ± 2.1 mL) in patients with MSICH ($p = 0.001$). Larger hematoma volume was the only independent risk factor for MSICH in multiple logistic regression analysis (OR = 1.012, 95%CI 1.004–1.021, $p = 0.004$).

Conclusions: Patients with MSICH have clinical characteristics and outcomes similar to patients with solitary ICH. They present with two significantly different hematoma sizes, both of which are significantly larger than patients with solitary ICH, suggesting that a larger hematoma can trigger smaller hematomas. A future prospective study with a larger number of patients will explore the precise mechanism of this rare entity.

1. Introduction

Multiple simultaneous intracerebral hemorrhages (MSICH) in different arterial territories are rare but known clinical events. The incidence is reported to be 0.9% to 5.6% of all ICHs [1–5,13,14]. However, etiologic factors and typical clinical course have yet to be elucidated. In particular, whether MSICHs share the same causative factors as solitary ICHs has been controversial [8–11,14]. The present study aims to document a detailed clinical presentation of MSICH and clarify the risk factors compared with solitary ICH.

2. Materials and methods

2.1. Study population

Medical charts of 313 consecutive patients with spontaneous and non-traumatic ICH treated at the Department of Cerebrovascular Surgery, International Medical Center, Saitama Medical University between April 2011 and September 2014, were retrospectively reviewed. MSICH was defined by the following criteria: (1) two solitary high-density areas on computed tomographic (CT) scan; (2) high-density areas located in typical sites specific to hypertensive ICH; (3) no other etiologic factors including arteriovenous malformation, cavernous malformation, moyamoya disease, venous thrombosis, coagulopathy, vasculitis, and hemorrhagic transformation of cerebral infarction [10,15–21]. Patients with multiple lobar hemorrhages possibly affected by amyloid angiopathy were excluded. We obtained the following parameters from all patients on admission: Glasgow Coma Scale (GCS) score, age, sex, blood pressure on arrival, hematoma volume, presence of secondary intraventricular hematoma (IVH), history of antihypertensive agents, use of antiplatelet/anticoagulation drugs, and clinical outcome (modified Rankin Scale score, mRS) on discharge.

2.2. CT imaging and measurement of the hematoma volume

The diagnosis of ICH was based on CT scans in all patients. CT scans

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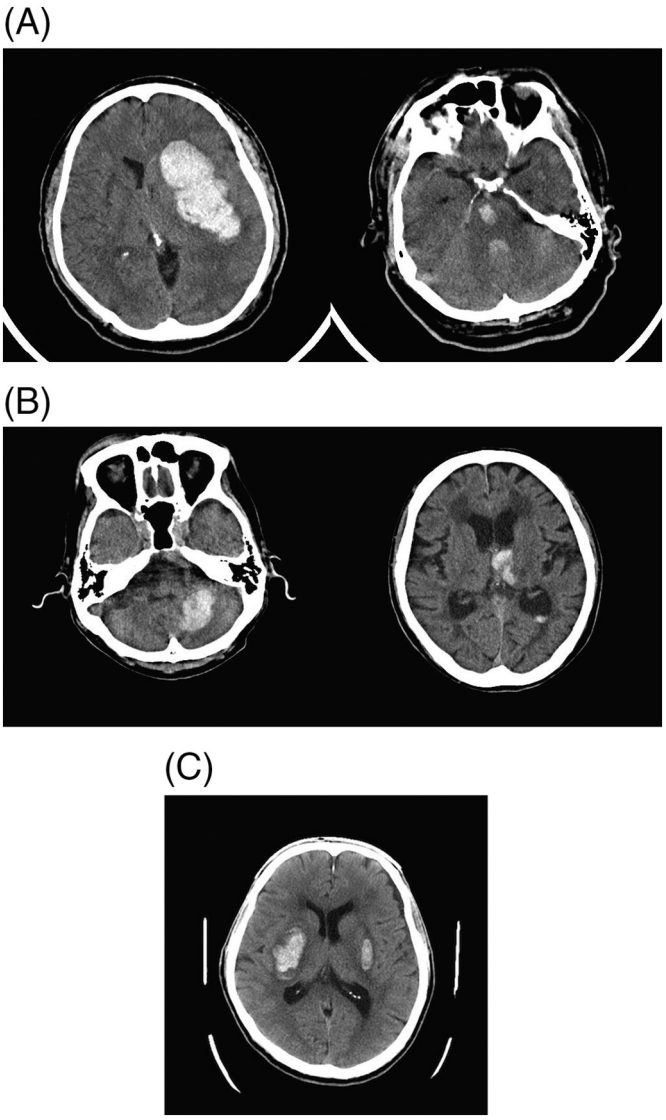

Fig. 1. Computed Tomography (CT) scans of representative cases of multiple simultaneous intracerebral hemorrhages (MSICH). There were significant differences in size between larger and smaller hematomas.
A) Representative case of a more-than-100-times difference in hematoma size (case no. 17)
B) Representative case of 10-to-100-times differences in hematoma size (case no. 8)
C) Representative case of 2-to-10-times differences on hematoma size (case no. 12)

of 5-mm slice thickness were performed in the emergency department in all patients. Hematoma volume was measured using the ABC/2 method [22]: The longest diameter (A) on the perpendicular line (B) of the hematoma was calculated in the slice with the largest area of ICH. The height of the hematoma (C) was calculated by the number of 5-mm interval slices. In the MSICH group, we measured two hematoma volumes respectively.

2.3. Statistical analysis

The unpaired *t*-test and chi-square test were employed to compare the 10 variables mentioned above between patients with solitary ICH and MSICH. Moreover, multiple logistic regression analysis with Firth's bias reduction [23] was used to correlate age, sex, hematoma volume, blood pressure on arrival, and history of antihypertensive use. All analyses were performed using SAS JMP version 12.1.0 and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

2.4. Ethics committee

The Institutional Review Board (IRB) at Saitama Medical University International Medical Center approved all aspects of this study (application number 15-164).

3. Results

3.1. Clinical presentation and outcome of MSICH

In all ICH patients, immediately after admission, efforts were made to reduce systolic BP to a normotensive level (< 140 mm Hg) with bolus and/or continuous intravenous administration of a calcium channel blocker (verapamil or nicardipine) as previously described [32]. Selected patients underwent urgent craniotomy and evacuation of hematoma based on the Japanese Guidelines for Stroke Management [33].

MSICH occurred in 17 patients (5.4% of 313). Clinical characteristics of the patients are summarized in Table 1. There were 14 men and 3 women, and the mean age was 68.5 ± 12.8 years. Hematomas were bilateral in 12 cases and unilateral in 5 cases. The most common lesion was in the putamen (n = 16), followed by the thalamus (n = 7), cerebellum (n = 6), brainstem (n = 3), and frontal lobe (n = 2). The most common combination was putamen and thalamus (n = 4). A combination of supratentorial and infratentorial hematoma was seen in 9 patients, putamen and brainstem in 3, putamen and cerebellum in 3, and thalamus and cerebellum in 3.

There were significant differences in size between larger hematomas (mean 59.2 ± 69.1 mL) and smaller hematomas (mean 1.7 ± 2.1 mL) in MSICH cases (p = 0.001). The size differences were > 100 times in 4 patients (23.5%, Fig. 1A), from 10 to 100 times in 6 (35.3%, Fig. 1B), and from 2 to 10 times in 7 (41.2%, Fig. 1C).

The conscious levels of patients on admission included clear (GCS 15) in 2, somnolence (GCS 13–14) or stupor (GCS 10–12) in 9, semi-coma (GCS 6–9) in 2, and coma (GCS 3–5) in 4. Mean systolic blood pressure on arrival was 184.1 ± 41.7 mm Hg, but ranged from 119 to 261 mm Hg. Four patients (23.4%) had been receiving antihypertensives.

Six patients (35.3%) underwent craniotomy and evacuation for larger hematomas in the acute stage without complication, whereas 11 patients were managed conservatively. At discharge, good outcomes (mRS 0–2) were observed in 5 patients (29.4%).

3.2. Comparison of MSICH and solitary ICH

Clinical variables and statistical relationships between solitary ICH and MSICH are summarized in Table 2. In univariate analysis, MSICH patients had a significantly less frequent history of antihypertensive agents than solitary ICH patients (23.4% versus 41.9%, p = 0.002). Although mean hematoma volume was larger in MSICH patients (59.2 ± 69.2 mL) than in solitary ICH patients (32.9 ± 38.9 mL), the difference was not statistically significant (p = 0.126). Also, there were no significant differences in other variables including age, sex, GCS score and blood pressure on arrival, use of antithrombotic drugs, and patient outcome at discharge. Conversely, the only significant risk factor for MSICH was large hematoma volume (odds ratio [OR] = 1.010, 95% confidence interval [CI] 1.002–1.019, p = 0.0132) in multiple logistic regression analysis (Table 3).

4. Discussion

The present study reveals that patients with MSICH have similar characteristics to those with solitary ICH with regard to age, sex, neurological presentation, SBP on arrival, and clinical outcome at discharge.

Conversely, larger hematoma volume was the only independent risk