Contralateral delayed hematoma secondary to anticoagulant treatment-related intracerebral hemorrhage

Libo Sun [1*], Yufei Gao [1*], Chao Fu [1], Fang Li [2], Xiaoxuan Fang [1], Conghai Zhao [1]

1 Department of Neurosurgery, China-Japan Union Hospital, Jilin University, Changchun, Jilin Province, China
2 Department of Neurosurgery, China-Japan Friendship Hospital, Beijing, China

** Authors contributed equally to this work*

Correspondence to: Conghai Zhao, MD.
Department of Neurosurgery, China-Japan Union Hospital, Jilin University, Changchun 130033, Jilin Province, China.
TEL: +86 13104318588; FAX: +86 0431 84995625; E-MAIL: conghai@jlu.edu.cn

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Abstract

The incidence of anticoagulant treatment (AT)-related intracerebral hemorrhage (AT-ICH) is increasing in consequence of the increased incidence of ischemic stroke due to an aging population. AT-ICH is associated with a risk of ongoing bleeding, death, or disability. Cerebral amyloid angiopathy (CAA), a common pathological finding among the elderly that is associated with macro- and microscopic hematoma development, might increase the risk of ICH. We report a rare case of contralateral delayed hematoma in the context of CAA secondary to acute ICH after AT for intracerebral ischemic stroke.

CASE REPORT

INTRODUCTION

The increasing incidence of anticoagulant treatment (AT)-related intracerebral hemorrhage (AT-ICH) may be attributed to the increased incidence of atrial fibrillation due to an aging population, the larger number of elderly patients who are receiving ATs, the increased use of combined anticoagulant or antiplatelet therapies, and the expanded use of oral ATs for secondary ischemic stroke or prevention of transient ischemic attack. In the United States, about 5% to 12% of intracerebral hemorrhage (ICH) cases are related to AT use, and the annual incidence of AT-ICH is currently estimated at nearly 3,000 cases (Cervera *et al.* 2012). The ICH incidence in patients receiving ATs is 7- to 10-fold higher than that in patients who are not receiving ATs. Notably, the incidence of AT-ICH in stroke-prone patients is as high as 1.8% per year (Steiner *et al.* 2006). AT-ICHs are most frequently located in the deep or lobar regions of the brain, and they show an increased hemorrhage expansion rate (>33% increase in volume) compared to spontaneous ICHs (Cucchiara *et al.* 2008). AT-ICHs are detected later in the hospital course than ICHs that are not associated with AT use (Flibotte *et al.* 2004).

We report a case of contralateral delayed hematoma secondary to acute ICH after AT. To the best of our knowledge, this paper represents the first report of this type of bleeding pattern.

CASE REPORT

A 76-year-old male with a >20-year history of multiple lacunar infarctions and 15-year history of myocardial ischemia (MI) was admitted to the hospital and treated for corona radiata ischemic stroke with anticoagulant and antiplatelet medications for 3 weeks (Figure 1). He was discharged without neurologic deterioration. At discharge, he was prescribed enteric-coated aspirin and an antihypertensive regimen (oral, once daily).

Five weeks after discharge, the patient presented with abrupt aphasia and hemiparesis on the left side that had begun 1 hour prior to admission. On admission, his blood pressure was 135/85 mmHg and pulse rate was a regular 70 beats/min. Computerized tomography (CT) showed a hematoma in the left basal ganglia region (Figure 2a). Blood samples indicated a prothrombin time (PT) of 14.2 seconds, international normalized ratio (INR) of 1.28, partial thromboplastin time (PTT) of 31.2 seconds, thrombin time (TT) of 22.5 seconds, and fibrinogen level of 3.68 g/L. Prothrombin complex concentrates (PCCs) were infused within 2 hours after onset and repeated 12 hours later. The INR was 1.06 at 24 hours.

At 34 hours after onset, the patient was deeply unresponsive, with a Glasgow Coma Scale score of 13. A repeated CT scan of his brain showed a large hemotoma in the right parietooccipital intracerebral region (Figure 3a,b). The midline was not obviously shifted. Medical therapy was chosen without surgical treatment. PCC was infused daily in for the next 3 days. Samples taken on the seventh day after admission indicated a PT of 12.9 seconds, INR of 1.18, PTT of 27.3 seconds, TT of 16.6 seconds, and fibrinogen level of 2.86 g/L. Thromboelastography indicated a reaction time (R-value) of 3.80 minutes, angle of 72.30°, and maximum amplitude (MA) of 70.70 minutes (Table 1). Enteric-coated aspirin was administered. A CT scan 1 month after onset showed that the hemorrhages had resolved (Figure 3e,f).

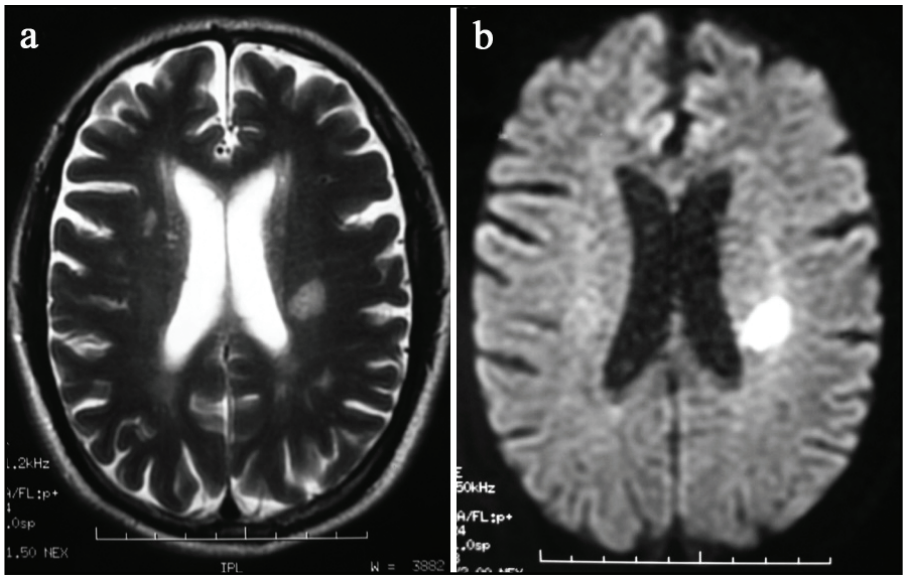

Fig. 1. T2-weighted and diffusion-weighted magnetic resonance images demonstrating acute ischemic stroke in the left corona radiata region and a history of multiple lacunar infarctions in the region of both middle cerebral arteries.

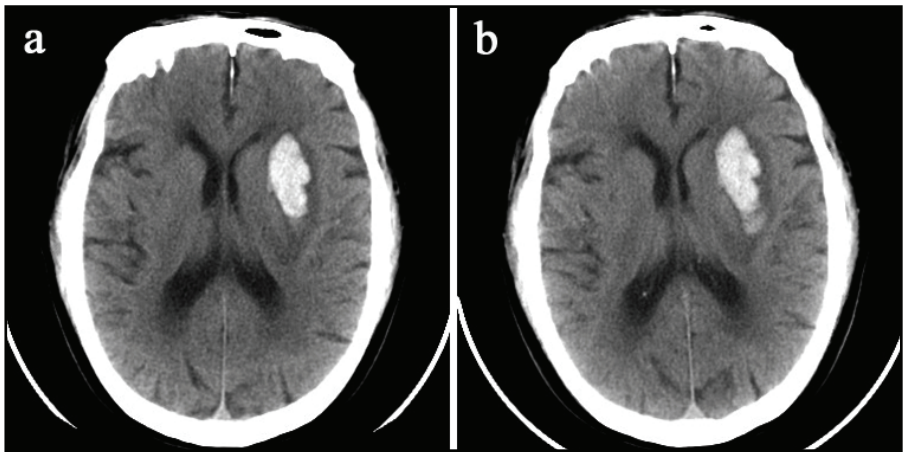

Fig. 2. (a) Computed tomography scans on admission showing an intracerebral hemorrhage in the region of the left middle cerebral artery. **(b)** Computed tomography scan at 24 hours after the first hemorrhage, revealing no further bleeds.

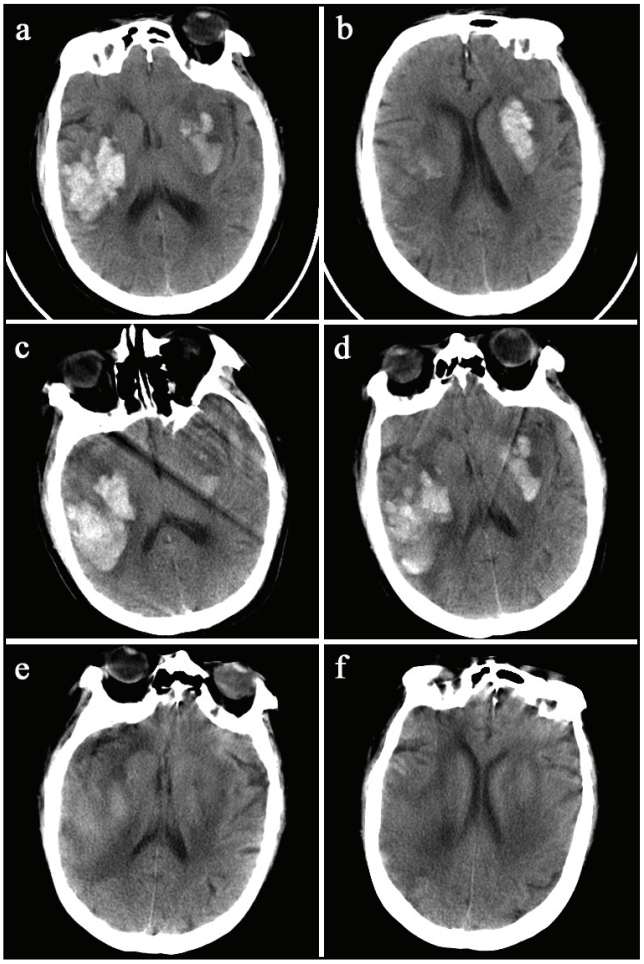

Fig. 3. Computed tomography scans at 34 hours **(a, b)** and 48 hours **(c, d)** after the first hemorrhage, demonstrating a right temporal-occipital hemorrhage (multiple hemorrhages), without evidence of a midline shift. Follow-up computed tomography scan 1 month **(e, f)** after the first hemorrhage, showing resolution of the hemorrhages.

Tab. 1. Thromboelastography results.

Variable (unit)	Value	Normal range
R (min)	3.80	5.00–10.00
K (min)	1.20	1.00–3.00
Angle (°)	72.30	53.00–72.00
MA (min)	70.70	50.00–70.00
G (°/s)	12000.00	4500.00–11000.00
EPL (%)	0.10	0.00–15.00
A (mm)	71.40	
CI	3.50	–3.00–3.00
LY30 (%)	0.10	0.00–8.00
A30 (mm)	70.10	

Values in bold text are outside of the normal range for that variable. R: reaction time; K: clotting time; Angle: alpha angle; MA: maximum amplitude; G: clot elasticity; EPL: estimated percent lysis; A: clot strength; CI: coagulation index; LY30: clot lysis at 30 min; A30: amplitude at 30 min.

DISCUSSION

In this study, we report a rare case of contralateral delayed hematoma secondary to acute ICH, which was observed in the context of cerebral amyloid angiopathy (CAA). The elderly patient was treated for ischemic stroke with anticoagulant and antiplatelet medications for 3 weeks, and oral antiplatelet therapy was discontinued after presentation. The PT and INR were higher than normal levels at the onset of ICH.

Upon diagnosis of AT-ICH, it is vital that AT be reversed. However, there are currently no standardized guidelines for reversing the anticoagulant effect in patients with AT-ICH. The goal of these therapeutic measures is to decrease the INR to ≤1.4 (preferably, to ≤1.2) (Morgenstern *et al.* 2010; Steiner *et al.* 2006; Ageno *et al.* 2009). PCCs are considered the first therapeutic choice in AT-ICH and are superior to fresh-frozen plasma or vitamin K1 (Masotti *et al.* 2011). PCCs are advantageous because they offer a range of coagulation factors and rapid therapeutic onset with a small dosage volume, without significantly increasing the risk of disseminated intravascular coagulation or thrombosis (Leissinger *et al.* 2008).

In the current case study, the patient developed contralateral delayed hematoma even though he showed normal PT and INR levels after PCC treatment. The delayed hematoma likely developed as a result of CAA, a pathologic condition that results from the deposition of β-amyloid (Aβ) within the arterial media and adventitia. CAA is a common underlying vasculopathy for elderly patients who receive thrombolysis (Mehndiratta *et al.* 2012). Severe CAA can lead to vessel fragility and rupture, as well as the formation of macroscopic or microscopic hematomas. Unlike hypertensive arteriolar hemorrhages that occur in the penetrating subcortical vessels, CAA-associated hemorrhages are superficial in location, due to the preferential involvement of vessels in the cerebral cortex and meninges. CAA most frequently (and most severely) occurs in the occipital lobe, followed by the frontal, temporal, and parietal lobes, respectively.

Up to 20% of hemorrhages in patients receiving thrombolysis for acute ischemic stroke occur outside of the ischemic penumbra (NINDS t-PA Stroke Study Group 1997). The medical management of CAA-associated ICH does not differ from that in other causes of ICH, which focus on the control of early hematoma growth. Surgical management may be employed for prevention of hematoma expansion, reduction of mass effect and edema, and decompression to improve local perfusion. In this case, a nonshifted midline on CT and a Glasgow Coma Scale score of 13 led us to recom-

mend medical therapy without surgery. As a result of treatment, the hemorrhage did not enlarge and no new hemorrhages developed.

To date, no prospective, randomized, controlled clinical trial has compared various strategies in their ability to reduce the enlargement rates of AT-ICHs. Even if the PT and INR levels are normal after PCC treatment, there is still a risk of hematoma enlargement or new hematoma development. CAA is an important cause of AT-related lobar ICH in the elderly. Treatment approaches should seek to lower the high risk of ongoing bleeding, death, or disability associated with AT-ICH.

Conflicts of interest: *None.*

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