Case Report

Vitamin K, fresh frozen plasma, and platelet transfusion used to arrest progression of intracranial hemorrhage after traumatic brain injury in a patient taking anticoagulant and antiplatelet agents

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Case: An 89-year-old man fell from stairs and sustained head trauma. He was taking warfarin and aspirin. Upon arrival at our hospital, his Glasgow Coma Scale score was 14. Initial head computed tomography showed small acute subdural hematoma. We immediately administered vitamin K and ordered fresh-frozen plasma. Repeat computed tomography 3 and 6 h after trauma revealed the acute subdural hematoma had increased to 14 and 20 mm, respectively, and there were several new intracranial hemorrhages. Fresh-frozen plasma and platelet transfusion were initiated.

Outcome: Follow-up computed tomography revealed no further progression of intracranial hemorrhages, and the patient's consciousness did not deteriorate further.

Conclusion: Appropriate administration of vitamin K, fresh-frozen plasma, and platelets successfully arrested progression of traumatic intracranial hemorrhages in this patient taking anticoagulant/antiplatelet agents and may have averted brain surgery.

Key words: Anticoagulant, fresh frozen plasma transfusion, platelet transfusion, traumatic brain injury, vitamin K

INTRODUCTION

IN RECENT YEARS, the increasing proportion of elderly citizens in Japan has led to an increased incidence of traumatic brain injury (TBI) in older people.¹ Anticoagulants and prescription antiplatelet (ACAP) agents are widely used by older adults, who are prescribed these drugs for cardiovascular disease. A recent study of trauma patients showed a nearly threefold increase in the number of patients using antiplatelet drugs during a 5-year period.² Another study reported that traumatic intracranial hemorrhage (ICH) in patients on anticoagulants is “epidemic in patients over 55 years of age.”³ Older adults are at increased risk of TBI-related hospitalization and death.⁴ Furthermore, patients with TBI who are taking ACAP agents experience a higher rate of inpatient mortality com-

pared to those not on ACAP agents.⁴ To the best of our knowledge, there are no controlled clinical trials or clinical guidelines regarding the reversal of ACAP for patients with TBI.

We report our experience with a patient who sustained a TBI while taking warfarin and aspirin. The extent of his traumatic ICH increased, but it was successfully arrested with administration of vitamin K, fresh-frozen plasma (FFP), and platelet transfusion. We propose a practical protocol in the emergency department to reverse ACAP in patients with ICH caused by TBI.

CASE

AN 89-YEAR-OLD JAPANESE man was transferred to our hospital due to head trauma after falling down several steps. His past medical history included Parkinson's disease, left ventricular aneurysm after myocardial infarction, hypertension, dyslipidemia, chronic kidney disease, and dementia. He was taking 700 mg levodopa/day for Parkinson's disease, 2 mg warfarin/day for left ventricular aneurysm, and 100 mg aspirin/day for myocardial infarction.

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On arrival, the patient's Glasgow Coma Scale (GCS) score was 14 (E4, V4, and M6). His vital signs were 22 breaths/min respiratory rate, 89 b.p.m. heart rate, 150/85 mmHg blood pressure, and 36.8°C body temperature. Coagulofibrinolytic measurements showed that prothrombin time-international normalized ratio (PT-INR) was prolonged to 2.62 (Table 1).

Initial head computed tomography (CT) was carried out 1 h after trauma and showed a small acute subdural hematoma (ASDH) at the right surface of the cerebral cortex and a small contusion in the right white matter near the ventricular wall (Fig. 1A). We immediately administered 20 mg vitamin K to reverse the effects of warfarin and ordered 960 mL FFP to supply coagulation factors. Repeat CT was carried out 3 h after trauma and revealed that the right ASDH had increased in thickness from 7 to 14 mm, with a midline shift of 4 mm to the left side. In addition, several hemorrhagic lesions were newly apparent (Fig. 1B). We started to transfuse 480 mL FFP, which was now ready to use, and ordered 10 units of platelets.

Six hours after trauma, the patient's consciousness level had dropped to GCS 11. Computed tomography showed that the right ASDH had further increased to 20 mm in thickness and the contusional hemorrhage in the left frontal lobe had also increased to 15 mm from 8 mm in diameter, but the midline shift toward the left did not change (Fig. 1C, D). Because the patient's PT-INR had been corrected to 1.43 at this time (Table 1), we did not supplement with further FFP. Ten units of platelets were then ready, and transfusion of these platelets began 7 h after trauma. Consequently, further progression of ASDH or contusional hemorrhage was not observed on the follow-up CT, and the patient's GCS score remained at 11–13 after admission. We stopped ACAP therapy, and no associated adverse events occurred. The patient was conservatively treated and received rehabilitation to avoid disuse syndrome. His consciousness recovered gradu-

ally, and he was ready to move into a convalescent hospital. However, he died of food aspiration on post-trauma day 72.

DISCUSSION

IN OUR CASE, appropriate administration of vitamin K, FFP, and platelet transfusion successfully arrested progression of ICH after TBI in a patient taking ACAP agents and may have averted brain surgery. The patient died not long after treatment, but his death was due to aspiration related to Parkinson's disease and was not a consequence of TBI.

Patients taking anticoagulants are more likely to have progression of initial ICH after head injury and to experience new hemorrhagic foci upon second CT compared to those who are not taking anticoagulants.⁴ Among all patients with progression of ICH after TBI, patients on preinjury ACAP agents are significantly more likely to die compared to non-ACAP users.⁴

Ivascu *et al.* reported a rapid warfarin reversal protocol in anticoagulated patients with traumatic ICH and a decrease in mortality to 10% from 48% after implementation of the protocol. The protocol included immediate physician evaluation, head CT, and FFP and vitamin K administration in warfarin anticoagulated patients with documented ICH.^{5,6} A North American survey of 100 trauma surgeons in 2005 revealed that only 12% of institutions had a protocol addressing reversal of anticoagulation.⁷ Platelet transfusion has been used in clinical practice to reestablish platelet aggregation in patients with TBI who were taking prescription antiplatelet agents before the injury, but established guidelines or recommendations have not been established.⁸ Currently, there are no clinical guidelines regarding treatment of patients with TBI who are taking ACAP agents. The protocol for reversal of ACAP in the setting of acute TBI in our institution is shown in Table 2.⁹

Vitamin K is not a fast-acting agent because the effect on reversal of warfarin appears 3 h after i.v. administration according to the drug information sheet. Thus, patients taking warfarin with head injury should undergo head CT without delay and immediately receive vitamin K if traumatic ICH is documented on CT, regardless of a PT-INR value. The treatment target of PT-INR by FFP transfusion has not been established in traumatic ICH. Regarding spontaneous ICH, a PT-INR above 2.0 was reported to be one of the predisposing factors for enlargement of ICH in patients taking warfarin.¹⁰ For the patients whose PT-INR values on admission were above 2.0, early administration of prothrombin complex concentrate (PCC) reduced the frequency of hematoma enlargement.¹¹ Thus, we temporarily set the target to reduce PT-INR with FFP administration below 2.0. For patients who are candidates for neurosurgical procedures,

Table 1. Blood coagulation data of an 89-year-old man who suffered head trauma after falling down stairs

	On arrival	6 h after trauma
PT-INR	2.62	1.43
APTT, s	40.7	29.0
Fibrinogen, mg/dL	377	N.E.
D-dimer, mg/L	6.3	10.3
Platelets, $\times 10^4/\text{mm}^3$	17.6	13.6

APTT, activated partial thromboplastin time; N.E., not examined; PT-INR, prothrombin time-international normalized ratio.

Fig. 1. Computed tomography (CT) sequence of the brain of an 89-year-old man who suffered head trauma after falling down stairs. A, Initial CT 1 h after trauma. Arrow, small acute subdural hematoma (ASDH); arrowhead, small contusion in the deep white matter. (B) CT 3 h after trauma. Arrows, enlarged ASDH; arrowheads, new lesions of intracranial hemorrhage in the right ventricle, left frontal, left basal ganglia, and left Sylvian fissure. (C, D) CT 6 h after trauma. Arrows, further progression of ASDH; arrowheads, increasing contusional hemorrhages.

the therapeutic endpoint of FFP and vitamin K administration is recommended to achieve PT-INR less than 1.6.¹² Prothrombin complex concentrate may be more effective to normalize PT-INR than FFP in warfarin anticoagulated patients, as previously reported.¹³ However, we recommend FFP, not PCC, in the protocol (Table 2), because use of PCC is currently off-label for traumatic/spontaneous ICH in Japan. An optimal dosage of FFP to supplement coagulation factors has been unclear. Warfarin-induced coagulopathies can be effectively reversed by administration of 15 mL/kg FFP and 10 mg vitamin K i.v.^{5,12} In a warfarin reversal protocol reported by Ivascu *et al.*, patients with CT confirmation of ICH were rapidly given the two units of uncross-matched FFP, and further doses of FFP were given according to a value of PT-INR.^{5,6} They began to thaw FFP while the primary survey was being carried out, before ICH was documented on CT. Unused FFP that has been thawed may be allotted to another trauma patient in a high volume trauma center. However, in the situation of a common emer-

gency medical center in Japan, practically, it seems to be acceptable that a sufficient dose of FFP is thawed when ICH on CT and a prolonged PT-INR value have been identified.

In the present case, platelets were actually ordered after an increase in ICH was recognized on the repeat CT, not immediately after the initial CT that documented the small ASDH. As a result, platelet transfusion started 7 h after the trauma. We are not sure whether the late platelet transfusion contributed to avert surgery in our case. Although the insignificant amount of ICH on the initial CT led us to hesitate in ordering FFP or platelet transfusion, emergency doctors should note that it takes time for FFP or platelets to be prepared, because FFP cannot be thawed at high temperature and hospitals often do not have stocks available for platelet transfusion.

Because the number of older patients with TBI who are taking ACAP agents is increasing, specific treatment options for reversal by a blood product is becoming a major issue in trauma care. A population-based cohort analysis of 8,450

Table 2. Protocol to reverse anticoagulant and prescription antiplatelet (ACAP) agents in patients with traumatic intracranial hemorrhage (ICH)

ACAP agent	Traumatic ICH on CT within 6 h of injury		Increase in ICH on follow-up CT
	PT-INR < 2.0	PT-INR ≥ 2.0	
Warfarin	10–20 mg vitamin K i.v.†	10–20 mg vitamin K i.v. + 480 mL FFP d.i.v.	Additional 480 mL FFP d.i.v., if PT-INR still ≥ 2.0†
Factor Xa or thrombin inhibitor	Prepare FFP 480–960 mL†		480–960 mL FFP d.i.v.
Antiplatelet agent	Prepare 5–10 units platelets§		5–10 units platelets d.i.v.

For patients who have any of the following risk factors, immediate transfusion of †fresh-frozen plasma (FFP) or §platelets should be considered: a) patient age ≥70 years, b) cortical contusion evident on computed tomography (CT) (high-density area or salt-and-pepper sign in the brain parenchyma), c) any risk factor for increased bleeding such as history of hemorrhagic disorder, recent surgery for brain disease, or systolic blood pressure 180 mmHg.

d.i.v., intravenous drip. [Correction added on 26 September 2016, after first online publication: The presentation of the following values 'Prepare FFP 480-960 mL' and 'Prepare 5-10 units platelets' have been corrected in Table 2].

elderly patients who survived an incident of major trauma and were receiving warfarin before injury showed that cessation of warfarin therapy was not associated with an increased risk of arterial thrombotic events.¹⁴ Another recent study of 42,913 elderly anticoagulated patients with atrial fibrillation or flutter revealed that risk of eventual death with head injury exceeded annualized stroke risk for patients with CHA₂DS₂-VASc scores of 0–2.¹⁵ Physicians and family doctors should consider the risk/benefit analysis before prescribing ACAP agents to prevent ischemic events in the heart or brain for older patients, especially those at high risk of falling because of a past or concurrent illness or daily activity.

CONFLICT OF INTEREST

NONE.

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