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Case Report

Mechanical Thrombectomy for Acute Ischemic Stroke in a Patient Treated with Dabigatran

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Ischemic Stroke: A Cerebrovascular Accident

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Keywords

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Abstract

Newer anticoagulants such as dabigatran have been widely used for the prevention of ischemic stroke in patients with nonvalvular atrial fibrillation (AF). A 64-year-old man treated with dabigatran 110 mg twice daily for chronic AF presented with total aphasia, right homonymous hemianopsia, and right hemiparesis at 90 minutes after the last intake. His prothrombin time-international normalized ratio (PT-INR) was 1.14 (normal range: 0.7-1.5) and activated partial thromboplastin time (aPTT) was 33.8 seconds (normal range: 24-38 seconds). Clotting activity could not be measured because of the dabigatran intake; however, clotting activity was predicted to increase to its highest level at 90-120 minutes after the last dabigatran dose. Angiography results showed total occlusion of the left middle cerebral artery (MCA), and mechanical thrombectomy with the Penumbra System (Penumbra, Inc.) was performed instead of intravenous administration of recombinant tissue plasminogen activator (rt-PA). The patient showed recanalization of the MCA and neurological improvement. Mechanical thrombectomy can be used as a supplement to intravenous administration of rt-PA for the treatment of acute ischemic stroke in patients receiving newer anticoagulants such as dabigatran. The indication of thrombolysis for acute ischemic stroke in patients taking dabigatran should be discussed after considering the aPTT value and the time since the last intake of dabigatran.

ABBREVIATIONS

aPTT: activated Partial Thromboplastin Time; **PT-INR:** Prothrombin Time-International Normalized Ratio; **MCA:** Middle Cerebral Artery; **NIHSS:** National Institutes of Health Stroke Scale; **rt-PA:** Recombinant Tissue Plasminogen Activator; **TICI:** Thrombolysis in Cerebral Infarction Score

INTRODUCTION

According to the guidelines for intravenous administration of recombinant tissue plasminogen activator (rt-PA) for acute ischemic stroke, patients receiving anticoagulants such as warfarin or heparin, and those with prothrombin time-international normalized ratio (PT-INR) > 1.70 or activated partial thromboplastin time (aPTT) > 40 seconds are excluded because of the increased risk of intracranial hemorrhage [2,10]. However, no guidelines have been established to date regarding thrombolysis for acute stroke in patients treated with newer anticoagulants such as dabigatran. Here, we report on a patient treated with dabigatran who presented with onset of acute ischemic stroke and underwent mechanical thrombectomy with the Penumbra System (Penumbra, Inc.) instead of IV rt-PA because the dabigatran treatment prevented the assessment of changes in clotting activity.

CASE PRESENTATION

A 64-year-old man with a history of hypertension, atrial fibrillation (AF), and ventricular tachycardia was treated with dabigatran 110 mg twice and aspirin 100 mg once daily. He underwent cardiac resynchronization therapy for ventricular tachycardia and defibrillation for chronic AF in the department of cardiovascular medicine of our hospital. Three days later, he presented with total aphasia, right homonymous hemianopsia, and right hemiparesis, with a time of onset at 90 minutes after the last intake of dabigatran. The National Institutes of Health Stroke Scale score was 18. Emergency CT scan showed loss of corticomedullary differentiation in only the left opercular cortex (CT ASPECTS 9/10 points; Figure 1). His coagulation parameters were as follows: platelet count, 31.9×10^4 (normal range: 15–45

× 10^4); PT-INR, 1.14 (normal range: 0.7–1.5) ; and aPTT, 33.8 seconds (normal range: 24–38 seconds).

Thrombolysis by mechanical thrombectomy was the treatment of choice instead of intravenous rt-PA because the dabigatran treatment prevented assessment of changes in clotting activity. We predicted that the clotting activity should increase to its highest level at 90–120 minutes after the last intake of dabigatran. After obtaining informed consent, mechanical thrombectomy was performed with the Penumbra System. The first diagnostic angiography showed total occlusion of the left middle cerebral artery (MCA; thrombolysis in cerebral infarction [TICI] score: 0; Figure 2A). We started continuous suction of the clot with the 041 Penumbra System at 100 minutes after stroke onset. After 15 minutes of continuous suction, total recanalization of the MCA was achieved (TICI 3; Figure 2B). The patient showed neurological improvement of the speech disturbance and motor weakness. A head CT scan obtained after the procedure did not show hemorrhage or enlargement of the ischemic area (Figure 3). Two weeks later, the patient was transferred to the acute rehabilitation care unit with minimal motor aphasia. At 6 months after stroke, his modified Rankin Scale was 1.

DISCUSSION

Since 2011, newer anticoagulants such as dabigatran have been used for primary and secondary preventive treatment of ischemic stroke in patients with nonvalvular AF [5]. They are used as a fixed dose medication in most circumstances and do not require routine blood testing. These drugs do not show major interactions with most foods or medications [12]. Dabigatran is an orally administered prodrug that is rapidly converted by tissue esterases to dabigatran, a direct thrombin inhibitor [5]. It has been shown to be more effective in the prevention of ischemic stroke and systemic embolisms than warfarin and to be associated with a lower risk of intracranial hemorrhage [5].

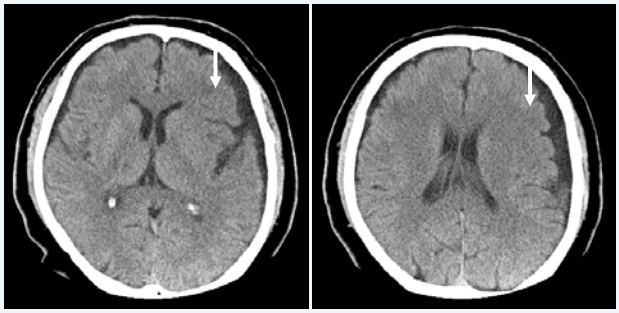

Figure 1 Emergency CT scan showing loss of corticomedullary differentiation in the left opercular cortex (arrow).

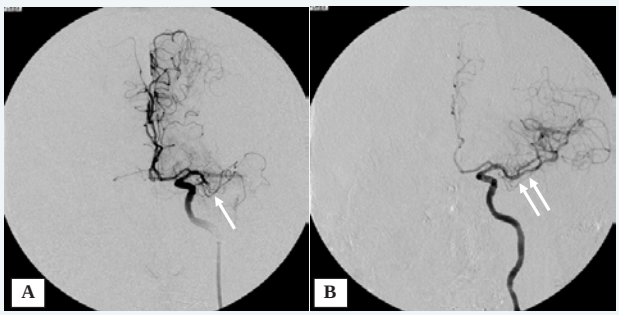

Figure 2 Anteroposterior view of the first diagnostic angiography of the left internal carotid artery showing total occlusion of the middle cerebral artery (arrow) (A). After continuous suction of the clot, the left MCA was totally recanalized (double arrows) (B).

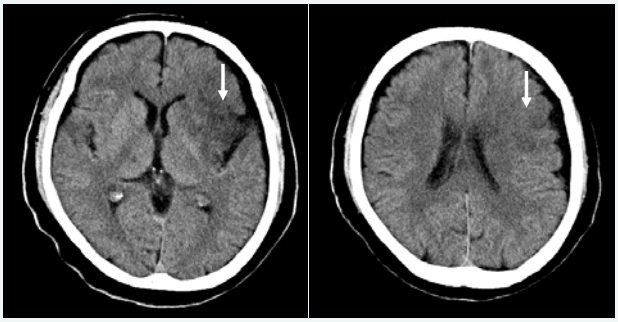

Figure 3 Head CT scan performed on the day after the procedure showing no hemorrhagic change and no enlargement of the ischemic area (arrow).

Dabigatran does not need routine monitoring of the anticoagulant effects [5,12]. However, in clinical situations, if a patient taking dabigatran requires thrombolysis for ischemic stroke, it would be helpful to determine the indication for thrombolysis by measuring the anticoagulant effect [1,5]. The guidelines for the use of intravenous rt-PA exclude patients receiving anticoagulant therapy and those with PT-INR > 1.70 [2,10]. Although the ecarin clotting time is considered to be the most accurate measure of the anticoagulant effect of dabigatran [5,12], this test cannot be performed in Japan or in most countries in emergency situations because the measurement hardware is not available. The aPTT partially correlates with plasma concentrations of dabigatran, but the quantitative assessment of the anticoagulant effect of dabigatran is difficult using only the aPTT value [1,12].

There are 6 case reports of patients taking dabigatran who had an acute ischemic stroke and were treated with intravenous rt-PA [3,6-9,11]. Thrombolysis by intravenous rt-PA can result in serious cerebral and systemic hemorrhage in a patient taking dabigatran. In 5 of these cases, the time since the last dabigatran intake was described [3,6,8,9,11]. In these cases, one patient treated with rt-PA at 190 minutes after the last dabigatran intake developed intracranial hemorrhage and died [3]. The other four patients showed neurological improvement without hemorrhagic complications after the administration of rt-PA [6,8,9,11]. However, the aPTT values in all the cases were <40 seconds; therefore, they could not indicate the anticoagulant value or serve as a guide for the indication of thrombolysis by rt-PA (Table 1). The peak plasma concentrations and the anticoagulant effects of dabigatran reach a maximum level at approximately 2 to 3 hours after oral ingestion, and the drug has a half-life of 13 to 17 hours in patients with normal renal function [4,5,12]. Therefore, rt-PA administration even at 12 hours after the last intake of dabigatran might increase the risk of intracranial hemorrhage.

Mechanical thrombectomy using the Penumbra System or Merci Retriever can be used as an alternative thrombolysis method to rt-PA for the treatment of acute stroke. Mechanical

Table 1: Clinical characteristics of the patients taking dabigatran who underwent thrombolysis by intravenous administration of rt-PA.

Author	Age/Sex	Dabigatran dose (mg)	Last intake (hour)	PT-INR	aPTT (second)	NIHSS	rt-PA time (minute)	Outcome (NIHSS)
De Smedt	46/F	NA	7	1.20	34.8	19	270	Improved (12)
Matute MC	76/F	220	15	1.00	30.6	4	120	No symptoms (0)
Casado Naranjo I	62/M	220	3	1.29	37.1	18	190	Hemorrhage Death
Lee VH	64/M	300	N.D.	1.10	37.6	8	205	No symptoms (0)
Sangha N	51/M	300	3.5	1.07	30.7	6	153	Improved (1)
Marrone LC	73/M	220	7	1.13	38.0	14	120	No symptoms (0)
Present case	65/M	220	1.5	1.14	33.8	18	100 (Penumbra)	Improved (1)

Abbreviations: aPTT: activated Partial Thromboplastin Time; NIHSS: National Institutes of Health Stroke Scale; PT-INR: Prothrombin Time-International Normalized Ratio; rt-PA: recombinant tissue Plasminogen Activator

thrombectomy does not require thrombolytic agents and might not increase the risk of hemorrhagic complications. Intravenous administration of rt-PA is the only treatment approved by the US Food and Drug Administration for patients presenting with acute ischemic stroke [2], and there are no data available regarding endovascular interventions for acute stroke in patients receiving dabigatran, which requires a detailed study in the future.

CONCLUSION

The indication for thrombolysis in patients treated with dabigatran should be determined according to the aPTT value and the time since the last intake of dabigatran. Mechanical thrombectomy can be performed instead of intravenous administration of rt-PA in patients with a high risk of hemorrhage.

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