Case Studies

Thrombolytic Therapy in Severe Cardioembolic Stroke After Reversal of Dabigatran with Idarucizumab: Case Report and Literature Review

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Whether idarucizumab, an antidote of dabigatran, can be used effectively and safely before thrombolytic therapy with recombinant tissue plasminogen activator (rt-PA) in patients with stroke undergoing treatment with dabigatran remains unknown. We herein describe a 57-year-old man who developed severe cardioembolic stroke with a National Institutes of Health Stroke Scale score of 22 in the left middle cerebral artery territory while undergoing treatment with dabigatran for nonvalvular atrial fibrillation and who was treated with rt-PA after the reversal of dabigatran with idarucizumab. The thrombolytic therapy following the use of idarucizumab significantly improved the patient's neurological symptoms without hemorrhagic complications, although acute arterial occlusion of the right lower limb was found during the clinical course. **Key Words:** Cardioembolic stroke—dabigatran—idarucizumab—nonvalvular atrial fibrillation—recombinant tissue plasminogen activator.

Background

Direct oral anticoagulants are widely used to prevent cardioembolic stroke in patients with nonvalvular atrial fibrillation (NVAF). However, cardioembolic stroke can still occur during anticoagulation therapy in some patients.[1] The therapeutic strategy for thrombolytic therapy in such patients is now heavily discussed. Idarucizumab, a humanized monoclonal antibody fragment, is now available as the specific antidote for the direct oral thrombin inhibitor, dabigatran.[2] In the literature, there have been only a few reports that have described the use of idarucizumab before thrombolytic therapy with recombinant tissue plasminogen activator (rt-PA) in patients with cardioembolic stroke with severe neurological symptoms. We herein report a Japanese patient with severe cardioembolic stroke who was administered idarucizumab before rt-PA therapy.

Case Presentation

A 57-year-old man with hypertension, diabetes, and NVAF treated with dabigatran at 110 mg twice daily was admitted to our hospital 39 minutes after the development of sudden-onset aphasia and right hemiplegia. He

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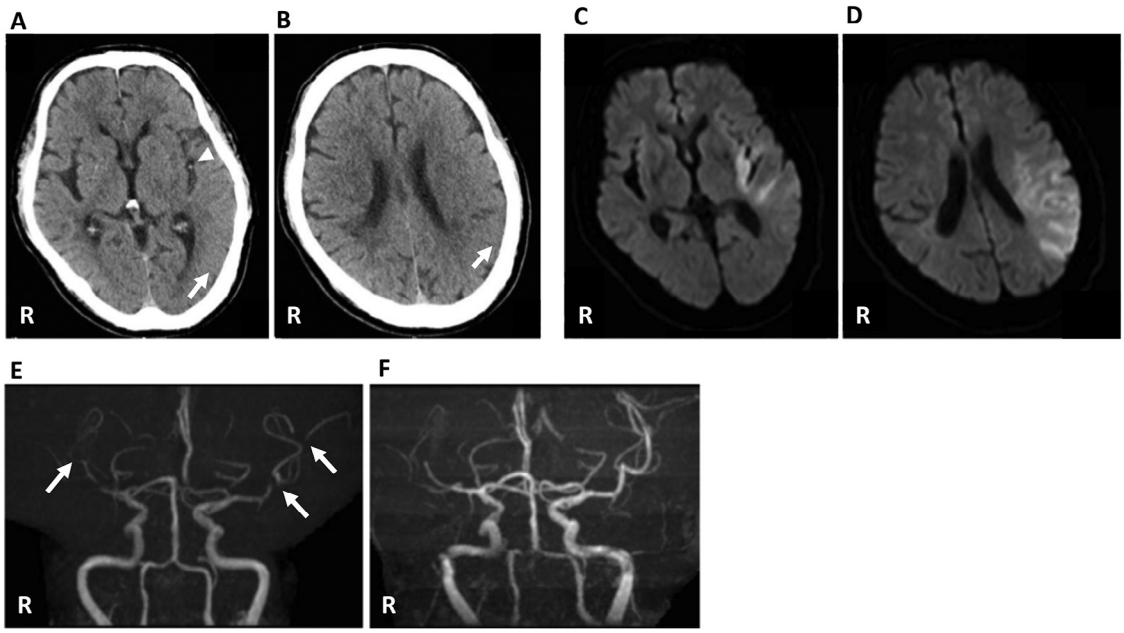

Figure 1. *(A, B) Brain computed tomography at 60 minutes after symptom onset showed reduced contrast attenuation of the cerebral parenchyma of the left temporoparietal lobe (arrow) and a dot sign on the left middle cerebral artery (arrowhead). (C, D) Diffusion-weighted images 60 minutes after the initiation of recombinant tissue plasminogen activator (rt-PA) therapy showed high-intensity areas in the left middle cerebral artery (MCA) territory. (E) Brain magnetic resonance angiography 60 minutes after the initiation of rt-PA therapy showed arterial defects (arrow) in the bilateral distal M1 and left M2 segment. (F) Brain MRA on day 4 showed the recanalization in the left MCA. The M1 of the right MCA appears to be occluded asymptomatically. "R" indicates the right side.*

presented with global aphasia, right hemispatial neglect, right hemiplegia, and severe hypoesthesia of the right side of the body. His National Institutes of Health Stroke Scale (NIHSS) score was 22 points in the emergency room. Head computed tomography (CT) at 60 minutes after symptom onset showed reduced contrast attenuation of the cerebral parenchyma of the left temporoparietal lobe with an Alberta Stroke Programme Early CT Score of 8 and a dot sign on the left middle cerebral artery (MCA) without hemorrhage (Fig 1A, B). Transcranial color flow imaging showed blood flow with low end-diastolic velocity (13.4 cm/s) in the M1 segment. Although we could not precisely determine when the patient had taken dabigatran last because of aphasia, the activated partial thromboplastin time was prolonged to 41.3 seconds on admission. We therefore infused idarucizumab at 5 g intravenously for 15 minutes at 78 minutes after symptom onset, then performed rt-PA therapy. Sixty minutes after initiation of the rt-PA therapy, his neurological symptoms had improved to 16 points on the NIHSS with Wernicke's aphasia, slight right hemispatial neglect, and moderate right hemiparesis. Diffusion-weighted images showed high-intensity areas in the left MCA territory (Fig 1C, D). Magnetic resonance angiography showed arterial defects in the distal M1 and M2 segments of the left MCA (Fig 1E). An echocardiogram showed no thrombi in all 4 chambers. We started an intravenous infusion of low-molecular-weight heparin (10,000 units/day) to prevent recurrent thrombotic events after confirming the absence of rt-PA-associated hemorrhagic complications on day 1. There were no signs of hemorrhage on CT on day 2 and on magnetic resonance imaging on day 4. Magnetic resonance angiography on day 4 showed a recanalization of the left MCA, whereas the right MCA remained occluded without any neurological symptoms, suggesting a pre-existing asymptomatic occlusion (Fig 1F). On day 4, we changed the anticoagulation therapy from heparin to rivaroxaban at 15 mg once daily. On the same day, we noticed a pulseless right dorsalis pedis artery and paleness of the right lower limb, although the patient did not have any complaints. Contrast-enhanced CT and angiography (Fig 2A) showed an arterial occlusion of the right popliteal artery, which was completely recanalized by endovascular thrombectomy (Fig 2B). On day 30, his neurological symptoms improved to 7 points on the NIHSS, and his modified Rankin scale score was grade 3.

Discussion

We have herein reported the first reported Japanese case of severe cardioembolic stroke treated with rt-PA after the reversal of dabigatran with idarucizumab. The thrombolytic therapy markedly improved the patient's neurologic symptoms without hemorrhagic complications. However, we cannot completely exclude the possibility that idarucizumab might have been associated with a thrombotic event in the right lower extremity.