Case Report

Catastrophic Secondary Infarctions with Onset Seizure Following Tissue Plasminogen Activator Therapy

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Fatalities following intravenous recombinant tissue-type plasminogen activator therapy have been reported. Major fatal complications following intravenous recombinant tissue-type plasminogen activator therapy include intracranial hemorrhage, aortic dissection, and extracranial bleeding. However, the possibility that intravenous recombinant tissue-type plasminogen activator therapy itself paradoxically induces synchronized multiple cerebral novel infarctions has never been considered. We herein report the first case of bilateral internal carotid artery infarction with onset seizure following intravenous recombinant tissue-type plasminogen activator therapy for a vertebral-basilar artery infarction. A 75-year-old man was transferred to our hospital and diagnosed with acute ischemic stroke in the basilar artery. His National Institute of Health Stroke Scale score was 4. The intravenous recombinant tissue-type plasminogen activator therapy was initiated 234 minutes after stroke onset because no contraindications were present. Almost 2 hours after the intravenous recombinant tissue-type plasminogen activator therapy, the patient suddenly fell into a deep coma with generalized convulsions. A huge secondary infarction was found in the bilateral anterior circulation territories, and he died 7 days after stroke onset. This case alerts clinicians to the possibility of synchronized multiple cerebral infarctions following intravenous recombinant tissue-type plasminogen activator therapy as a dangerous complication in patients with multiple severe stenoses in the cerebral arteries.

Key Words: rt-PA—onset seizure—multiple infarctions—complication—intracranial arterial stenosis

Introduction

Some cases of stroke result in death following intravenous recombinant tissue-type plasminogen activator (IV rt-PA) therapy.[1-4] However, the possibility that IV rt-PA therapy itself paradoxically induces multiple cerebral novel infarctions has not been reported. We herein present the first report of a man with catastrophic multiple novel infarctions following IV-rt-PA therapy for minor stroke.

Case Report

A 75-year-old right-handed man suddenly developed gait disturbance and dysarthria while farming. He had medically treated hypertension and hyperlipidemia but no other medical history. He had received no antiplatelet

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or anticoagulant therapy. He was transferred to our hospital 139 minutes after symptom onset.

At arrival, his consciousness was clear, but dysarthria and visual agnosia were present. His blood pressure level was 161/83 mmHg and National Institute of Health Stroke Scale (NIHSS) score was 4. Laboratory examination showed no remarkable abnormalities including the platelet count (272,000/μL) and blood sugar level (127 mg/dL). Cranial magnetic resonance imaging showed acute ischemic lesions in the right posterior cortex and the bilateral thalamus. White matter lesions, but not ischemic lesions, were present in the middle cerebral artery area (Fig 1A-D). Cranial magnetic resonance angiography showed multiple stenoses in the bilateral intracranial internal carotid arteries and basilar artery (Fig 1E). The patient was diagnosed with acute ischemic stroke in the vertebrobasilar artery, and we initiated IV rt-PA therapy with edaravone 234 minutes after symptom onset because no contraindications were present.

One hour after initiating IV rt-PA, the visual agnosia disappeared and the NIHSS score improved to 1. The blood pressure preserved proper value (151/81 mmHg at 15 minutes after IV rt-PA, 142/72 mmHg at 30 minutes after, 164/104 mmHg at 45 minutes after, and 169/84 mmHg at 60 minutes after). However, almost 2 hours after IV rt-PA, the patient suddenly entered a deep coma with generalized convulsions starting with clonic convulsion. Although we initiated diazepam at 10 mg, fosphenytoin at 22.5 mg/kg, phenobarbital at 15 mg/kg, and levetiracetam at 2000 mg, the generalized convulsive status continued. Thus, we administered midazolam at 0.2 mg/kg/h under mechanical ventilation. We initially suspected intracranial hemorrhage following IV rt-PA therapy. However, cranial computed tomography showed no hemorrhagic change (Fig 1F). All through clinical course, no atrial fibrillation was detected in the electrocardiogram monitoring. We also performed the carotid ultrasonography and transcranial color-coded sonography, and data are shown in Supplemental material. We were unable to perform angiography to control the relentless seizure and ventilation. After generalized convulsions, the NIHSS score became worse to 40 and the blood pressure level decreased to 85/43 mmHg at the minimum for several minutes due to the anticonvulsant drugs. Thus, we preserved blood pressure of 110/60 mmHg with dopamine and norepinephrine.

The next morning, computed tomography revealed a huge infarction in the bilateral anterior circulation area (Fig 1G). Although supportive treatment was performed, cranial edema developed (Fig 1H), and the patient died 7 days after symptom onset. A summary of the clinical course is shown in Fig 1I.

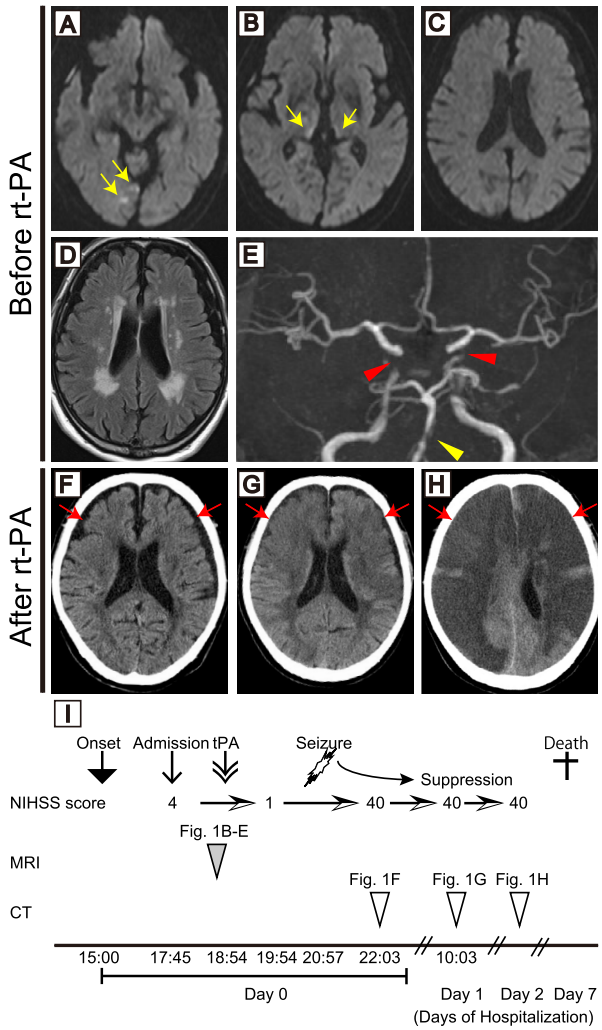

Figure 1. *(A-D) Cranial magnetic resonance imaging (MRI) and (E) magnetic resonance angiography (MRA) before intravenous recombinant tissue plasminogen activator (IV rt-PA) therapy. (A-C) Cranial diffusion-weighted imaging (DWI) and (D) fluid-attenuated inversion recovery (FLAIR) imaging. (E) MRA view. Red arrowheads show internal carotid artery stenosis, and yellow arrowheads show basilar artery stenosis. The Diffusion-Weighted Imaging-Alberta Stroke Program Early Computed Tomography Score (DWI-ASPECTS) was 10. Cranial computed tomography images (F) 3 hours, (G) 16 hours, and (H) 2 days after IV rt-PA therapy. Red arrows show novel bilateral middle cerebral artery infarctions. (I) Summary of the patient's clinical course showing the relationship among events, changes in the National Institutes of Health Stroke Scale, and image examinations. (Color version of figure is available online.)*

Discussion

We speculate the stroke pathology in this case be atherosclerotic based on the examinations results; however, the classification should be unknown with TOAST criteria. There are several hypotheses regarding why synchronized multiple cerebral novel infarctions occurred following IV rt-PA therapy in this case (Supplemental material).

A limitation of our study is the lack of pathological analysis because of the lack of consent for autopsy. A recent study showed that IV rt-PA therapy for minor nondisabling ischemic stroke did not significantly improve outcomes compared with aspirin.[5] Therefore, it is important to note the possibility of multiple embolisms

following IV rt-PA therapy in patients with multiple severe stenoses in the cerebral arteries.

Authors' Contributions

K.M., L.N., and M.S. were the attending doctors of the present case. K.M. drafted the manuscript. Y.K., T.O., T.M., H.S., and R.K. helped to draft the manuscript. S.F. conceived the study, participated in its coordination, and helped to draft the manuscript. All authors read and approved the final manuscript.

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Supplementary Materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2018.12.045.

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