Online October 20, 2020
Journal of Neuroendovascular Therapy 2021; 15: 240–245 DOI: 10.5797/jnet.cr.2020-0053

Case Report

Rupture of Anterior Communicating Artery Aneurysm after Intravenous Thrombolysis for Acute Ischemic Stroke: A Case Report

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Objective: Rupture of intracranial aneurysms after tissue plasminogen activator (t-PA) administration for acute ischemic stroke with an unruptured cerebral aneurysm is rare. We report a case of ruptured cerebral aneurysm after t-PA administration.

Case Presentation: A 74-year-old woman with dysarthria and left hemiparesis was admitted to our hospital, and acute lacunar infarction was found in the right corona radiata. One hour after t-PA administration, she complained of sudden headache and nausea, and her consciousness level deteriorated. Subarachnoid hemorrhage due to rupture of the anterior communicating aneurysm was confirmed and coil embolization was performed.

Conclusion: T-PA administration for acute ischemic stroke with an unruptured cerebral aneurysm risks rupture of the cerebral aneurysm, and careful judgment is needed in each case.

Keywords ▶ tissue plasminogen activator, acute cerebral infarction, unruptured intracranial aneurysm, subarachnoid hemorrhage

Introduction

Tissue plasminogen activator (t-PA) therapy for acute ischemic stroke with an unruptured cerebral aneurysm requires careful administration.[1)] However, the incidence of symptomatic intracranial hemorrhage after t-PA administration has not increased and the possibility of cerebral aneurysms rupture is markedly low. Many studies demonstrated that the benefits of t-PA administration exceed its risks.[2–6)] In this study, we report a patient in whom an unruptured anterior communicating artery aneurysm ruptured immediately after t-PA administration for acute ischemic stroke, leading to subarachnoid hemorrhage.

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Case Presentation

Patient: A 74-year-old woman.
Medical history: Hypertension and hyperlipidemia.
Present illness: At 8:00, dysarthria, dizziness, and numbness of the left hand and foot were noted while eating breakfast. She consulted a local clinic and was referred to our hospital under a tentative diagnosis of cerebral infarction. The time of arrival was 11:25.
Findings on admission: The Glasgow Coma Scale (GCS) score was E4V5M6. Left hemiparesis (manual muscle testing (MMT) of the upper limb: 3/5, MMT of the lower limb: 3/5, and mild left facial paralysis) and dysarthria were observed. The National Institutes of Health Stroke Scale (NIHSS) score was 5. According to the in-hospital protocol, emergency brain magnetic resonance imaging (MRI) was performed. Fresh infarction of the right corona radiata was detected. The diffusion-weighted imaging-Alberta Stroke Program Early CT Score (DWI-ASPECTS) was 10. Magnetic resonance angiography (MRA) revealed no occlusion of a major artery, but an anterior communicating artery aneurysm measuring 3 mm in diameter was found (**Fig. 1**).
Course after arrival: After receiving informed consent, t-PA was administered 4 hours and 18 minutes after onset based on the patient's and her family's wishes because there was no factor indicating careful administration other

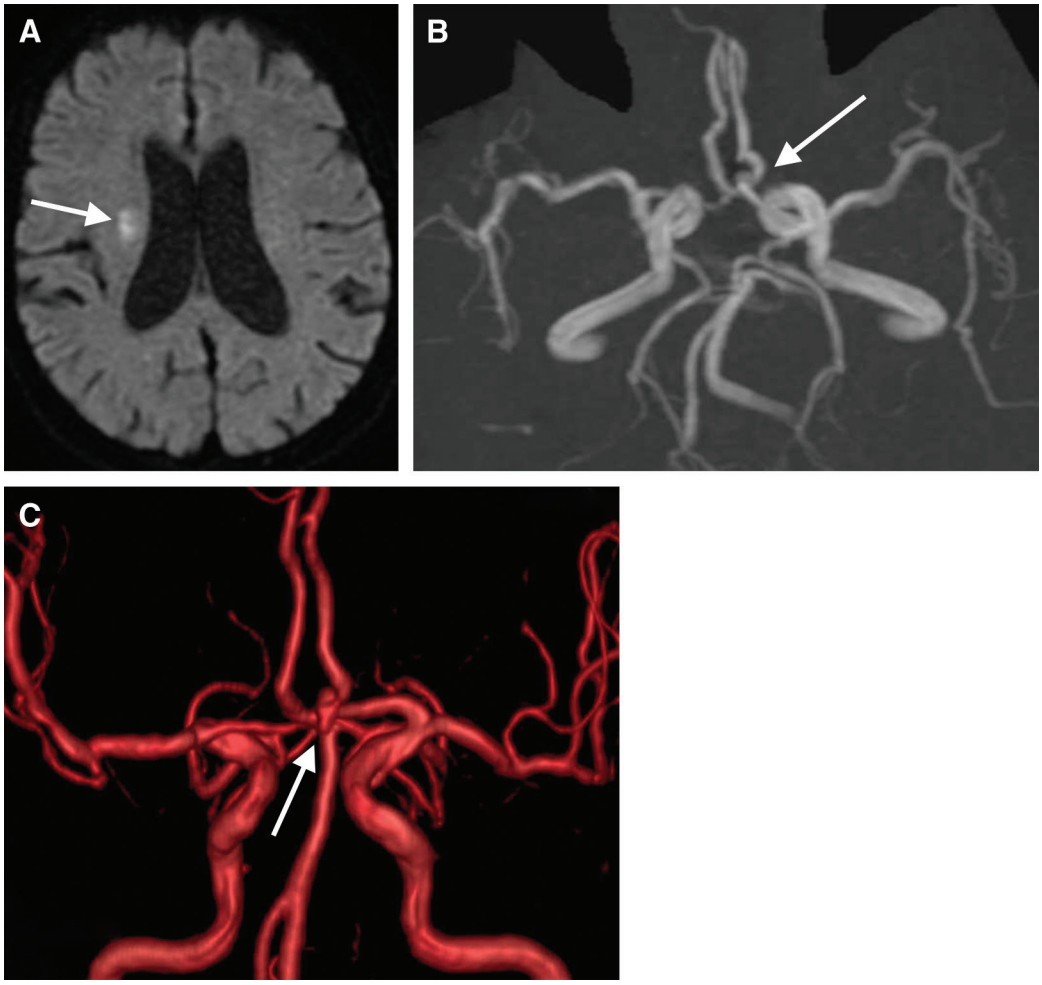

Fig. 1 (**A**) DWI on admission showed a high-intensity area in the right corona radiata (arrow). (**B**) MRA (3D-TOF) showed a small aneurysm in the anterior communicating artery (arrow). (**C**) MRA (volume rendering) suggested appearance of bleb at the tip of the aneurysm (arrow). 3D-TOF: three-dimensional time of flight; DWI: diffusion-weighted imaging; MRA: magnetic resonance angiography

than an unruptured cerebral aneurysm and paralysis was relatively marked. After the start of administration, the systolic blood pressure reached ≥190 mmHg and nicardipine was administered to control it at ≤185 mmHg. Paralysis of the left upper limb reduced 1 hour after the start of administration and the NIHSS score was 3. No abnormality was noted on brain computed tomography (CT). Thereafter, the patient immediately complained of headache and nausea, and her consciousness level rapidly deteriorated, reaching a GCS score of E1V1M5. Brain CT revealed Fisher group 3 diffuse subarachnoid hemorrhage. CT angiography (CTA) demonstrated an anterior communicating artery aneurysm (**Fig. 2**), as detected on MRA. After blood pressure control and sedation, endotracheal intubation was conducted and the patient was moved to the intensive care unit (ICU) (**Fig. 3**).

Emergency cerebral angiography was performed. Three-dimensional (3D)-rotational angiography (RA) revealed an anterior communicating artery aneurysm measuring 3.5 × 2.5 mm in diameter with bleb formation (**Fig. 4A**), leading to a diagnosis of subarachnoid hemorrhage related to the rupture of this aneurysm. Subsequently, coil embolization of the cerebral aneurysm was performed (**Fig. 4B**). We considered the use of rescue devices, such as a balloon catheter, in preparation for intraoperative rupture, but the aneurysm ruptured after t-PA administration and embolization was conducted using a simple technique as promptly as possible. A 6Fr 25-cm sheath (Terumo, Tokyo, Japan) was inserted into the right femoral artery. A 6Fr Envoy 90 cm (Johnson & Johnson (J&J), Tokyo, Japan) was inserted to the petrous portion of the left internal carotid artery coaxially with a 4Fr CX catheterJB2 125 cm (KATECS, Kanagawa, Japan) using a Surf 0.035-inch 150-cm guidewire (PIOLAX, Inc., Kanagawa, Japan). A 3.4Fr TACTICS 120 cm (Technocrat, Aichi, Japan) was used as an intermediate

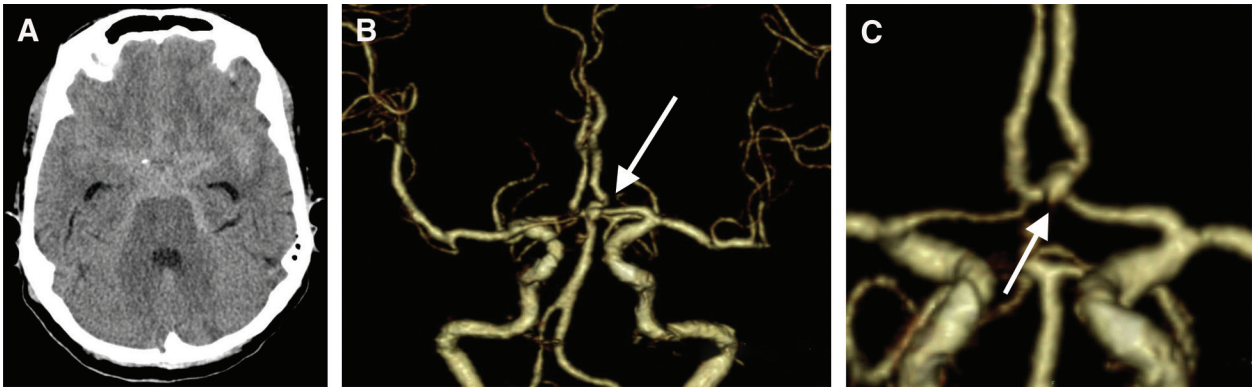

Fig. 2 (**A**) CT showed diffuse subarachnoid hemorrhage in the basal cistern. (**B**) CTA showed an aneurysm (3.0 mm) in the anterior communicating artery (arrow). (**C**) Bleb was suspected at the tip of the aneurysm (arrow). CT: computed tomography; CTA: CT angiography

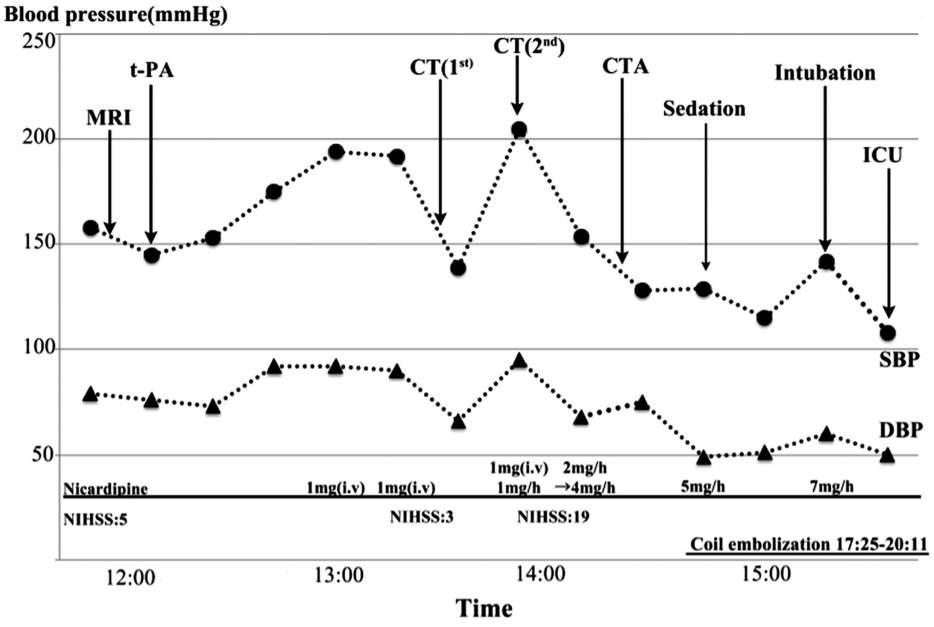

Fig. 3 Blood pressure change from arriving to our hospital to entering the ICU. DBP: diastolic blood pressure; ICU: intensive care unit; i.v.: intravenous injection; SBP: systolic blood pressure

catheter. An Excelsior SL-10 preshaped 45° 150 cm (Stryker, Kalamazoo, MI, USA) was inserted into the aneurysm using a Traxcess 14 200 cm (Terumo). A frame was prepared using a GALAXY COMPLEX EXTRA-SOFT 3 mm/4 cm (J&J) and two coils of GALAXY G3 mini 2 mm/3 cm (J&J) were inserted. After confirming the disappearance of intra-aneurysmal contrast enhancement, the procedure was completed (**Fig. 4C**). No rebleeding was noted on brain CT the day after coil embolization. The administration of aspirin at 100 mg was started, and anti-vasospasm treatment using fasudil hydrochloride and ozagrel was initiated.

After coil embolization, there was no symptomatic cerebral vasospasm. After 6 weeks, ventriculoperitoneal shunt for secondary normal-pressure hydrocephalus was performed. The patient was referred to a rehabilitation hospital with a modified Rankin Scale score of 3.

Discussion

According to previous studies, the incidence of intracerebral hemorrhage after intravenous thrombolysis using t-PA ranges from 10.5% to 24.8%, and symptomatic hemorrhage accounts for 1.9%–5.9%.[3–5,7] According to the guidelines for t-PA treatment in Japan, t-PA should be carefully administered to acute ischemic stroke patients with unruptured cerebral aneurysms.[1] However, retrospective studies of intravenous thrombolysis using t-PA

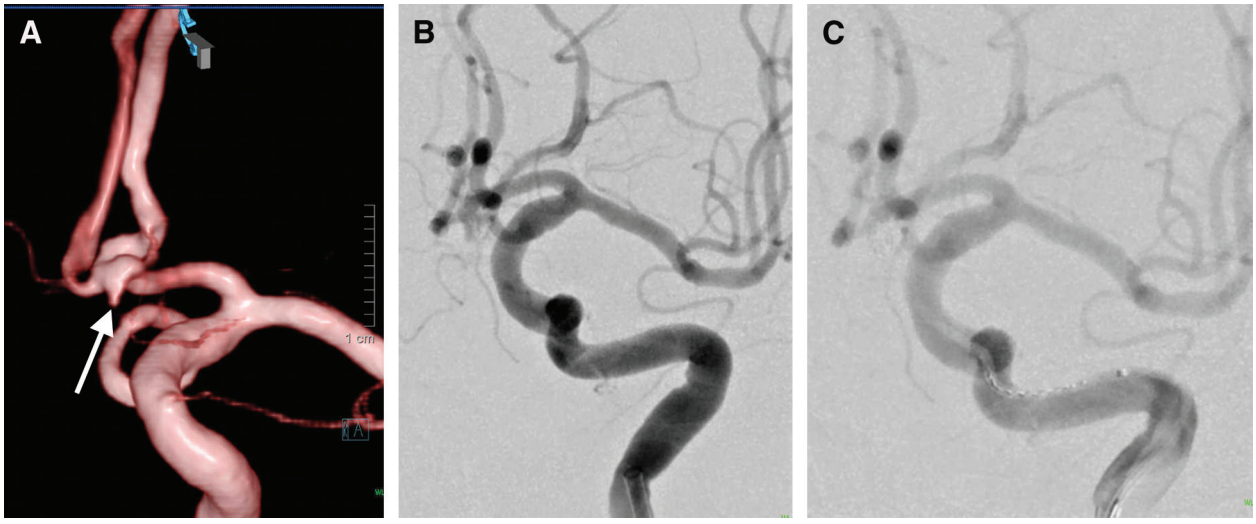

Fig. 4 (**A**) 3D-RA rotation angiography showed an aneurysm (3.5 × 2.5 mm) with bleb in the anterior communicating artery (arrow). (**B**) Angiography before coil embolization. (**C**) Angiography after the treatment showed the neck remnant. 3D-RA: three-dimensional rotation angiography

involving acute ischemic stroke patients with unruptured cerebral aneurysms reported that there was no significant difference in the incidence of intracerebral hemorrhage, including symptomatic hemorrhage, between patients with and without cerebral aneurysms, and that there was no subarachnoid hemorrhage related to cerebral aneurysmal rupture,[2–6] suggesting that t-PA can be used relatively safely even in patients with cerebral aneurysms. Four patients with myocardial or cerebral infarction and unruptured cerebral aneurysms in whom aneurysmal rupture after t-PA administration caused subarachnoid hemorrhage have been reported (**Table 1**).[8–11] The mean age of the patients, including ours, was 66.6 years, and four were females. Concerning the disease-type classification of infarction, myocardial infarction was noted in one patient, cardiogenic cerebral embolism in two, internal carotid artery dissection in one, and lacunar infarction in one patient. Concerning the aneurysmal site, three patients had anterior communicating artery aneurysms. In five of six cerebral aneurysms (five patients), the presence of a daughter sac was observed. The interval from t-PA administration until cerebral aneurysmal rupture varied. In three patients who died after cerebral aneurysmal rupture, the aneurysmal size was large and the post-rupture state was serious. An increase in the blood pressure after cerebral infarction may be primarily involved in the rupture of unruptured cerebral aneurysms after t-PA administration. In the acute phase of cerebral infarction, activation of the sympathetic nervous system promotes catecholamine and brain natriuretic peptide secretion, increasing the blood pressure in many cases.[12–14] According to several studies, t-PA induces matrix metalloproteinase-9 (MMP-9) production,[15] and MMP-9 production occurs in an infarcted area, causing hemorrhage through destruction of the vascular basement membrane.[16,17] Since the possibility that t-PA is also involved in cerebral aneurysmal rupture cannot be excluded, the use of t-PA for acute ischemic stroke should be carefully considered patients with unruptured cerebral aneurysms. Furthermore, anterior communicating artery aneurysms may rupture even when the diameter is small,[18] as demonstrated in the present case. Bleb presence itself is a risk factor for rupture[19]; therefore, the site and shape of a cerebral aneurysm and risk of rupture must be considered before t-PA administration. When administering t-PA to patients with acute ischemic stroke, MRA or CTA should be performed to identify a blood vessel responsible for cerebral infarction or to search for an unruptured cerebral aneurysm rather than evaluating whether t-PA administration is appropriate based on plain CT findings alone. If an unruptured cerebral aneurysm is detected, the risk of rupture after t-PA administration must be considered. If the neurological severity is low in the absence of major artery occlusion, the risks and benefits of t-PA administration should be carefully assessed. After t-PA administration, strict systolic blood pressure control reduces the incidence of intracranial hemorrhage.[20] Therefore, it may be appropriate to consider downward adjustment of blood pressure control from after t-PA administration in acute ischemic stroke patients with unruptured cerebral aneurysms.

Table 1 Patient characteristics of subarachnoid hemorrhage due to rupture of cerebral aneurysm after t-PA administration

Case	Author	Age	Sex	Type of infarction	NIHSS	Cerebral aneurysm	Size	Daughter sac	Onset time	WFNS	Treatment	mRS
1	Lagares, 1999	66	F	Myocardial infarction	0	Anterior communicating a.	N/A	+	8h	V	None	6
2	Rammos, 2012	51	F	Af (cardiogenic embolism)	20	Anterior communicating a.	7 mm	+	N/A	IV	Thrombectomy	6
				MCA occlusion							Coling	
3	Haji, 2014	71	M	ICA dissection	15	Posterior communicating a.	6 mm	–	5h	V	None	6
				MCA occlusion		Posterior inferior cerebellar a.	8.5 mm	+				
4	Zaldivar, 2015	71	F	Af (cardiogenic embolism)	11	Middle cerebral a.	6 mm	+	24h	I	Clipping	1
				MCA occlusion								
5	Present case	74	F	lacunar infarction	5	Anterior communicating a.	3 mm	+	1h	IV	Coiling	3

N/A:not available; Onset time:the time when SAH confirmed from t-PA administration; ICA: internal carotid artery; MCA: middle carotd artery; mRS: modified Rankin Scale; t-PA: tissue plasminogen activator

Conclusion

We reported a patient in whom an unruptured anterior communicating artery aneurysm ruptured after t-PA administration for acute ischemic stroke, causing subarachnoid hemorrhage. The use of t-PA for patients in acute ischemic stroke with unruptured cerebral aneurysms must be carefully decided based on the risk of cerebral aneurysmal rupture and neurological severity of cerebral infarction.

Disclosure Statement

The authors declare no conflict of interest.

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