

Effective Intravenous Thrombolytic Therapy in a Patient with Cerebral Infarction Associated with Left Atrial Myxoma

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Abstract

A 70-year-old man presented with sudden onset of global aphasia and right hemiplegia. Brain MRI revealed occlusion of the left middle cerebral artery. He was diagnosed as having a hyperacute cerebral infarction. Intravenous thrombolytic therapy was started, and the neurological symptoms were resolved after 11 h. Echocardiography showed a mobile mass in the left atrium, suspicious of a myxoma. The tumor was resected and pathologically diagnosed as a myxoma. In this patient, intravenous thrombolytic therapy was effective, and no adverse effects were observed. This suggests that, even with complications of myxoma, thrombolytic therapy can be considered if there are no contraindications.

Key words: cerebral infarction, myxoma, intravenous thrombolytic therapy, recombinant tissue plasminogen activator (rt-PA)

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Introduction

Myxoma is a benign tumor of the heart, occurring most commonly in the left atrium (1). It can embolize to any organs, and patients with various symptoms of cerebral infarction have been reported (2-4). The embolic source may be composed of tumor itself or thrombus (5). Currently, thrombolytic therapy is generally given to patients with cerebral infarction (6). However, the guidelines do not discuss stroke with myxoma (7-9), and only a small number of cases have been reported (10-17). Myxoma may also cause cerebral aneurysm formation (3, 4), and there is a risk of cerebral hemorrhage with thrombolytic therapy. Therefore, thrombolytic therapy in cerebral infarction with myxoma is still controversial. A patient with cerebral infarction associated with left atrial myxoma in whom thrombolytic therapy was

effective is reported.

Case Report

A 70-year-old man with no past history developed sudden weakness of the right side of his body and difficulty speaking. He was rushed to the emergency room of our hospital and arrived 32 minutes after symptom onset. On examination, his level of consciousness was Glasgow coma scale (GCS) E4V1M5 and Japan coma scale (JCS) I-3. The patient was unable to follow commands. Blood pressure was 117/78 mmHg, and pulse was 64 beats/min and regular. The general physical examination was unremarkable. On neurologic examination, the patient had global aphasia, right facial paralysis, and right upper and lower limb paralysis, and he was unresponsive to pain stimulation on the right side. The National Institutes of Health Stroke Scale (NIHSS)

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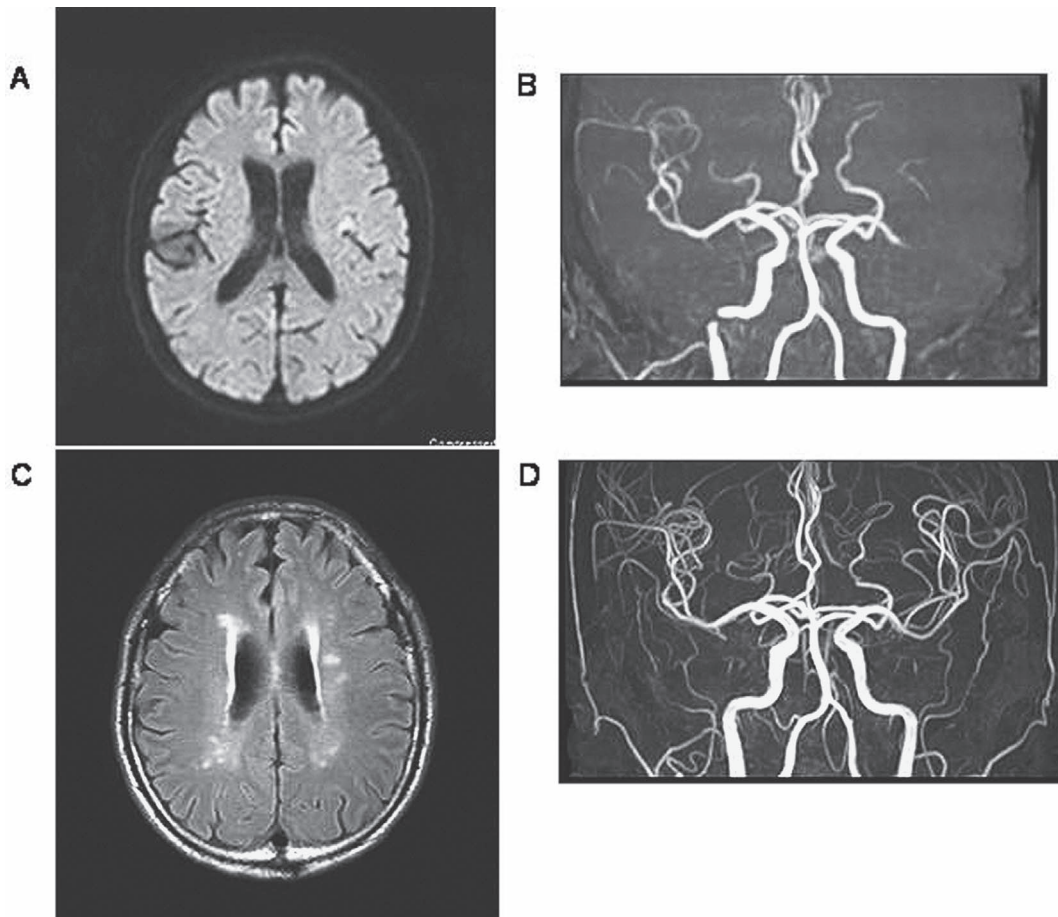


Figure 1. Brain MR images before and after thrombolytic therapy. At 50 min after symptom onset, a slightly high signal region was seen in the left insular cortex on DWI (A); the brain MRA showed poor flow distal from the horizontal segment of the left MCA (B). On day 11, a faint high signal was depicted in the left corona radiata on FLAIR (C). MRA showed reperfusion distally from the horizontal segment of the left MCA (D). DWI: diffusion-weighted imaging, MRA: magnetic resonance angiography, MCA: middle cerebral artery, FLAIR: fluid attenuated inversion recovery

score was 11. Laboratory findings showed no abnormalities except for slight increases in lactate dehydrogenase (LDH) and creatinine (Cr) as follows: white blood cell count (WBC) $4,910/\mu\text{L}$, hemoglobin (Hb) 13.2 g/dL, platelet count (Plt) $12.1 \times 10^4/\mu\text{L}$, aspartate aminotransferase (AST) 30 IU/L, alanine aminotransferase (ALT) 18 IU/L, LDH 286 IU/L, creatine phosphokinase (CK) 89 IU/L, Cr 1.23 g/dL, LDL cholesterol 66 mg/dL, blood sugar 118 mg/dL, HbA1c 5.0%, brain natriuretic peptide (BNP) 23.3 pg/mL, C-reactive protein (CRP) 0.09 mg/dL, prothrombin time (PT) 11.9 seconds (international normalized ratio 1.0), and activated partial thromboplastin time (APTT) 24.5 seconds (control 29.0 seconds). The ECG was normal with sinus rhythm. The brain computed tomography (CT) at 40 minutes after onset showed no early CT signs. The brain magnetic resonance imaging (MRI) showed a faint high signal in the left insular cortex on diffusion-weighted imaging (DWI) (Fig. 1A). Magnetic resonance angiography (MRA) revealed occlusion in the horizontal segment of the left middle cerebral artery (MCA) (Fig. 1B).

The patient was diagnosed as having a hyperacute cere-

bral infarction due to occlusion of the left MCA. At 92 min after the symptom onset, alteplase [0.6 mg/kg of recombinant tissue plasminogen activator (rt-PA)] was intravenously infused for 1 hour. Edaravone (30 mg twice a day) was also given for 1 week. Just before administration of alteplase, the NIHSS score was 11. At 15 minutes after the start of administration of alteplase, the right hemiplegia had begun to improve, and the patient could follow commands. After 4 hours, the aphasia and dysarthria began to improve greatly. After 11 hours, the symptoms were completely resolved, and the NIHSS score improved to 0.

ECG monitoring showed no atrial fibrillation, and carotid artery ultrasound revealed no plaque formation. During observation, the patient had no abdominal pain, back pain, hematuria, or cyanosis of the legs, but because the creatinine and LDH showed transient mild elevations during hospitalization, the possibility of asymptomatic systemic embolism could not be ruled out. There were no risk factors for atherothrombotic cerebral infarction, and the symptoms occurred suddenly during the daytime. There were no arteriosclerotic lesions of the cerebral or carotid arteries, but the

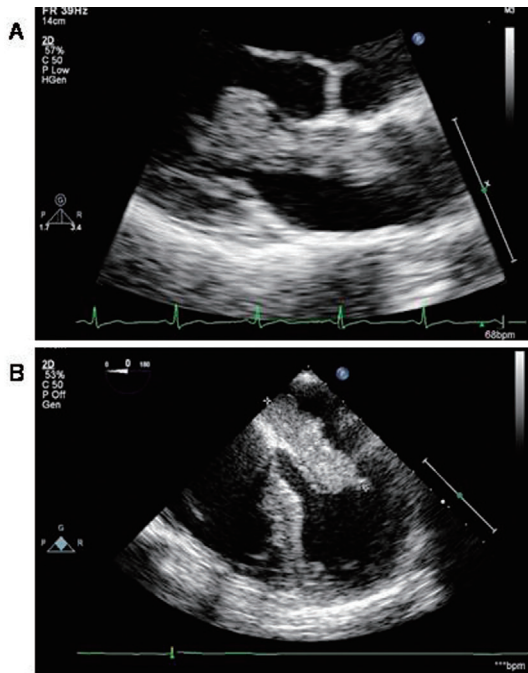


Figure 2. Echocardiography before surgical resection. Transthoracic long axis precordial view (A) and transesophageal four-chamber view (B) show a pedunculated mobile mass in the left atrium arising from the atrial septum. There is no thrombus in the left atrial appendage.

left MCA was completely occluded. Because of these reasons, cardiogenic cerebral embolism was suspected clinically, and oral warfarin was started. On day 11, brain MRI/MRA confirmed recanalization of the left MCA (Fig. 1D), and only a small cerebral infarct was noted (Fig. 1C).

On day 15, transthoracic echocardiography showed normal left ventricular contraction, without any valvular diseases including mitral stenosis, but there was a mobile mass, suspicious of myxoma, in the left atrium (Fig. 2A). On day 18, transesophageal echocardiography was performed. No intracardiac shunt or thrombus in the left atrial appendage was observed (Fig. 2B). There was neither anemia nor elevation of interleukin-6 (IL-6) (1.78 pg/mL, normal range: ≤ 2.41 pg/mL). No cerebral bleeding complications occurred. Since this tumor was considered the cause of the cerebral infarction, on day 20, the tumor was resected under cardiopulmonary bypass. It was intraoperatively confirmed that a pedunculated polypoid tumor (70 × 25 × 15 mm) arose from the fossa ovalis in the left atrium. Histopathology revealed a PAS-positive myxoid stroma, proliferation of mildly atypical tumor cells, intratumoral bleeding, and thrombus formation (Fig. 3). The final diagnosis was left atrial myxoma. During the operation, the tumor and the atrial septum where it originated were excised, and the atrial septum was closed using a GORE-TEX® patch (3 cm × 6 cm).

Anticoagulation with warfarin was continued for 3 months postoperatively, until the atrial septal patch was expected to be endothelialized. After 1 year, echocardiography

showed no recurrence of myxoma, and there was no cerebral aneurysm formation on brain MRI. There have been no arrhythmias. To date, the patient is asymptomatic and doing well (modified Rankin scale 0).

Discussion

Myxoma is a benign tumor of the heart most commonly occurring in the left atrium and attached by a pedicle to the fossa ovalis in the atrial septum. Clinical symptoms include the classic triad of embolic, obstructive, and constitutional signs, such as cerebral infarction, syncope, dyspnea, fever, weight loss, and arthralgia. In the present patient, there was no past history of obstruction; cerebral infarction was the initial presentation, and CRP was mildly elevated. The treatment of myxoma is surgical resection, and when it is resected without residual tumor, recurrence is uncommon, and the prognosis is good. Some myxomas occur as part of the familial myxoma syndrome, Carney syndrome, and multiple tumors, and recurrences have been reported (1). However, in the present patient, it was an isolated lesion and a sporadic case.

Myxoma can generally be diagnosed easily by transthoracic echocardiography. In cases such as the present, where there are no risk factors for cerebrovascular disorder and atrial fibrillation is not present, it is important to suspect the possibility of myxoma as a cause of cerebral embolism, despite its rarity. If time constraints and available facilities permit, transthoracic echocardiography should be performed.

Causes of cerebral infarction include tumor emboli and thrombotic emboli (5). Morphologically, tumors with a villous surface are prone to embolization (18). In the present patient, a thrombotic embolus was considered because the histopathology showed an irregular surface and thrombus formation, and thrombolytic therapy was highly effective.

A literature search for articles or abstracts in English dealing with thrombolytic therapy for cerebral infarction associated with myxoma yielded eight case reports (10-17). Two cases were given intra-arterial infusion of urokinase (10, 11), one case was given intra-arterial infusion of rt-PA (12), and five cases were given intravenous infusion of rt-PA (13-17). Among these eight cases, treatment was effective in five cases (10, 12, 14, 15, 17) and not effective in three cases (11, 13, 16). Only 1 case was complicated with cerebral hemorrhage (13). Cerebral angiography was performed in that case, but no cerebral aneurysm was present (13). Cerebral infarction complicated with myxoma is rare, and the number of cases is insufficient for a full evaluation of efficacy and safety. It is important to note that, even in cases of myxoma associated with tumor embolism, however, thrombolytic therapy has been effective in some cases, meaning that there is scope for the consideration of thrombolytic therapy even if myxoma is present. Conversely, in cases in which thrombolytic therapy is ineffective, the possibility of tumor embolism would be considered. It is to be hoped that, as more cases are accumulated in the future, it

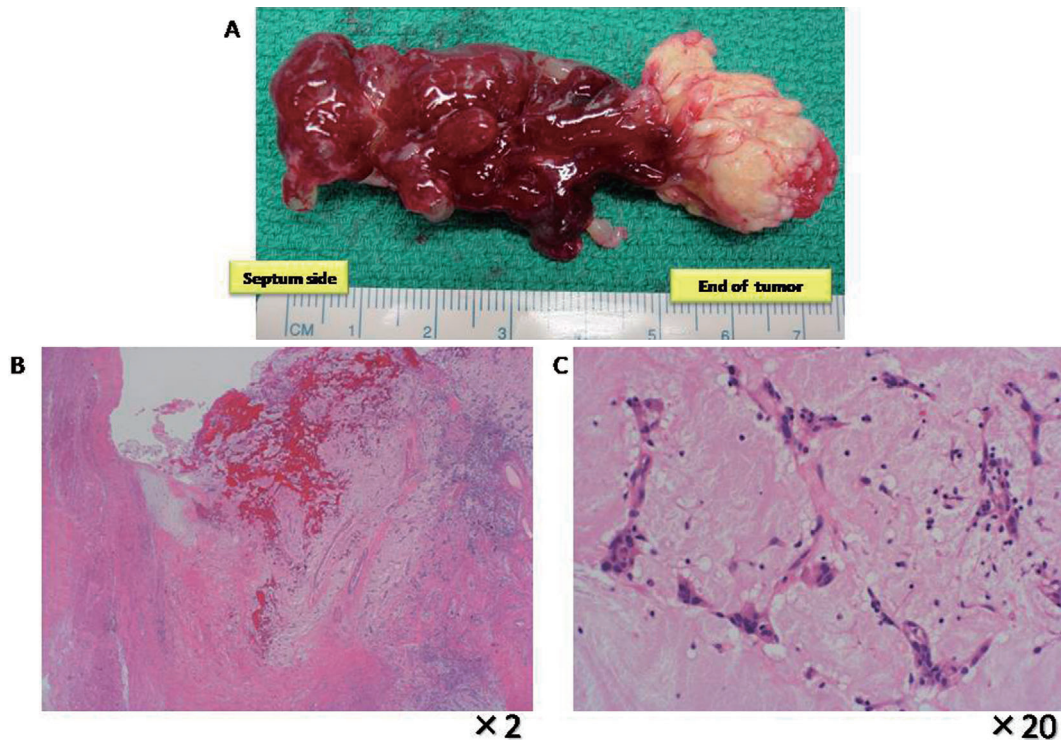


Figure 3. Gross and microscopic pathology. The excised myxoma measured 70 × 25 × 15 mm and weighed 14 g. There was a pedicle on the septal side, and the tip was papilliform (A). Histopathology showed bleeding within the tumor and on the surface, and there was thrombus formation (× 2) (B). Spindle-shaped tumor cells were interspersed within a myxoid stroma (× 20) (C). There were no malignant findings.

will become possible to establish clinical methods for distinguishing between tumor embolism and thrombotic embolism.

We used alteplase at 0.6 mg/kg, which is lower than the internationally approved dosage of 0.9 mg/kg, because a previous report showed that the clinical efficacy and safety of 0.6 mg/kg alteplase in Japanese patients were compatible with those of 0.9 mg/kg in patients in North America and the European Union (19).

In myxoma, the formation of a small cerebral aneurysm has been reported on long-term follow-up; the mechanism involves tumor cell invasion into the vessel walls (3, 4).

According to a review by Sabolek et al of 32 cases of delayed cerebral aneurysm associated with myxoma whose courses were observed by angiography, as well as cranial MRI and MRA, the median number of aneurysms present per individual was three, of which 91% were fusiform aneurysms and the remainder saccular. Their size was 3-10 mm, the site of occurrence was the MCA area in 74% of cases, and the median time from cardiac surgery to discovery of aneurysm was 36 months (4). Since new cerebral aneurysms may occur, careful follow-up monitoring is also important in the present case.

In the small number of reported cases of thrombolytic therapy to date, cerebral aneurysm as a clinical cause of cerebral hemorrhage has not been reported. However, aneurysms that are complications of myxoma may be minute aneurysms, like bacterial aneurysms, that are undetectable

on MRI or cerebral angiography. In the case reported by Chong et al, subarachnoid hemorrhage in the left cranial region occurred following thrombolytic therapy, and although subsequent cerebral angiography did not show a cerebral aneurysm, a minute aneurysm might have been present. With thrombolytic therapy, the risk of hemorrhage from an undetectable minute aneurysm must be taken into account when determining the indications. Local arterial infusion via a catheter is another choice of administration that can be considered with the objective of reducing the risk of hemorrhage (13).

In conclusion, a patient with sudden cerebral infarction associated with myxoma in whom thrombolytic therapy was highly effective, and pathologic findings from resected samples also suggested thrombotic embolism, was reported. Complications of tumor embolism and cerebral aneurysm must also be taken into account, but thrombolytic therapy may be effective even if myxoma is present, and its indications could be carefully considered.

The authors state that they have no Conflict of Interest (COI).

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