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# Cerebral Embolism Associated with Left Atrial Myxoma That Was Treated with Thrombolytic Therapy

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## Key Words

Cerebral embolism · Myxoma · Thrombolytic therapy · Recombinant tissue plasminogen activator · Mechanical embolus retrieval in cerebral ischemia

## Abstract

We present a case of cerebral embolism associated with a left atrial myxoma that was treated with intravenous thrombolytic therapy. A 79-year-old right-handed man with no history of neurological or psychiatric illnesses was referred to our hospital because of confusion. He had been self-supported in the activity of daily living and could enjoy gardening until just before his admission. He had aphasia, left conjugate deviation, right hemiparesis, and right pathological reflexes. His NIHSS score was 24. Cranial DWI showed hyperintense lesions in the left middle cerebral artery territory, and MRA revealed left middle cerebral artery occlusion. We started treatment with the recombinant tissue plasminogen activator alteplase intravenously 3 h after the onset. However, the therapy was ineffective, and the NIHSS score was 25 on the second day. A transthoracic echocardiogram and heart MRI showed a left atrial myxoma. However, surgery was contraindicated because of the patient's poor general condition. Although intravenous recombinant tissue plasminogen activator is a reasonable treatment for stroke patients, even with a cardiac myxoma, we cannot always expect good effects, especially if the emboli are parts of the tumor itself. In this case, we could not perform an endovascular mechanical embolectomy; however, we speculate that mechanical embolus retrieval in cerebral ischemia might be effective in such cases.

## Introduction

Embolic events occur in approximately 40–50% of patients with cardiac myxoma [1]. Embolic complications of an atrial myxoma are due to fragments of the myxoma itself or surface emboli [2]. Some cases of cerebral infarction associated with cardiac myxoma have been treated successfully with intravenous thrombolytic therapy [1, 3–6]. However, thrombolytic therapy is not always effective.

A phase I study showed that cerebral embolectomy with the Merci Retriever is safe and that successful recanalization could benefit a significant number of patients, even when performed in an extended 8-hour time window [7].

We report a patient who suffered from cerebral embolism associated with a left atrial (LA) myxoma and who was unsuccessfully treated with thrombolytic therapy. We discuss the efficacy of mechanical embolus retrieval in cerebral ischemia (MERCİ) in such cases.

## Case Report

A 79-year-old right-handed man with no history of neurological or psychiatric illnesses was referred to our hospital because of altered consciousness. He was being treated medically for hypertension, but he had not been on antithrombotic or anticoagulant treatment at the time of stroke onset. He had never undergone an echocardiogram. On arrival at the emergency room, his blood pressure was 159/67 mm Hg, and he had a regular heart rate of 54 beats per minute with normal heart sounds. His consciousness scores on the Glasgow Coma Scale were E2, V1, and M4. A neurological examination revealed left conjugate deviation, right hemiparesis, and right pathological reflexes. The National Institutes of Health Stroke Scale (NIHSS) score was 24.

Cranial CT showed slight blurring of the border between the gray and white matter, with sulcal effacement in the left frontotemporal lobe, but without a hyperdense middle cerebral artery (MCA) sign (online suppl. fig. 1a; [www.karger.com/doi/10.1159/000336179](http://www.karger.com/doi/10.1159/000336179)). Cranial DWI showed hyperintense lesions in the left MCA territory (online suppl. fig. 1b), and MRA revealed occlusion of the left MCA (online suppl. fig. 1c). The laboratory data were normal, and an electrocardiogram demonstrated sinus rhythm with no abnormal findings. We started treatment with the recombinant tissue plasminogen activator (rtPA) alteplase intravenously 3 h after symptom onset. On the second day, brain CT showed a slight oozing hemorrhage in the area of the left MCA. A transthoracic echocardiogram showed a 21 × 12-mm myxoma in the LA (online suppl. fig. 2). His neurological symptoms did not improve, and the NIHSS score was 25. On admission, we performed 24-hour ECG monitors for 3 days, but significant findings such as atrial fibrillation were not detected. On day 6, FLAIR (online suppl. fig. 1d) and T<sub>2</sub>\*-weighted (online suppl. fig. 1e) brain MRI showed hemorrhagic infarction, and MRA showed no recanalization (online suppl. fig. 1f). A cardiac MRI performed on day 15 showed an 11 × 8-mm elevated lesion in the LA, which was slightly hyperintense in the T<sub>1</sub>-, T<sub>2</sub>-, and fat-suppressed T<sub>2</sub>-weighted images (online suppl. fig. 3). However, surgery was contraindicated because of the patient's poor general condition. We introduced anticoagulant treatment with warfarin 14 days after stroke onset with PT-INR: 2.0–3.0.

Although his consciousness improved to E4, V1, and M4 on the Glasgow Coma Scale, the right hemiparesis and aphasia did not improve. The patient had an NIHSS score of 21 and a modified Rankin scale score of 4 when he was moved to a rehabilitation hospital on day 36.

## Discussion

Primary tumors of the heart are rare, with an incidence of approximately 0.02%, corresponding to 200 tumors in 1 million autopsies [8]. Three quarters of cardiac tumors are benign, and nearly half of these tumors are myxomas. Most patients are between the third and sixth decade of life [9]. About 75% of cardiac myxomas originate in the LA and 15–20% in the right atrium [9]. Embolism occurs in 40–50% of the patients with myxomas [1]. Emboli caused by atrial myxomas can be composed of fragments of the myxoma itself or surface emboli [2]. Though there is still no evidence-based medicine to prevent from embolic complications other than surgical resection of myxoma, we introduced anticoagulant treatment, and fortunately, the patient had no stroke recurrence.

Intra-arterial local thrombolysis is effective for treating cerebral embolism associated with cardiac myxoma [10, 11]. Cases of cerebral infarction associated with cardiac myxomas have been treated successfully with intravenous thrombolytic therapy [1, 3–6]. However, there are also published cases with an unfavorable outcome. Chong et al. [12] presented a patient with an acute ischemic stroke associated with an LA myxoma who was treated with intravenous rtPA and developed hemorrhage remote from the location of the ischemic stroke. Another patient with cerebral embolism associated with atrial myxoma was treated with intravenous rtPA and developed cerebral microbleeds due to cardiac myxoma [13]. In these patients, the tumors were later resected, but the histopathological findings of the emboli were not described [1, 3–6, 10–13]. However, we cannot always expect thrombolytic therapy to be effective, especially in tumor emboli.

A phase I study showed that cerebral embolectomy with the Merci Retriever was safe and that successful recanalization could benefit a significant number of patients [7]. However, there are still only a few studies available about the efficacy of MERCI in larger population, and MERCI is not a well-established therapy in Japan. In our case, the thrombolytic therapy was ineffective, and we could not perform neurosurgery. We had been preparing to introduce MERCI to our hospital, but the introduction had not been completed at that time. The main inclusion criteria for MERCI are: NIHSS score  $\geq 10$ ; treatment performed within 8 h from symptom onset and contraindication to intravenous thrombolysis; no large hypodensity on CT, and occlusion of a major cerebral artery on the angiogram [7]. Safety is defined by the absence of vascular injury or symptomatic intracranial hemorrhage [7]. Our patient met all criteria for MERCI, and neither vascular injury nor symptomatic intracranial hemorrhage was present. Therefore, MERCI could have been a choice of treatment.

Bhatia et al. [14] reported a case of stroke caused by a tumor embolus that was diagnosed histopathologically by removing the embolus from the distal left internal cerebral artery using the MERCI Retrieval device. This patient had a history of breast cancer and was diagnosed with a metastatic pulmonary lesion on chest CT, and a mechanical thrombectomy was performed without thrombolytic therapy. Histopathologically, the retrieved embolus was consistent with a phyllodes tumor of the breast, matching the result of the endobronchial lesion biopsy.

No doubt, intravenous rtPA is a reasonable treatment for stroke patients with cardiac myxomas. However, thrombolytic therapy is not always effective. Endovascular

mechanical embolectomy using MERCI is effective for achieving revascularization in patients with acute ischemic stroke, including those in whom intravenous rtPA is ineffective [15]. In the present case, we could not confirm whether the embolus was a blood clot or tumor itself. However, when thrombolytic therapy is not successful for treating a stroke, even without a known neoplasm, we should suspect tumor emboli. With tumor fragment emboli, it is possible to remove the emboli from the cerebral vasculature with a mechanical embolectomy, such as MERCI [14].

Most patients with myxomas are between the third and sixth decade of life [9]. Although they are comparatively young, the risk of hemorrhage is greater than in those patients without myxomas because of occult tumor emboli or microaneurysms. The risk of hemorrhage might be higher in older cases, especially when the onset-to-treatment times are longer [6]. Our patient was relatively old, and the onset-to-treatment time was 3 h, but he did not show complication of symptomatic intracranial hemorrhage. We administered 0.6 mg/kg of alteplase according to the guidelines of the Japan Stroke Society, which is a lower dose than the internationally approved dosage of 0.9 mg/kg. In patients receiving 0.6 mg/kg alteplase, the risk of symptomatic intracranial hemorrhage within 36 h is lower than thresholds determined by calculating data reported in North America and the European Union for a 0.9-mg/kg dose [16].

For stroke associated with a known myxoma, intra-arterial thrombolysis may be preferable to intravenous thrombolysis, since intra-arterial therapy allows the identification of aneurysms, which may enable the clinician to focus treatment on the occluded artery, thereby avoiding areas more likely to bleed [12]. Realistically, at stroke onset, one rarely knows if a patient has a myxoma, and it is difficult to evaluate all patients with echocardiography before starting thrombolysis. However, we should perform echocardiography as soon as possible to rule out a myxoma in acute ischemic stroke. In addition, we should not hesitate to introduce MERCI, as it may improve the prognosis of such patients. Further research in a larger population is necessary to determine safe and effective therapies for infarction associated with cardiac myxomas.

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