

# Cerebrovascular Complications of Atrial Myxoma

*Sheri L. Novendstern, MD*

*Scott L. Silliman, MD*

*Robert P. Booth, MD*

**A**lthough stroke is generally perceived to be a disease of middle-aged and older adults, it can occur in young adults as well. Data collected in Europe and the United States have demonstrated an annual incidence of 4 to 28 stroke events per 100,000 people younger than 45 years.<sup>1</sup> Most strokes in young adults are ischemic.

Atrial myxomas are a rare cause of stroke, accounting for fewer than 1% of all ischemic strokes.<sup>2</sup> Although rare, atrial myxoma should be considered in the differential diagnosis of any young adult who presents with ischemic stroke. Detection of this tumor is relatively easy, and surgical removal of the myxoma is usually a permanent measure to prevent subsequent strokes. This article presents the case of a 37-year-old woman with an atrial myxoma who had 2 strokes. The etiology of stroke in young adults is considered in the context of this patient's differential diagnosis. The pathogenesis and management of the clinical manifestations of atrial myxoma, including cerebral embolism and aneurysm formation, are discussed, as is the management of the tumor itself.

## CASE PRESENTATION

### Patient Presentation and History

A 37-year-old woman was admitted to the hospital several hours after abruptly developing weakness in her right limb. Her medical history was notable only for depression. She had no known history of diabetes, hypertension, deep venous thrombosis, or cardiac disease. Nine months earlier, she had an episode of transient numbness on the right side of her body. Diagnostic evaluation at that time, consisting of a brain computed tomographic (CT) scan and carotid ultrasonography, revealed no abnormal findings. Her only medication was sertraline. She reported no history of cigarette smoking, alcohol abuse, or illicit drug use.

### Physical Examination

On admission to the hospital, the patient was afebrile,

with a pulse of 66 bpm, blood pressure of 112/64 mm Hg, and respiratory rate of 18 breaths/min. She was awake and alert. Her general physical examination was normal, and no abnormal heart sounds, carotid bruits, or supraclavicular bruits were auscultated. A neurologic examination revealed slight weakness in the right lower part of the face and 4+/5 strength in the right arm and leg. Reflexes were 2+ in all limbs. The patient had no language impairment, visual deficits, or abnormalities of sensation or coordination.

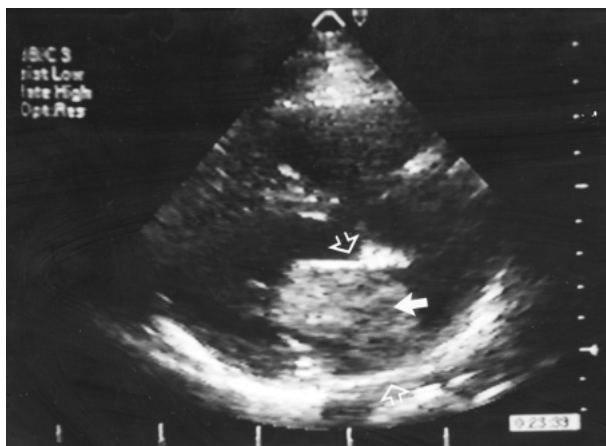
### Diagnostic Evaluation

Results of initial diagnostic testing, including serum electrolyte levels, coagulation studies, complete blood count, and chest radiograph, were within normal limits, except for a slight normocytic, normochromic anemia. An electrocardiogram showed normal sinus rhythm, and a CT scan of the brain, which was conducted within 24 hours of symptom onset, appeared normal. Homocysteine level was normal, as was a hypercoagulation profile consisting of protein S activity, protein C activity, antithrombin III level, and anticardiolipin antibodies.

Magnetic resonance imaging (MRI) of the brain showed an acute infarct in the left basal ganglia and an old left pontine infarct. A cerebral angiogram revealed no abnormalities in the extracranial or intracranial portions of the cerebrovasculature, except for mild fibromuscular dysplasia (FMD) involving the distal extracranial segment of the left internal carotid.

---

*Dr. Novendstern is a Senior Resident, Department of Internal Medicine, University of Florida Health Sciences Center, Jacksonville, FL. Dr. Silliman is an Assistant Professor of Neurology, Department of Neurology, and Director of the Comprehensive Stroke Program, University of Florida Health Sciences Center, Jacksonville, FL. Dr. Booth is an Associate Professor of Radiology, Department of Radiology, and Director of Neuroradiology, University of Florida Health Sciences Center, Jacksonville, FL.*



**Figure 1.** Transesophageal echocardiogram view of the case patient demonstrating an atrial myxoma (solid arrow). The tumor protrudes through the cusps of the mitral valve (open arrows).

A transesophageal echocardiogram revealed a 15-cm<sup>2</sup> mass in the left atrium. This mass was attached to the interatrial septum and measured 5 cm × 2.5 cm × 0.9 cm (Figure 1). Mild mitral regurgitation occurred from the tumor protruding into the mitral valve during systole. A stalk attached the mass to the posterior commissure.

### Treatment and Outcome

The cardiac mass was removed via sternotomy. An incidental atrial septal defect was identified and repaired. Pathologic examination of the mass was consistent with a myxoma. The patient was transferred to a rehabilitation facility. One month after transfer from the hospital, her right arm and leg strength was 5-/5, and she was walking with the help of a cane.

## DISCUSSION

### Etiology of Stroke in Young Adults

Causes of ischemic stroke in young adults differ from those in older adults. In older adults, most ischemic strokes are caused by cerebrovascular atherosclerosis or cardiogenic emboli related to atrial fibrillation, cardiomyopathy, or valvular disease. In young adults, most ischemic strokes are caused by hypercoagulability, migrainous infarction, nonatherosclerotic arteriopathies, illicit drugs, and emboli originating from structural cardiac abnormalities.<sup>1</sup> Such cardiac abnormalities include patent foramen ovale, atrial septal defect, aortic or mitral valve disease, bacterial endocarditis, and atrial myxoma.

The case patient had several structural anomalies that have been associated with ischemic stroke—FMD,

an atrial septal defect, and an atrial myxoma. Mild FMD was present only in the left internal carotid artery. FMD was not observed in the arteries supplying blood flow to the pons, the site of the patient's first brain infarction. Thus, it is unlikely that FMD contributed to her strokes. Although paradoxical emboli through her atrial septal defect cannot be excluded as the cause of her strokes, the patient did not have any risk factors for venous thrombosis, such as an identified hypercoagulable state, recent surgery, immobilization, or estrogen use. For these reasons, we believe that emboli originating from the left atrial myxoma caused her 2 strokes.

### Epidemiology of Atrial Myxoma

Primary tumors of the heart are rare, with an incidence between 0.0017% and 0.19% in unselected patients at autopsy.<sup>3</sup> Myxomas are the most common primary tumor of the heart, constituting 50% of all cardiac tumors.<sup>3</sup> Of these tumors, 90% occur in the atria, with a left-to-right ratio of 4:1.<sup>4</sup> Myxomas occur in all age groups, but they are particularly frequent between the third and sixth decades of life, with women predominating in most series.<sup>3</sup> Myxomas usually occur sporadically, but in rare cases, they may be inherited in an autosomal dominant fashion.

### Clinical Manifestations of Atrial Myxoma

Three types of symptoms may characterize patients harboring a cardiac myxoma: (1) symptoms due to obstruction of cardiac outflow; (2) constitutional symptoms; or (3) symptoms due to embolism. Obstructive symptoms, such as dyspnea and syncope, reportedly occur in approximately one half of patients with atrial myxoma.<sup>3</sup> Larger tumors and those with pedicles, which make the tumors mobile, increase the likelihood that obstructive symptoms will be present. The obstructive symptoms are caused by the blockage of blood flow across the valves of the heart, especially the mitral valve, since the left atrium is the most common location of a myxoma.

Constitutional symptoms are present in many patients with atrial myxoma.<sup>4</sup> These are nonspecific and include myalgia, fatigue, fever, and weight loss. The etiology of these symptoms is unknown, but it has been proposed that they may be caused by dislodgment of fragments of the friable myxoma into the systemic circulation<sup>5</sup> or by release of interleukin 6 by the tumor.<sup>6</sup>

Myxomas can fracture and release emboli. The emboli are composed of tumor cells, fibrin clot, or both.<sup>7</sup> Because most myxomas are located in the left atrium, embolism into the systemic arterial circulation

is not infrequent, occurring in 20% to 45% of patients with myxoma.<sup>4,8</sup>

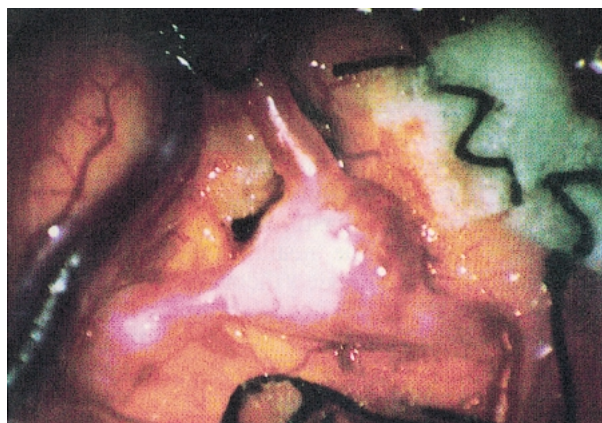
Neurologic events are common in patients with myxoma, occurring in approximately one third of these patients.<sup>3</sup> Most of these events are cerebrovascular in etiology. Myxomas are associated with ischemic and hemorrhagic cerebrovascular events, which are sequelae of tumor embolism into the brain.

Ischemic stroke is the most frequent embolic manifestation of atrial myxoma.<sup>3</sup> Within the brain, the middle cerebral artery and its branches are the most common sites of embolic occlusion. In patients with brain emboli, cerebral angiography often demonstrates emboli in multiple vessels.<sup>9</sup> Acute treatment of ischemic stroke caused by these emboli is supportive, focusing on prevention of medical and neurologic complications that can occur in any patient with ischemic stroke. Detection of the myxoma, followed by its resection, is the only currently recognized modality for preventing further ischemic strokes.

Thrombolytic agents, such as tissue plasminogen activator, have not been systematically studied as a treatment for brain emboli. Thrombolytics would presumptively be beneficial as an acute therapy if the emboli are fibrin rich, but not if the emboli are comprised of myxomatous remnants. A single case report describes a patient with a middle cerebral artery occlusion who was treated with urokinase that was administered intra-arterially prior to the detection of her atrial myxoma.<sup>7</sup> The artery partially recanalized, but the patient's clinical condition did not improve.<sup>7</sup>

Intracranial arterial aneurysms can occur after myxomatous fragments embolize. These aneurysms are thought to arise following tumor cell invasion of the vascular endothelium and media. Invasion of the vascular wall by these cells weakens the media and ultimately may lead to aneurysmal dilatation.<sup>4</sup> Myxomatous proliferation has been found in the walls of the aneurysms at autopsy in some patients.<sup>10</sup> The aneurysms are often fusiform in shape, but they may be saccular (**Figure 2**). The location of these arterial aneurysms is usually distal to the circle of Willis, a rare site for congenital or atherosclerotic aneurysms. Often, multiple aneurysms are present.<sup>9</sup> Rupture of these aneurysms produces subarachnoid or intracerebral hemorrhage.

The true incidence of myxomatous aneurysms is unknown because long-term studies evaluating the likelihood of aneurysm formation have not been conducted. The length of time for development of these aneurysms is not well known. Case studies suggest that the formation of myxomatous aneurysms can occur as long as several years after the initial cerebral embolic



**Figure 2.** Intraoperative photograph showing a fusiform aneurysm at a vessel bifurcation. This aneurysm was located peripherally in the middle cerebral artery circulation. Reprinted with permission from Furuya K, Sasaki T, Yoshimoto Y, et al. Histologically verified cerebral aneurysm formation secondary to embolism from cardiac myxoma. Case report. *J Neurosurg* 1995;83:170-3.

event.<sup>10</sup> The aneurysms may remain asymptomatic for years. Detection of an aneurysm has been reported as long as 19 years after resection of the primary cardiac tumor.<sup>11</sup> The natural history of myxomatous aneurysms is variable. Over time they can remain stable in size, enlarge, or regress completely.<sup>12</sup>

No therapy has proven to be effective in treating these intracranial aneurysms. Although fusiform aneurysms cannot be clipped because they lack a stem, successful surgical excision of these aneurysms has been reported.<sup>12</sup> The risks and benefits of this procedure, however, have not been delineated in clinical trials. Chemotherapy of an enlarging aneurysm has been attempted in a single patient without success.<sup>13</sup>

In rare instances, tumor emboli can lead to the formation of intracerebral masses. It has been postulated that these metastatic masses arise from tumor cells that transgress through the arterial wall and invade neighboring brain tissue.<sup>9</sup> Single and multiple brain metastases have been reported.<sup>2</sup> Mass effect associated with these tumors produces symptoms such as headache, limb weakness, and sensory loss; however, the masses can be excised.<sup>6</sup>

#### **Diagnosis and Management of Atrial Myxoma**

Imaging techniques that can detect cardiac myxoma include dye ventriculography, cardiac CT scan, and echocardiography. Echocardiography is widely available and often utilized as a diagnostic test in patients with

ischemic stroke. Transesophageal echocardiography detects myxomas more reliably than transthoracic echocardiography.<sup>14,15</sup>

Removal of atrial myxoma carries an operative mortality rate of 5% or less.<sup>16</sup> Atrial myxomas can recur following surgical resection. The overall risk of recurrence is approximately 12% for familial tumors and only 1% to 3% for sporadic tumors.<sup>3</sup> Incomplete resection, intraoperative displacement of tumor material, embolization, transformation from a benign to a malignant lesion, and multifocal genesis have been proposed as possible explanations for recurrence of atrial myxoma.<sup>3</sup> Recurrence usually occurs within 1 to 2 years following removal, but reappearance can occur several years later.<sup>4,16</sup> Periodic echocardiography is recommended following initial tumor removal to monitor for recurrences. Because there are no prospective natural history studies on atrial myxomas, accepted guidelines regarding timing and duration of echocardiographic surveillance do not exist.

## CONCLUSION

Atrial myxoma should be included in the differential diagnosis of any young adult with an acute ischemic stroke. Detection of the tumor by echocardiography, followed by surgical excision, significantly reduces the risk of subsequent ischemic strokes.

Aneurysmal subarachnoid hemorrhage is a potential complication of brain emboli originating from an atrial myxoma. There are no evidence-based guidelines that delineate when cerebral angiography or aneurysm resection should be conducted in patients with cerebrovascular manifestations of atrial myxoma. We recommend that catheter angiography be considered in any patient who presents with an atrial myxoma-associated stroke. If an aneurysm is discovered by angiography, neurosurgical consultation can be obtained to assess the feasibility of aneurysm resection. The decision to operate must be individualized in each patient. **HP**

## REFERENCES

1. Warlow CP, Dennis MS, van Gijn J, et al. The organization of stroke services. In: Warlow CP, Dennis MS, editors. *Stroke: a practical guide to management*. Oxford: Blackwell Science; 1996:598–631.
2. Knepper LE, Biller J, Adams HP Jr, Bruno A. Neurologic manifestations of atrial myxoma. A 12-year experience and review. *Stroke* 1988;19:1435–40.
3. Reynen K. Cardiac myxomas. *N Engl J Med* 1995;333:1610–7.
4. Markel ML, Waller BF, Armstrong WF. Cardiac myxoma. A review. *Medicine (Baltimore)* 1987;66:114–25.
5. Browne WT, Wijdicks EF, Parisi JE, Viggiano RW. Fulminant brain necrosis from atrial myxoma showers. *Stroke* 1993;24:1090–2.
6. Wada A, Kanda T, Hayashi R, et al. Cardiac myxoma metastasized to the brain: potential role of endogenous interleukin-6. *Cardiology* 1993;83:208–11.
7. Bekavac I, Hanna JP, Wallace RC, et al. Intra-arterial thrombolysis of embolic proximal middle cerebral artery occlusion from presumed atrial myxoma. *Neurology* 1997;49:618–20.
8. St John Sutton MG, Mercier LA, Giuliani ER, Lie JT. Atrial myxomas: a review of clinical experience in 40 patients. *Mayo Clin Proc* 1980;55:371–6.
9. Desousa AL, Muller J, Campbell R, et al. Atrial myxoma: a review of the neurological complications, metastases, and recurrences. *J Neurol Neurosurg Psychiatry* 1978;41:1119–24.
10. Furuya K, Sasaki T, Yoshimoto Y, et al. Histologically verified cerebral aneurysm formation secondary to embolism from cardiac myxoma. Case report. *J Neurosurg* 1995;83:170–3.
11. Friedman DP, Rapoport RJ. Giant fusiform oncotic aneurysm: MR and angiographic findings [letter]. *AJR Am J Roentgenol* 1996;167:538–9.
12. Branch CL Jr, Laster DW, Kelly DL Jr. Left atrial myxoma with cerebral emboli. *Neurosurgery* 1985;16:675–80.
13. Roeltgen DP, Weimer GR, Patterson LF. Delayed neurologic complications of left atrial myxoma. *Neurology* 1981;31:8–13.
14. Salmon K, Decoodt P, Capon A. Detection of a left atrial myxoma by systematic transesophageal echocardiography in stroke. *Am Heart J* 1991;122:580–3.
15. Obeid AI, Marvasti M, Parker F, Rosenberg J. Comparison of transthoracic and transesophageal echocardiography in diagnosis of left atrial myxoma. *Am J Cardiol* 1989;63:1006–8.
16. Hall RA, Anderson RP. Cardiac neoplasms. In: Edmunds LH, editor. *Cardiac surgery in the adult*. New York: McGraw-Hill; 1997:1345–62.

Copyright 2001 by Turner White Communications Inc., Wayne, PA. All rights reserved.