Neurologic Manifestations of Atrial Myxoma
A 12-Year Experience and Review
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We present the results of a 12-year retrospective analysis of 11 patients, eight women and three men, aged 16–76 years, with pathologically documented atrial myxomas. Nine of the 11 patients were found to have a left atrial myxoma; right atrial myxomas were identified in two. Five of the 11 patients (45%) had abnormalities on neurologic examination, and five of five had computed tomographic evidence of nonhemorrhagic cerebral infarction. Neurologic symptoms were the initial presentation in four patients. Six patients reported a history of cardiac disease; eight of the 11 had abnormalities on cardiac auscultation. Echocardiography in 10 patients was diagnostic in all but one. Gated magnetic resonance imaging of the heart in two patients demonstrated myxoma position and movement. Follow-up examinations (varying from 1 month to 7 years after tumor resection) in nine of 11 patients demonstrated no recurrent neurologic symptoms. Cerebral infarction is a common complication of atrial myxomas and may be the presenting feature. Recurrent cerebral emboli before surgery is not uncommon. Cardiac auscultation may be normal, and electrocardiographic changes are often nonspecific. Delayed neurologic events following surgery are rare. (Stroke 1988;19:1435–1440)

Atrial myxoma can cause embolic cerebral infarction or intracranial hemorrhage, which may be its initial manifestation. Recurrent cerebral ischemic events can occur if the tumor is not detected and surgically removed. Cardiac signs and symptoms are frequently nonspecific. Atrial myxoma may masquerade as mitral stenosis, mitral insufficiency, collagen-vascular disease, infective endocarditis, constrictive pericarditis, and other less common entities. These patients remain a diagnostic challenge and are often initially misdiagnosed.

Subjects and Methods
We reviewed the clinical records and radiologic studies of 11 patients with atrial myxomas who were seen at the University of Iowa Hospitals between 1975 and 1987. The University of Iowa Hospitals and Clinics serve as the state of Iowa’s comprehensive tertiary health care center and serve primarily the state of Iowa and the northwestern part of Illinois. In the last 10 of the 12 years covered in this study, 2,109 acute stroke patients were seen. We project that of about 2,500 acute stroke patients assessed during the 12 years, 15 patients presented with cardiac tumors. Only 11 tumors were pathologically proven to be myxomas; one patient had a rhabdomyoma, and three patients refused surgery. All 11 patients had medical and neurologic examinations. Chest roentgenography, twelve-lead electrocardiography (ECG), complete blood count with differential, and standard biochemical and urine tests were performed in all 11 patients; nine patients had Westergren erythrocyte sedimentation rates (ESRs). Echocardiography was performed in 10 of the 11 patients; one patient had evidence of an atrial mass on cardiac catheterization. Gated magnetic resonance imaging (MRI) of the heart was performed in two of the 11 patients. Five of the 11 patients had cranial computed tomography (CT), and two had cranial MRI. Two of the 11 patients underwent cerebral angiography; one had sequential angiography studies following two separate neurologic events.

Results
Eight women and three men, ranging from 16 to 76 (mean 58.4) years of age were seen. Nine patients had left atrial myxomas, and right atrial myxomas were found in two; one with a patent foramen ovale had bialtral myxomatous proliferation. Two patients were found to have two separate myxomas at surgery. The most frequent presenting complaints were dyspnea (45%), neurologic symptoms (36%), and...
TABLE 1. Neurologic Manifestations of Atrial Myxoma

<table>
<thead>
<tr>
<th>Pt/sex/age</th>
<th>Location</th>
<th>Symptoms</th>
<th>Signs</th>
<th>Computed tomography</th>
<th>Cranial MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/57</td>
<td>L atrium</td>
<td>Diplopia, ataxia, sleep apnea</td>
<td>Memory impairment; slow vertical saccades</td>
<td>R thalamic infarct</td>
<td>Bilateral medial thalamic infarcts</td>
</tr>
<tr>
<td>2/F/31</td>
<td>R atrium (PFO)</td>
<td>Recurrent L hemiparesis, headaches</td>
<td>L homonymous hemianopia, hemiparesis; bilateral extensor plantar responses</td>
<td>R MCA and R ACA infarcts; subarachnoid hemorrhage</td>
<td>ND</td>
</tr>
<tr>
<td>3/F/76</td>
<td>L atrium</td>
<td>Dizziness</td>
<td>R central facial paresis</td>
<td>L subcortical infarct</td>
<td>ND</td>
</tr>
<tr>
<td>4/F/57</td>
<td>L atrium</td>
<td>R hemiparesis, aphasia</td>
<td>Aphasia; R hemiparesis</td>
<td>L MCA infarct</td>
<td>ND</td>
</tr>
<tr>
<td>5/M/75</td>
<td>L atrium</td>
<td>Monocular blurred vision</td>
<td>Anosognosia, prosopagnosia; total loss of vision except R superior temporal quadrant; L optic disk pallor</td>
<td>Old L frontal, parietal, occipital infarcts; new R posterior temporal, occipital infarcts</td>
<td>Old L frontal, parietal, occipital infarcts; new R temporal, occipital infarcts</td>
</tr>
</tbody>
</table>

Palpitations (36%). Two patients had recurrent neurologic events before diagnosis and surgical resection of the myxoma despite anticoagulation with warfarin; nine patients reported constitutional symptoms including fatigue, malaise, dizziness, anorexia, and weight loss. The average time from the onset of neurologic manifestations in two to diagnosis was 7 years; the average time from the onset of symptoms in nine to diagnosis was 3.2 years. Cardiac auscultation was abnormal in eight of the 11 patients: seven had systolic murmurs, four had a diastolic rumble, and three had an extra heart sound. Neurologic abnormalities were found on examination in 45% of the 11 patients. Westergren ESR was elevated in eight of nine patients, with a mean of 65 mm/hr. Echocardiography was diagnostic in nine of 10 cases; it failed to demonstrate a right atrial mass in one patient. Gated MRI of the heart performed in two patients gave clear images of the myxoma, delineating its size, position, attachment, and motion.

Cerebral infarctions were found on CT scan in all five patients examined (Table 1); three had multiple cerebral infarctions. Cerebral emboli most commonly involved the middle cerebral artery and its branches. The carotid circulation was involved in four patients and the posterior circulation in three. Sequential cerebral angiography in one of the two patients so examined demonstrated a right middle cerebral artery thrombus in the first examination and a right pericallosal artery thrombus in the second; no aneurysms were visualized in either study.

Tumor resection was complete in 10 of the 11 patients; there were no surgical complications. One patient died of a dissecting aortic aneurysm 2 years after resection of the atrial myxoma. A second death resulted from intractable congestive heart failure 2 years after the incomplete resection of a large, highly vascular, left atrial myxoma. Eight patients were followed for up to 8 (mean 3.8) years without report of a subsequent neurologic event.

Two patients who initially presented to our service illustrate some of the neurologic complications of atrial myxomas.

Case 1
A 57-year-old man with a history of sleep apnea presented with diplopia and ataxia. Two weeks before admission, he had a 1-hour episode of binocular vertical diplopia. That same night, his wife noted loud snoring and periods of apnea and was unable to awaken him. He was taken to the local hospital and awoke after endotracheal intubation with amnesia for the events of the preceding day. During the next several days he continued to be lethargic, with intermittent apnea during sleep. He also noted objects "sliding to the right" of his visual field, and he had occasional difficulty finding the correct words. An overnight sleep study revealed evidence of obstructive and central sleep apnea. His medical history was notable for an overnight admission for chest pain 4 months previously. A myocardial infarction was excluded at that time and results of an exercise stress test were normal.

Results of cardiac auscultation were normal. Neurologic examination revealed slow vertical saccadic eye movement. ESR was 50 mm/hr. ECG revealed nonspecific T wave changes. A hypodense area was seen in the right thalamus on CT scan. MRI of the brain demonstrated bilateral mesial thalamic infarctions (Figure 1). Echocardiography showed left atrial enlargement and a left atrial mass. Gated MRI of the heart revealed a 3-cm soft tissue mass attached to the left atrial septum with no evidence of prolapase (Figure 2). Pathology of the resected atrial mass was consistent with myxoma. He has had no further neurologic events in the last 10 months.

Case 5
A 75-year-old man developed a right homonymous hemianopia in 1974 and was placed on warfarin. He did relatively well until March 1987, when he noticed decreased vision in his left eye. There
was a loud S1 and a grade II/VI holosystolic murmur heard at the apex and radiating to the axilla. He had jugular venous distention and bibasilar pulmonary rales. Neurologic examination revealed confabulation, denial of visual loss, and prosopagnosia. He was blind in his left eye and had a pale left optic disk. Vision in his right eye consisted of sparing only of the right superior temporal quadrant to finger counting and confrontation. Chest roentgenogram revealed cardiomegaly and prominent pulmonary vasculature. ECG showed evidence of a previous inferior wall infarction and left ventricular hypertrophy with strain. ESR was 21 mm/hr. Cranial CT revealed old left frontal and occipital infarctions and a new right posterior temporal occipital infarction. MRI of the brain confirmed these findings (Figure 3). There was a long pedunculated left atrial mass on two-dimensional echocardiography. MRI of the heart revealed that this large mass was attached to the posterior wall of the left atrium (Figure 4).

This patient underwent resection of a 3×1.5×1 cm mass on a slender stalk, with pathology documenting myxomatous tissue. He has had no recurrences in the last 4 months.

Discussion

In 1952, Goldberg et al reported the first ante-mortem diagnosis of atrial myxoma in a 3-year-old boy who presented with a recurrent right hemiparesis. In the last 35 years, several series of atrial myxomas have been reported. The age, sex distribution, and location of myxomas in our series are in accordance with previously reported studies.

Classic presenting manifestations include constitutional, obstructive, and embolic symptoms. Constitutional symptoms, reported previously in 30–89% of cases, occurred in 82% of our patients. Obstructive symptoms were reported in 45% of our patients and have previously been reported in 30–70% of cases. Embolization to the spleen, adrenals, intestine, kidneys, abdominal aorta, coronary arteries, and mesentry and limb arteries have been reported in 10–45% of cases. Excluding cerebral embolization, there were no episodes of clinically apparent peripheral embolization in our patients.

Neurologic manifestations of atrial myxomas are frequent and have been reported in 25–45% of cases. The neurologic signs and symptoms are usually a result of embolization. Emboli are most often myxomatous but may also arise from thrombus adherent to the tumor. Embolization from a left atrial myxoma has been reported to cause cerebral infarction in 27% of cases. Cerebral embolic events often occur before the onset of
constitutional or obstructive symptoms and did so in four of our patients with neurologic symptoms. Recurrent cerebral infarction before myxoma resection is common.13-17 Two of our patients had recurrent cerebral embolization before diagnosis despite anticoagulation. Retinal myxomatous emboli have been described and are usually associated with emboli to the ipsilateral middle cerebral artery.8,9,18,19 Multi-infarct dementia has been reported as a result of recurrent cerebral embolization.20 Spinal cord embolus, resulting in paraplegia, has also been reported.21

Emboli from atrial myxomas can cause multiple cerebral aneurysms that may be found before or after resection of the cardiac lesion.22,23 Aneurysms are usually fusiform but may have a saccular component. They are often multiple and occur on peripheral branches of the intracranial arteries.24,25 Myxomatous proliferation has been found at autopsy in the walls of the aneurysms. The pathologic mechanism leading to aneurysm formation has been debated. Most authors believe that myxomatous emboli result in weakening and dilatation of the arterial wall. These aneurysms may resolve after resection of the primary tumor.22 Although one of our patients presented with a subarachnoid hemorrhage, neither of those studied angiographically had evidence of intracranial aneurysms.

Rarely, atrial myxoma can cause neurologic symptoms as a result of a mass effect from myxomatous proliferation. A large left temporal myxoid mass arising from the choroid plexus was reported by Rankin and DeSousa26 and DeSousa et al.27 Multiple enhancing lesions, noted on CT scan in a patient with intellectual decline, were found at surgery to be myxomatous tissue in a case reported by Frank et al.28 These presentations are apparently quite rare. We found no evidence of intracranial mass lesions on CT in our patients.

Early studies reported delayed neurologic complications following atrial myxoma resection including aneurysms and intracranial mass lesions,26,27,29,30 but more recent series have found delayed neurologic complications to be infrequent.31,32 There have been no subsequent neurologic events in our patients following resection of the myxoma.

Echocardiography remains the most frequently used imaging method to detect atrial myxomas. Two-dimensional echocardiography with a four-chamber view is believed to be optimal.33 Atrial
myxomas have also been imaged using gated, ultra-fast cardiac CT scan,34,35 MRI of the heart, as in two of our patients, may be preferred to visualize atrial myxomas in patients with chronic obstructive pulmonary disease or obesity, which can make echocardiographic evaluation less reliable.36

In summary, cerebral emboli remain frequent presentations and complications of atrial myxomas. Atrial myxomas are relatively rare but should be considered in the differential diagnosis of cerebral infarction, particularly when multiple cerebral infarctions have occurred and constitutional symptoms are reported. Cerebral infarction may occur before the onset of constitutional or obstructive symptoms. Once detected, removal of an atrial myxoma should be considered urgent due to the great embolic potential of this condition. Improved imaging techniques such as gated cardiac MRI continue to facilitate the diagnosis of this potentially curable cause of stroke.

References
1. Goldberg HP, Glenn F, Dotter CT, Steinberg I: Myxoma of the left atrium: Diagnosis made during life with operative and post-mortem findings. Circulation 1952;6:762–767

KEY WORDS • cerebral infarction • echocardiography • magnetic resonance imaging • myxoma