

Young Stroke, Cardiac Myxoma, and Multiple Emboli: A Case Report and Literature Review

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Abstract- Cardiac myxoma is a source of emboli to the vascular tree, especially to the central nervous system. Although it is rare, its early recognition is particularly important because of its unique clinical features of subsequently leading to intracerebral or subarachnoid hemorrhage, even brain metastases, and its potential for surgical cure. Missing the diagnosis may lead to devastating results, including stroke, even sudden death. A 40-year-old male with no other conventional vascular risk factors such as hypertension, diabetes or hyperlipidemia presented with right hemiplegia, global aphasia, vomiting, and fever. Infarction over the left middle cerebral artery was disclosed on magnetic resonance imaging study, and echocardiogram showed a huge mass, about 5cm in size, on the mitral valve which was histopathologically proved to be a cardiac myxoma. He also presented with multiple emboli to the kidneys and the left eye. There is uncertainty about the role of anticoagulation. The treatment of choice remains surgical excision of the cardiac myxoma which may lead to normalization of serum interleukin-6 levels and resolution of constitutional symptoms, and the intracranial aneurysms may regress and resolve.

Key Words: Cardiac myxoma, Stroke, Cardiac emboli

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INTRODUCTION

Stroke of uncertain origin in a patient always poses a challenge to and a burden on every neurologic practitioner to uncover the underlying cause by means of a thorough and concise workup. Cardiac myxoma is an uncommon cause of stroke. However, it is the most common benign cardiac tumor, found more frequently in young adults with stroke or transient ischemic attack (1 in 250) than in older patients (1 in 750)⁽¹⁾. Clinical

suspicion and prudent interventions are required for early diagnosis, which is the key to reducing the morbidity and mortality. However, non-specific systemic symptoms and minor embolic phenomena may be overlooked in the absence of any history of cardiac problems. In this situation, cardiac evaluation may not be performed or ignored, and the diagnosis of this rare condition may be delayed until the onset of a more significant embolic disease, such as stroke, with functional impairment. We present a patient with atrial myxoma

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and acute cerebral infarction over the left middle cerebral arterial territory who underwent immediate surgical intervention with fair functional recovery.

CASE REPORT

A 40-year-old married male without any systemic illness before, including hypertension, diabetes mellitus, hyperlipidemia and smoking, cardiopulmonary distress or syncope, had an episode of minor stroke with one-week admission to a medical center about 6-7 years ago. No traceable risk factors were noted at that time. There was no regular medications taken and no follow-up after discharge. He developed rapid onset of right-sided weakness and aphasia, and fell to the ground on the day of admission. Several episodes of vomiting, high-grade fever of above 39 °C along with profused sweating were noted later. He was transferred to our hospital and neurological examination showed an awake but lethargic patient with Glasgow Coma Scale (GCS) of 10 (E3V1M6). Right hemianopia, global aphasia, right hemiplegia with muscle power grading at 2/5, and right Babinski sign were present. NIH Stroke Scale (NIHSS) score was 26 and Barthel index (BI) was 0 on admission. Physical examination showed low-grade fever with body temperature of 37.8 °C, coffee-ground substance from the nasogastric tube, a deep-colored urine, smooth respiration, clear breathing sounds, regular heart beats and no murmurs. Laboratory data revealed peripheral leukocytosis (13,300/mm³) but no anemia (Hemoglobin 14.6 gm/dL), elevated C-reactive protein (CRP) (5.7 mg/dl, normal <0.8), and microhematuria. Chest X-ray showed no evidence of active lung lesions, electrocardiogram was normal, and sonogram of abdomen did not reveal any lesions involving the genitourinary tracts, including the kidneys. Carotid duplex and transcranial duplex study disclosed stenotic flow at bilateral anterior and middle cerebral arteries, and vertebrobasilar arteries. Noncontrasted brain computed tomography (CT) showed multiple hypodense lesions over the left frontal and temporoparietal lobes, the anterior limb of left internal capsule and the caudate nucleus. Magnetic resonance imaging (MRI) of the brain disclosed hypointensities on

T1-weighted images, hyperdensities on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images involving the left basal ganglion and the cortical ribbons of the left frontoparietal, temporal, and occipital regions. However, the magnetic resonance angiography (MRA) was unremarkable (Fig. 1). Transthoracic echocardiogram was performed the next day after admission which revealed a huge vegetation (> 5cm) on the mitral valve (Fig. 2) but with normal heart size and systolic function. An initial impression of infective endocarditis was made and crystal penicillin was administered after blood cultures were taken. Emergent consultation with cardiovascular surgeon was performed and the patient underwent surgical intervention the next morning. Serial blood, urine, and sputum cultures dis-

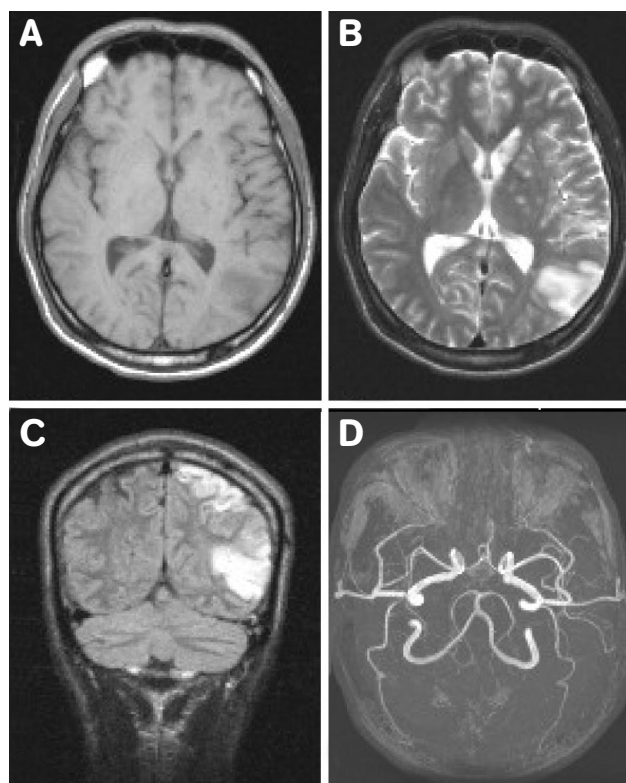


Figure 1. MRI of the brain disclosed hypointensities on T1-weighted images (panel A), hyperdensities on T2-weighted (panel B) and FLAIR images (panel C) involving the left basal ganglion, cortical ribbons of the left frontoparietal, temporal, and occipital regions; but magnetic resonance angiography (MRA) (panel D) was unremarkable.

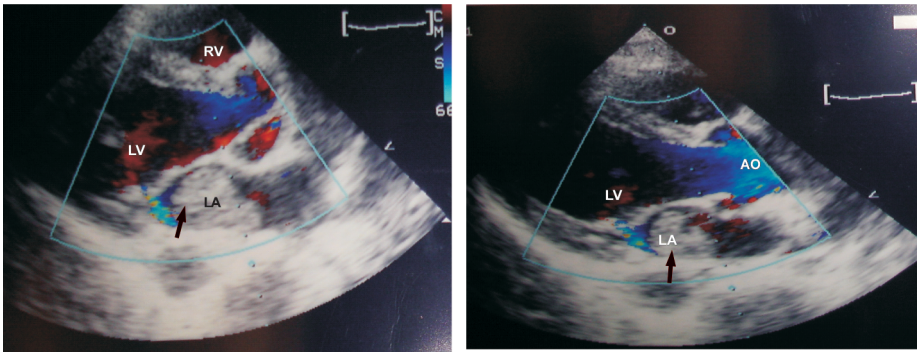


Figure 2. Transthoracic echocardiogram revealed a huge mass on mitral valve in left atrium (>5cm) (left: presystolic phase. right: systolic phase: LA: left atrium. LV: left ventricle. RV: right ventricle. AO: aorta)

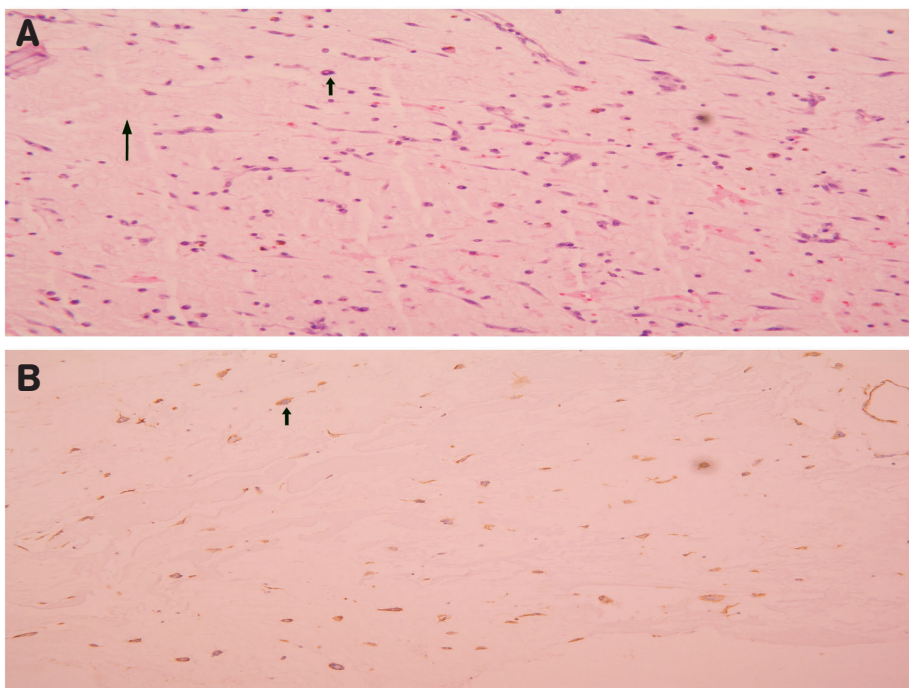


Figure 3. Microscopic (100× light microscopy, H&E stain) pictures of myxoma, composed of round, stellate cells (panel a.: short arrow) in a “mucoid” setting (panel a.: long arrow); and immunohistochemistry stain (CD34+++), (panel b.: short arrow).

closed no growth of bacteria and follow-up chest X-ray did not indicate any underlying source of infection. All of these findings indicated that the fever resulted from the mass itself rather than from a possible underlying infection. A large cardiac tumor over the left atrium, about 7×5cm in size, was noted during the operation. The gross histopathological examination showed a piece of grey-white, soft, polypoidal, lobulated mass, with a size of 4.0×3.0×1.5cm, and a weight of 9.0gm. Microscopically, it shows a picture of myxoma, and is composed of round, stellate cells in a “mucoid” setting with secondary changes of fibrosis, and focal hemor-

rhage with hemosiderin. The myxoma cells had a round or stellate shape, an ovoid nucleus, and a pink eosinophilic cytoplasm; they were scattered throughout the matrix. Immunohistochemistry study disclosed a strong positive result for CD34 (Fig. 3). The patient recovered very well. His sensory aphasia and muscle powers were the first to improve about 3 days after the operation. The NIHSS score was 15 and the BI was 10. About 3 weeks after the operation, the patient was able to express his blurred vision more precisely. An ophthalmological consultation was requested although hemianopia had been noted on initial clinical evaluation. Visual acuity of 1.0

at right eye, and only hand's movement at left eye, normal intra-ocular pressure, clear bilateral corneas, pale fundus with cherry red spot and macular edema at the left eye were noted. Central retinal artery occlusion was confirmed by the ophthalmologist via both the fundoscopic examination and color fundus examination. The VEP study was arranged later and disclosed a totally unresponsive left eye via both the pattern-field and the flashing-light stimulation. These findings outweighed our initial recognition that the visual defect was only due to the hemianopia which resulted from the hemispheric lesion. In the mean time, the NIHSS score improved to 11, and BI was 50. At 3-month follow-up, the patient lived a normal life independently. He could walk steadily without aids, could speak coherently and fluently with complete remission of global aphasia, had intact cognitive function, and mild numbness over the right hand; but his left eye regressed to total blindness without any light perception.

DISCUSSION

We present a patient with manifestations of multiple embolic phenomena, involving the brain (stroke), the kidney (microhematuria), and the left eye (central retinal artery occlusion). Early recognition of eye involvement may be delayed when it co-exists with cerebral hemispheric lesion, especially of the left side, along with aphasia.

Our patient presented with an initial manifestation of fever which originated from the tumor itself rather than an underlying infection, a subtle renal involvement, and an eye involvement beyond our expectation with a chance of fair functional recovery after appropriate management if it was recognized early.

Until 1953, when the first atrial myxoma was surgically resected, atrial myxoma was a diagnosis made exclusively at autopsy⁽²⁾. The mean age of all cases was 43 (range 6-82), and there was a female to male predominance of 3:2⁽³⁾. The annual incidence is 0.5 per million population, with 75% of cases occurring in the left atrium⁽⁴⁾. Although atrial myxoma is mostly sporadic, at least 7% of cases are familial (Carney complex)⁽⁵⁾. It is

transmitted in an autosomal dominant manner, through a causative mutation of the PRKAR 1 alpha gene located on the long arm of chromosome 17 (17q22-24 region)⁽⁶⁾. Delay in the diagnosis from the onset may range from 1 to 126 months⁽⁷⁾. There were overlapping neurological presentations. The most common presentation was ischemic stroke (83%), most often in multiple sites (41%)⁽³⁾. That means once the cardiac myxoma is diagnosed, a subsequent search for possible embolic targets should be done. In a series of 112 consecutive cases over a 40-year period, as reported by Pinede et al.⁽⁴⁾, signs of embolism were present in 33 patients (29%). The embolic locations were the central nervous system (73%), the retinal artery (3%), the upper and lower extremities (45%), and the coronary arteries (12%).

Patients with cardiac myxoma have various features of the classical triad of constitutional (30%), cardiac (60%), and embolic symptoms (30-40%)⁽⁸⁾. Constitutional symptoms include raised inflammatory markers with fever, weight loss, or symptoms resembling connective tissue disease due to cytokine (interleukin-6) secretion by the myxoma itself⁽⁵⁾, infection, or malignancy⁽²⁾. Cardiac symptoms include exertional dyspnea, orthopnea, acute pulmonary edema, syncope, sudden death, and right heart failure. Left sided tumors are more likely to embolize⁽⁵⁾.

Interestingly, physical exercise can dislodge an embolus from a myxoma of the left atrium, and based on reported studies, 12% of cases had intracerebral hemorrhage (ICH), and 5% had subarachnoid hemorrhage (SAH)⁽³⁾. Additionally, these aneurysms are often multiple and occur at the peripheral branches of the intracranial arteries, rather than at the base of the brain in the circle of Willis⁽⁹⁾. Aneurysmal formation was caused by the tumor fragment that infiltrates and weakens the vessel wall. Aneurysms are usually fusiform.

There are no clear guidelines for the immediate medical management. For cases with ischemic stroke and transient ischemic attack, the main issue is early secondary prevention while considering surgery⁽³⁾. Anticoagulants and antiplatelet agents are used with the presumption that some of the embolic component is a thrombus⁽¹⁰⁾, but may not be protective⁽¹¹⁾. Prior to com-

mencing therapy, hemorrhage needs to be excluded with CT or MRI, the latter preferably with MRA to help exclude large aneurysm formation associated with tumor embolization⁽³⁾.

The removal of the myxoma in a patient with recent stroke poses a difficult management problem. The concern has been that cardiopulmonary bypass and anticoagulation may exacerbate the neurological injury. Timing of surgery is still controversial, and needs to be clarified as more experience is accrued⁽³⁾. Resection of cardiac myxoma may lead to normalization of serum interleukin-6 levels and resolution of constitutional symptoms⁽¹²⁾, and the intracranial aneurysms may be regressed and resolved⁽¹³⁾.

The recurrence rate is low (5%), but long-term and serial echocardiography is advisable especially for young patients⁽⁴⁾.

CONCLUSION

The presence of embolic phenomena, especially in young patients with neurological symptoms, should prompt early neuroimaging and echocardiography, even in the absence of EKG or auscultation abnormalities. Here we emphasize the importance of MRA of the brain, VEP study and the early and routine consultation with ophthalmologist once the cardiac myxoma is proved. MRA of the brain is preferred for the exclusion of co-existing aneurysmal formation. Ophthalmological evaluation and VEP study can help in the early recognition of arterial occlusion of the ophthalmic or central retinal artery even when the patient does not complain of or is unaware of the visual problems.

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