

Unusual Multilocular Cardiac Myxomas Presenting with Syncope and Embolic Stroke: A Case Report

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The majority of cardiac tumors are metastatic neoplasms, but primary cardiac tumors are also an important cause of patient morbidity and mortality and occur in 3/1000 of all individuals. About half of primary cardiac tumors and 75% of benign primary cardiac tumors are myxomas. Lipomas, rhabdomyomas, and fibromas make up the majority of the remaining benign tumors. This work describes the clinical course of a symptomatic young female whose multilocular myxomas were not diagnosed initially, who then developed right hemiparesis resulting from cardiac embolization. Myxomas, if multilocular, are mostly biatrial in location. The patient had three myxomas in three chambers of the heart, including both atria and left ventricle, which were identified by transthoracic echocardiography. Multilocular myxomas most often occur in the familial setting, and are often recurrent. The patient's disease was nonfamilial. She received surgical resection successfully, and completely recovered without evidence of recurrence over an 18-month follow-up period.

Key Words: Cardiac myxoma • Syncope • Stroke

INTRODUCTION

Primary cardiac tumors of the heart are less common than secondary (metastatic) cardiac tumors. Some cardiac tumors are discovered incidentally when patients are being surveyed for other problems or during a physical examination. The majority of benign cardiac tumors are myxomas. Approximately, 75% of myxomas arise from the interatrial septum at the inferior border of the fossa ovalis of the left atrium, 15% of atrial myxomas arise from the right atrium, and the remaining cases (5 to 10%) arise from the left ventricle, or from multiple sites (5%). Left atrial myxomas are twice as

common in females compared to males. This work describes the clinical course of a symptomatic young female whose multilocular myxomas were not diagnosed initially, and who developed right hemiparesis resulted from cardiac embolization.

CASE REPORT

A 27-year-old female was sent to the emergency room with the chief complaint of an inability to move her right limbs for 3 days. She experienced a fall and transient loss of consciousness at that time, then dysarthria and hemiparesis of the right upper and lower limbs developed. She denied visual impairments, diplopia, fever, or urine incontinence. She was well in the past years, without systemic disease nor history of hypertension, diabetes or dyslipidemia. Over the past years, she had experienced intermittent dizziness and the episodes of near-syncope three to four times. Deteriorated dyspnea on exertion was also noted in recent months, but she did not pay any attention to it. She had

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no history of smoking, alcohol consumption, or illicit drug abuse, no weight loss, no myalgia or arthralgia.

On admission, the patient had a temperature of 36.2 °C, a regular heart rate of 70 beats/min, blood pressure of 108/69 mm Hg, and a respiratory rate of 20/min under room air. Physical examination revealed an alert and well-oriented female. She had no jugular venous distention, and her carotid impulse was normal, without bruits. Lungs were clear to auscultation. Cardiac examination revealed a regular heart rhythm; the first and second heart sounds were normal, but there was a distinct loud, low-pitched sound and soft systolic and diastolic murmurs at the apex. The patient had no edema of lower extremities. Dysarthria was noted; and the cranial nerves were intact. She had 1/5 motor strength of the right upper limb, 3/5 motor strength of the right lower limb, and normal strength of the left limbs. Her sensation was intact. Deep tendon reflexes were 1+/3+ bilaterally. Barbinski sign was negative bilaterally. The patient had no clonus, and Hoffman's sign was also negative. The remainder of the physical examination was unremarkable. Laboratory tests were normal. Electrocardiogram (ECG) revealed normal sinus rhythm with right axis deviation and counterclockwise rotation. Chest radiography showed mild enlargement of cardiac silhouette as well as left atrial enlargement, without evidence of masses or infiltrates. Head CT obtained in the emergency department revealed heterogeneous low density with faint contrast enhancement over the left basal ganglion and left temporal region; a subacute phase of cerebral infarction was considered.

On the following day, a magnetic resonance image (MRI) scan of the brain revealed multiple infarction and demyelination over grey, subcortical white matter and deep white matter, as well as both temporal-parietal lobes. A transthoracic echocardiogram demonstrated moderate dilatation of the left atrium with a homogeneous, huge, solid left atrial mass, 6.26 × 3.03 cm in size, occupied the left atrial chamber and protruded into the left ventricle through the mitral valve during diastole, but did not completely obstruct the mitral valve (Figures 1 and 2). The stalk could not be identified due to the mass occupying the whole left atrium. A left ventricular mass, 1.79 × 1.09 cm in size, arose from the left ventricular free wall, without obstruction of the outflow tract of left ventricular. A third tumor, 1.10 × 1.07 cm in

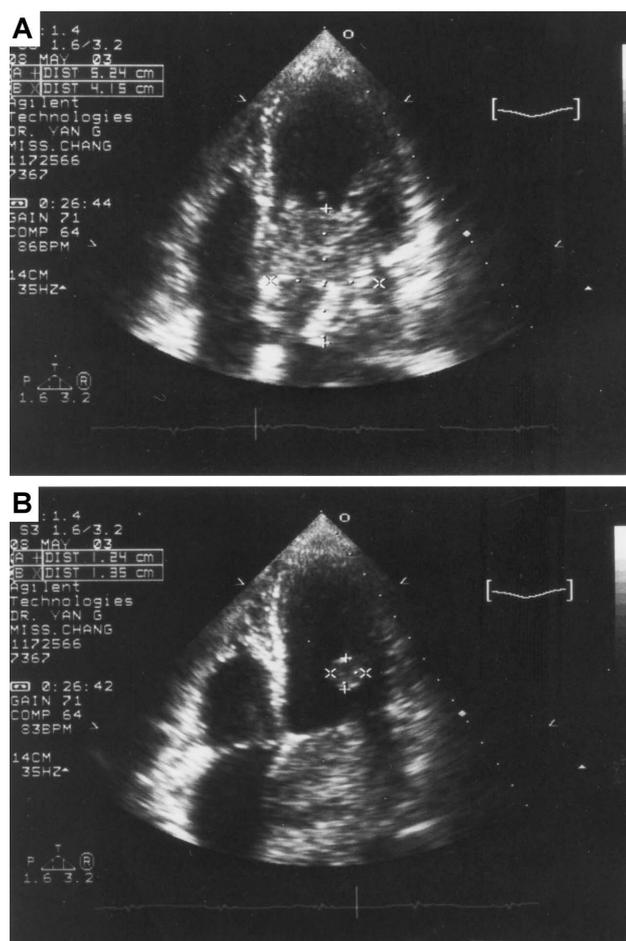


Figure 1. (A) The long-axis view of transthoracic echocardiogram demonstrated moderate dilatation of the left atrium with a homogeneous, huge, solid left atrial mass, 6.26 × 3.03 cm in size, occupied left atrial chamber, and protruded into the left ventricle through the mitral valve during diastole. (B) A smaller left ventricular tumor, 1.79 × 1.09 cm in size, arised from the left ventricular free wall, was also found during systole.

size, was noted at the right atrium, near the tricuspid ring, and prolapsed into the right ventricle during diastole (Figure 3); mild mitral regurgitation and moderate tricuspid regurgitation were detected. The transvalvular pressure gradient of the tricuspid valve was 29 mmHg. There was no pericardial effusion. The global left ventricular contractility and ejection fraction were within normal limits. The appearance of the masses was most consistent with a diagnosis of myxomas, although thrombus or other metastatic malignancy could not be excluded. The patient received surgery for excision of intracardiac tumors on the tenth day after admission without complication. Pathologic examination confirmed the multiple smooth,

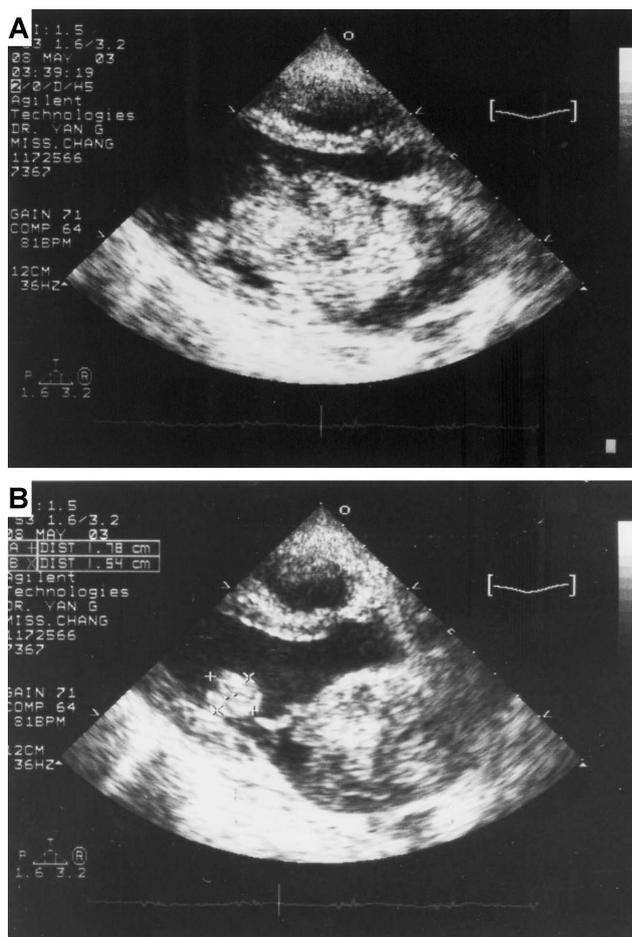


Figure 2 The apical four-chamber view of transthoracic echocardiogram demonstrated the left atrial and left ventricular mass. (A) diastole, (B) systole.

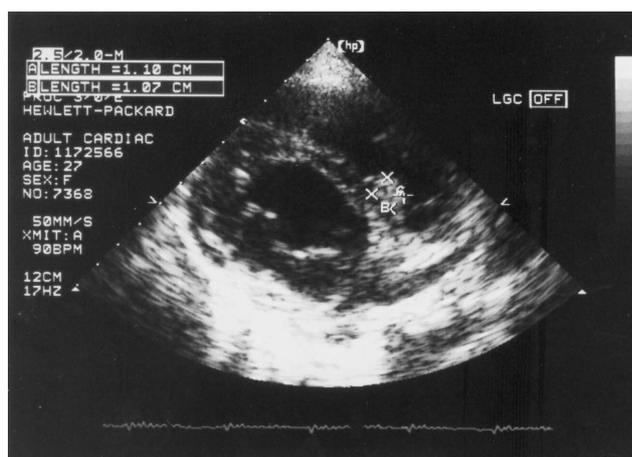


Figure 3. The short-axis view demonstrated a third tumor; 1.10 × 1.07 cm in size, was noted at the right atrium, near the tricuspid ring.

gelatinous myxomas (Figure 4). The patient had an improvement of her dysarthria and right hemiparesis. The

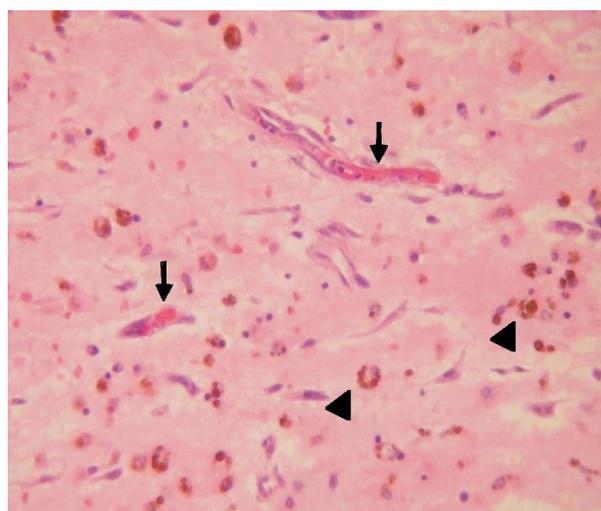


Figure 4. Microscopically, the section shows stellate myxoma cells proliferating and floating in the myxoid stroma accompanied with numerous small vessels (arrow). Occasionally, hemosiderin-laden histiocytes (arrowheads) infiltration is also noted. (hematoxylin and eosin stain, originally magnification × 200).

patient was discharged on day 6 after operation and was totally asymptomatic when she was followed at 6 and 18 months after surgery.

DISCUSSION

Some clues may be helpful to differentiate benign intracardiac tumor from malignant tumor before surgery. Rapid growth in tumor size, hemorrhagic pericardial effusion, the tumor on the right side of the heart, or in an atypical area such as the atrial free wall, presence of distant metastasis, local mediastinal invasion, or combined intramural and intracavitary tumors, extended into the pulmonary veins, all of these may be suggestive of malignancy. None were found in our patient, except location of the tumor on the both side of the heart. An intracavitary tumor that causes the obstruction of the right ventricular outflow is approximately 300 times more likely to be a malignant rather than a benign tumor.¹ Benign tumors are often located on the interatrial septum of the left atrium and display slow growth. Histologically, myxomas are benign, but they can be lethal based on their anatomic location, such as obstructing of the intracardiac flow.

Myxomas often have clinical manifestations as constitutional symptoms, such as fever, weight loss, malaise, fatigue, and weakness, which may be mediated by

interleukin-6, secreted by the myxoma itself.² Large or multicentric tumors are likely to induce constitutional signs, which are reversible after resection. Systemic embolization caused by cardiac myxoma is frequent, often occurring in the cerebrovascular and retinal arteries, and less often in the pulmonary artery. Recurrent strokes, as in our patient, are frequent; they may be embolic or hemorrhagic. Symptoms of heart failure due to mechanical obstruction of intracardiac inflow also develop rapidly, particularly in young patients without underlying heart disease. Sudden death or syncope may also occur due to total obstruction of intracardiac flow. The manifestations depend on the size, mobility, and location of the tumor. Friable tumors usually present with embolization, while the larger myxomas often present with cardiac manifestations. Previous studies on left atrial myxoma reported that symptoms of mitral valve obstruction were the most common (67%), followed by constitutional symptoms (34%) and embolism (29%); only a few patients were asymptomatic (10%).³

Abnormal cardiac auscultation is also an important clue, indicating pseudo mitral valve disease or a tumor "plop"; it was heard on our patient. Other abnormal cardiac findings may include the presence of a diastolic murmur in the mitral area (75%), systolic murmur (50%), increased S2 intensity as pulmonary hypertension (70%), third heart sound (33%), atrial fibrillation (15%), right heart failure (15%), clubbing fingers (5%), and Raynaud's phenomenon (5%).⁴ Occasionally, atrial myxomas become infected by bacteria or fungus, with subsequent endocarditis and systemic septic emboli.⁴ The most common ECG finding is left atrial enlargement. Also, arrhythmias are not uncommon. Atrioventricular block and ventricular tachycardia may occur if infiltration of the conduction tissue or irritation of the myocardium by the myxoma has developed. Serologic and hematologic data may be abnormal, especially in those with systemic symptoms, regardless of the size of the tumor. Elevated C reactive protein, globulin fraction, erythrocyte sedimentation rate, anemia, or thrombocytopenia also were reported, but none of them was noted in our patient. A connective tissue disease with autoantibodies may be suspected if myxomas have some extracardiac presentations.

Ninety percent of atrial myxomas are sporadic and occur as solitary tumors without specific genetic predisposition. Cardiac myxomas occur more commonly in

females (3:1 ratio) and are usually diagnosed between the ages of 50 to 70 years old.⁵ Around 7% of them are familial.⁶ Some young-age patients with multiple cardiac myxomas may have familial histories with autosomal dominant transmission pattern, and are considered as the familial myxoma syndrome (Carney complex). A causative mutation of a protein kinase, the *PRKAR1α* gene located on the long arm of chromosome 17 (17q22-24 region), was found by Kirschner.⁷ The Carney complex occurs at a mean age of 25 years old and has a lesser predominance in females.⁸ It is characterized by multiple recurrent cardiac myxomas, peripheral myxoid tumors, cutaneous spotty pigmentation, multiple lentiginos and blue nevi, endocrine overactivity, and psammomatous melanotic schwannoma.⁹ These manifestations were not found in our patient.

The diagnostic tools include ECG, chest X-ray, and echocardiography. ECG often shows nonspecific changes; about 33% of patients may demonstrate left atrial enlargement. Chest X-ray often shows nonspecific change, as left atrial enlargement and pulmonary hypertension changes may occur in 50% of patients.¹ Transthoracic echocardiography can identify the location, size, shape and mobility of a myxoma. In some conditions, transesophageal echocardiography (TEE) may give a better view to determine the detailed contents of myxoma, and the site of origin and extension. The diagnostic sensitivity by transthoracic echocardiography is 95.2%, and by TEE 100%, compared to 70% by computed tomography (CT) and MRI.¹⁰

Due to concern about intracardiac mechanical obstruction secondary to tumor or recurrent central/peripheral embolism, treatment of a cardiac myxoma is semi-urgent, and surgical excision is usually curative. So we arranged the surgical intervention for our patient as soon as possible. The prognosis of surgical intervention is good; survival rate was 95% after a median follow-up of 3 years.¹¹ Five percent of patients may have a recurrence, most of them occurring within 6 years after surgery, which suggests follow-up echocardiography is necessary.^{3,11} At long-term follow-up, the recurrence rate of myxoma in patients with a sporadic myxoma is 1 to 3%; in contrast, patients with a familial myxoma have a higher recurrence rate, so the latter should lifetime annual review with familial screening. Immunologic findings may play an additional role in confirming the diagnosis and the re-

currence of a myxoma.¹¹

CONCLUSION

Clinicians often misdiagnose cardiac myxomas in the absence of any history of cardiac problems. The non-specific systemic constitutional symptoms, physical findings and laboratory abnormalities emphasize the diagnostic difficulties. Diagnosis may be delayed until more severe symptoms occur, such as stroke or systemic embolization. Delay in diagnosis from symptom onset ranged from 1 to 126 months has been reported.¹² Conditions frequently confused with cardiac myxomas include rheumatic valvular disease, atrial septal defect, constrictive pericarditis, cardiomyopathy, mural thrombus, aortic stenosis, endocarditis, immunologic disorders (vasculitis including systemic lupus erythematosus), and neoplastic disorders (carcinoid syndrome). A surgical excision of the tumor is curative; therefore the challenge to the clinicians is to anticipate cardiac involvement in patients who have presented with the disease. At present, two-dimensional echocardiography plays a major role in the accurate and early diagnosis of cardiac myxoma. Surgery is the standard treatment and the long-term clinical results are excellent.

REFERENCES

1. Reynen K. Medical progress: cardiac myxomas. *N Engl J Med* 1995;333:1610-7.
2. Mendoza CE, Rosado MF, Bernal L. The role of interleukin-6 in cases of cardiac myxoma: clinical features, immunologic abnormalities, and a possible role in recurrence. *Tex Heart Inst J* 2001;28(1):3-7.
3. Pinede L, Pierre D, Loire R. Clinical presentation of left atrial cardiac myxoma: a series of 112 consecutive cases. *Medicine* 2001;80:159.
4. Braunwald E, Zipes DP, Libby P. Heart Disease: A Textbook of Cardiovascular Medicine. 6th Edition. Philadelphia: WB Saunders, 2001.
5. Le BD, De L, James A, et al. Left hemiparesis from atrial myxoma emboli. *Cardiol Rev* 2003 Jan-Feb;11(1):41-4.
6. Ejima K, Uchida T, Hen Y, et al. Complex myxoma detected by syncope: a case report. *J Cardiol* 2003 Feb;41(2):97-102.
7. Kirschner LS, Carney JA, Pack SD, et al. Mutations of the gene encoding the protein kinase type I-alpha regulatory subunit in patients with the Carney complex. *Nat Genet* 2000;26:89-92.
8. Percell RL, Henning RJ, et al. Atrial myxoma: case report and a review of the literature. *Heart Dis* 2003 May-Jun;5(3):224-30.
9. Carney JA. Carney complex: the complex of myxomas, spotty pigmentation, endocrine overactivity and schwannomas. *Semin Dermatol* 1995;14:90.
10. Engberding R. Diagnosis of heart tumors by transesophageal echocardiography: a multicentre study in 154 patients. European Cooperative Study Group. *Eur Heart J* 1993;14:1223-8.
11. Keeling IM, Oberwalder P, Anelli-Monti M, et al. Cardiac myxomas: 24 years of experience in 49 patients. *Eur J Cardio-Thorac Surg* 2002;22(6):971-7.
12. MacGowan SW, Sidhu P, Aherne T, et al. Atrial myxoma: national incidence, diagnosis and surgical management. *Ir J Med Sci* 1993;162(6):223-6.

不尋常多房性心臟黏液瘤引起之暈厥及中風 — 病例報告

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大部分的心臟腫瘤是轉移來的，但原發性心臟腫瘤也是重要的致病因，發生率約為千分之三。原發性心臟腫瘤將近半數是黏液瘤，而良性心臟腫瘤中黏液瘤更佔了 75%。其他良性心臟腫瘤還包括脂肪瘤，橫紋肌瘤，纖維瘤。本文章描述一年輕女性，一開始未診斷出心臟黏液瘤，後來導致右側偏癱。如果是多房性的心臟黏液瘤，通常會位於兩側心房，該病患則有三個黏液瘤，分別位於兩側心房及左心室。多房性的心臟黏液瘤通常有家族史，並容易復發，該患者則無家族史。經手術切除後，患者臨床症狀完全恢復，追蹤了 18 個月期間並未復發。

關鍵詞：心臟黏液瘤、暈厥、中風。