

## Case report

# Atrial Myxoma Presenting As a Cerebellar Stroke

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## Abstract

Primary tumors of the heart are rare. However, among them cardiac myxoma is the most common tumor accounting for half of the primary cardiac neoplasms. About 75% of cardiac myxomas are located in the left atrium, and 25% are located in the right atrium. These are thought to be arising from remnants of subendocardial vasoformative reserve cells or multipotential primitive mesenchymal cells in the fossa ovalis and surrounding endocardium, which can differentiate along a variety of cell lineages including epithelial, hematopoietic, and muscle cells. Although some cases are discovered incidentally by echocardiographic examination, it was recognized in most of the patients by various symptoms caused by the release of inflammatory cytokines such as interleukin-6 (IL-6), obstruction of intracardiac blood flow, or embolization. Cardiac myxoma has many undetermined interesting issues regarding its origin, nature as a tumor, varying clinical manifestations, and the presence of both sporadic and familial types. Recent evidence revealed that cardiac myxomas are benign neoplasms and slowly proliferating lesions. The existence of its malignant counterpart is controversial. However, recurrence after surgical excision or metastasis has been reported. We hereby present a case report of a young gentleman who presented with history of sudden onset of weakness and cerebellar signs. Urgent CT scan revealed hypodensities of bilateral occipital lobes and cerebellum suggestive of infarcts. Urgent echocardiography denoted large left atrial myxoma. The tumor was excised and the patient recovered well.

**Keywords:** Atrial myxoma, stroke, cerebellar signs, embolic phenomena

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## Introduction

Atrial myxoma is not an uncommon condition among patients. However, it is very uncommon for a patient with cardiac myxoma presenting with extra-cardiac symptoms and signs such as cerebellar manifestation. The commonest presenting feature of left atrial (LA) myxomas are mitral obstructive symptoms. Morphologically, LA myxoma are classified into two distinct types:- the round type characterized by round shape with non mobile surface and polypoid type, characterized by irregular shape with mobile surface. Studies suggest a higher incidence of embolic episodes in patients with friable polypoid type of

tumor (1). We present an unique case of a young man who had a very LA myxoma without mitral obstructive symptoms, but presented with cerebellar manifestation. Though, classically the polypoidal type of atrial myxoma tends to more prone for embolic phenomena, our case was an exception to this trend: resulting in multiple emboli despite belonging to the round type.

## Case Report

NAAZ, a 25-year-old Malay gentleman, who was previously well and apparently was about to get married the following week, presented to the

Emergency Department, HUSM, with history of sudden onset of weakness of both lower limbs and abnormal movement of upper limb one day prior to admission. He had no history of seizures, fall, trauma, fever or any symptoms suggestive of increased intracranial pressure. The weakness was progressively worsening the next day, associated with slurred speech. There was no history of dysphagia, nasal regurgitation, diplopia, bowel or bladder incontinence. He was not a diagnosed case of diabetes mellitus, hypertension, coronary artery disease or rheumatic heart disease. In fact, there is no similar illness in the family.

Upon admission, he was alert and conscious. His speech was slurred with dysarthria. The pulse was 76/min regular rhythm, normal character and good volume and the blood pressure was 130/75 mmHg. Cardiorespiratory examination revealed normal findings and per abdominal examination was normal. On neurological examination, this patient had bilateral intentional tremor, dysdiadochokinesis, positive past pointing test and heel to shin test. Cranial nerves were normal. Deep reflexes were brisk in all four limbs with extensor plantars bilaterally. No papilloedema was observed.

Urgent Computerised tomographic scan showed hypodensities of bilateral occipital lobes and cerebellum suggestive of infarcts. The ventricular system was normal and there was no midline shift. Echocardiography revealed a large (68 x 42 mm) homogeneous tumor attached to the interatrial septum, which was prolapsing into left ventricle during diastole. Mild mitral regurgitation was noted. The diastolic gradient across the mitral valve was insignificant. A diagnosis of LA myxoma with multiple brain emboli was made. There was no progressive deterioration of neurological status. This patient was referred to Cardiothoracic Unit for further management.

He was planned for excisional biopsy. Intraoperatively, we noted a round shaped with non mobile surface LA myxoma tumor attached to the interatrial septum, measuring 75x 45x68 mm. Intraoperative and postoperative outcome was uneventful. Patient recovered well with no residual neurological/ cerebellar symptom. Histopathological examination results confirmed atrial myxoma. Patient was seen twice during the follow up and he was very well with no evidence of recurrence.

## Discussion

Atrial myxomas represent approximately 50% of all cardiac tumors, occurring mainly in the 3rd–6th decade

of life (1). The annual incidence is 0.5 per million populations, (2) with 75% of cases occurring in the left atrium. There is a 2:1 female preponderance (3).

They originate from subendocardial mesenchymal cells mainly from the left atrium. Although atrial myxoma is mostly sporadic, at least 7% of cases are familial (4). The best described familial type is Carney complex, characterized by cutaneous spotty pigmentation, cutaneous and cardiac myxomas, nonmyxomatous extracardiac tumours and endocrinopathies. It is transmitted in an autosomal dominant manner, through a causative mutation of the *PRKAR1α* gene located on the long arm of chromosome 17 (17q22-24 region) (5).

Patients with LA myxoma usually present with signs of cardiac failure due to obstructed ventricular filling causing dyspnoea, pulmonary edema, and right heart failure. In some cases, it leads to syncope, sudden death, or signs of systemic embolism.

According to researchers, symptoms associated with embolic phenomena such as stroke or transient ischaemic attack is more common in young adults (1 in 250) than in older patients with these problems (1 in 750) (1). This patient conforms to most of the epidemiological studies as this young patient (in his 3<sup>rd</sup> decade) presented with neurological deficit due to embolic phenomena of atrial myxoma.

The presentation of atrial myxoma often comprises a diagnostic triad (summarized in Table 1). The embolization of tumor particles or thrombotic material covered with tumor cells occurs in 10–45% of myxoma patients. In at least half of the cases cerebral arteries are affected, leading to embolic ischaemic stroke (6). In contrast, the formation of intracranial aneurysms associated with left atrial myxomas is a less common phenomenon. Other rare neurologic complications include parenchymal brain metastases and intracerebral hemorrhage due to ruptured aneurysms (7, 8).

Atrial myxomas have been estimated to cause up to 0.5% of ischaemic strokes (9). In a recently published series, the median delay between onset of symptoms and diagnosis in myxoma patients with neurologic manifestation—mainly transient ischaemic attacks—was 36 months (10). Cerebral imaging often demonstrates multiple infarcts suggestive of an embolic cause, but in some cases it may show only small subcortical ischaemic lesions mimicking lacunar disease (11). Transthoracic echocardiography has a sensitivity of around 90% in detection of left atrial myxoma; the sensitivity of transesophageal examination is even higher (12).

**Table 1:** Diagnostic triad in presentation of atrial myxoma

Features	Manifestation	Frequency (% of patients)
Obstructive symptoms <sup>6,7</sup>	Heart failure, syncope, sudden death (rare)	54-95
Constitutional symptoms <sup>3,6</sup>	May mimic autoimmune disease or vasculitis; myalgia, arthralgia, weight loss, fatigue, fever, Raynaud's phenomenon. Finger clubbing	34-90
Embolic phenomena <sup>6-8</sup>	Emboli may travel to any organ, but 73% reach central nervous system, including spinal cord	10-45

Active illness is often accompanied by elevation of ESR and C-reactive protein, hyperglobulinemia and anemia. Constitutional symptoms may be mediated by interleukin-6, produced by the myxoma itself (13).

Morphologically, two distinct types of LA myxomas have been described; round type characterized by round shape with nonmobile surface and polypoid type, characterized by irregular shape with mobile surface (14). Studies by Moriyama et al (15) suggest a higher incidence of embolic episodes in patients with friable polypoid type of tumor.

Although cardiac myxomas usually present as a benign neoplasm, there are many reports suggesting its malignancy, including recurrence of the tumor, locally invasive myxoma, extension from the heart, and distant metastasis or peripheral tumor mass (16-18). Cardiac myxomas are generally thought curable by surgical resection of the primary tumor, but recurrence can occur at the site of the original tumor, at multiple intracardiac lesions, and at sites outside the heart.

Recurrence of cardiac myxoma has been observed in about 3% of patients in sporadic cases, and 20% in Carney complex. Cardiac recurrence may be secondary to incomplete resection of the tumor, implantation from the original tumor, unrecognized multicentric origin, or the new growth of pretumor or reserve cells (16). These recurrences may grow faster and be more infiltrative than the original tumor.

Gerbode et al. first reported recurrence of left atrial myxoma four years after initial excision (17). They postulated incomplete removal at the first operation and recommended wide resection of the interatrial septum around the base or stalk of the tumor. In English literature, Shinfeld et al. collected 584 patients with cardiac myxomas and found 42 patients

with first recurrence, and they found very few cases (1.3%) of repeated recurrence (18). They reported the age range at the time of first surgical resection was 7 to 62 years (mean, 32.7 years), and reoperation was performed at between 3 months and 14 years later (average, 3.9 years). Of the 42 cases of recurrence after left atrial myxoma, the second tumor appeared in the left atrium in 83%, in the right atrium in 14%, and at other sites in the heart in 7%. The tumor recurred at, or close to, the original site of the left atrium in 85% of cases.

Tumor emboli may go to any vascular bed and tumor cells may remain viable at the site of embolization, thus forming distant metastasis or peripheral tumor mass. As a benign tumor character of cardiac myxoma and tumor location of it in the cardiac chamber, its metastasis is usually intravascular and present delayed occurrence after resection of the cardiac lesion. Few researchers pointed out that malignancy of atrial myxomas is predicated on biologic behavior rather than on histologic appearance (19).

Researchers described a case of metastatic myxoma to soft tissue and bone (20). Cerebral metastasis from myxoma has also been reported (20). Wada et al. reported a case of a 70-year-old man who had an atrial myxoma and two metastatic myxomas in the brain (21).

The intracranial lesions were in fact diagnosed before the cardiac myxoma, since the patient developed hemiparesis before his cardiac symptoms occurred. Histopathological examination showed all lesions to be benign myxomas. Interestingly, high concentrations of IL-6 were present in the patient's serum and cardiac myxoma. Thus, they suggested that IL-6 may possibly potentiate metastasis of cardiac myxoma. Failure of constitutional symptoms to

resolve and of elevated gamma globulins and sedimentation rates to return to normal after technically successful resection of a primary cardiac tumor may suggest residual extracardiac tumor and may serve as a means of identifying the malignant cardiac myxoma. The potential for malignant change in cardiac myxoma is controversial. Shinfeld et al. reported same-site recurrence with more aggressive histology, then second recurrence with multiple smaller myxomas elsewhere in the left atrium (18). Although the first lesion was typically benign, the second recurrence was clearly malignant, and the patient died with extensive left atrial sarcoma. Sequential malignant transformation of cardiac myxoma is very rare.

#### *Appraisal of this case*

Several unique clinical features prompted us to report this case. First, though atrial myxoma presenting with embolic phenomena cause stroke due cerebral ischemia is quite common, but it is uncommon for cerebellar involvement whereby patient presenting with cerebellar signs, hitherto unreported, to our knowledge (2,3,4,5,6,7,8,9,10).

Second, the commonest presenting feature of LA myxomas are mitral obstructive symptoms which were absent in our case, despite the large size of the tumor. Neither did he have any constitutional symptoms (1, 6,7,8,9,12,13,14,15).

Thirdly the morphology and the presentation of the patient is interesting. As suggested by Ha JW et al (14), morphologically, LA myxoma are classified into two distinct types: the round type characterized by round shape with nonmobile surface and polypoid type, characterized by irregular shape with mobile surface. Studies suggest a higher incidence of embolic episodes in patients with friable polypoid type of tumor (15). Our case was an exception to this trend resulting in multiple emboli despite belonging to the round type. In fact, the tumours of round type are also less likely to prolapse into LV, unlike this patient.

#### **Conclusion**

Atrial myxoma is a benign cardiac tumour which could manifest in a various forms of clinical presentation. The spectrum of this disease can remain asymptomatic for many years or it can even present with embolic phenomena with severe neurological deficit and even death.

This is a unique case because:

1. Though atrial myxoma can present with embolic phenomena cause stroke due cerebral ischemia, but it is uncommon for cerebellar involvement.
2. The commonest presenting feature of LA myxomas are mitral obstructive symptoms which were absent in our case, despite the large size of the tumor. Neither did this patient have any constitutional symptoms.

The morphology and the presentation of the patient is interesting. Though studies suggest a higher incidence of embolic episodes in patients with friable polypoid type of tumor, our case was an exception to this trend resulting in multiple emboli despite belonging to the round type. In fact, the tumours of round type are also less likely to prolapse into LV, unlike this patient.

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