Clinical Investigation

Left Atrial Myxoma with versus without Cerebral Embolism:

Length of Symptoms, Morphologic Characteristics, and Outcomes

Zhi Zheng, MD
Guojun Guo, MD
Li Xu, MD
Lei Lei, MD
Xiang Wei, MD
Youmin Pan, MD

The aim of this study was to evaluate the embolic sequelae of left atrial myxomas and their influence on diagnosis, treatment, and prognosis.

Seventy-eight patients were retrospectively investigated. According to their symptoms and neurologic-imaging findings, these patients were classified into 2 groups: embolism (15 patients, 19%) and nonembolism (63 patients, 81%). The time from the first onset of symptoms to diagnosis (that is, the duration of symptoms) was significantly longer in the embolism group than in the nonembolism group (105 ± 190 vs 23 ± 18 d; P <0.01). The myxomas were divided into 2 types on the basis of clinicopathologic findings: type 1, with an irregular or villous surface and a soft consistency, and type 2, with a smooth surface and a compact consistency. There were 42 patients with type 1 myxoma and 36 with type 2. Type 1 myxoma was more frequently found in the embolism group (12 patients, 29%) than was type 2 myxoma (3 patients, 8%). The difference was significant (P=0.04). There were 2 perioperative deaths in the nonembolism group. No recurrence of cardiac myxoma or death was recorded in either group during follow-up. In the embolism group, neurologic symptoms were relieved by surgery, and no subsequent neurologic event was reported.

Because surgical resection is highly effective in left atrial myxoma, we should strive for early diagnosis in order to shorten the duration of symptoms and to avoid worse neurologic damage in patients in whom an embolic event is the initial manifestation. ***(Tex Heart Inst J 2014;41(6):592-5)***

Key words: *Cerebral infarction; heart neoplasms/complications; intracranial embolism/etiology; ischemic attack, transient; myxoma, left atrial/pathology; outcomes; retrospective studies*

From: *Department of Cardiothoracic Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, People's Republic of China*

Address for reprints: *Youmin Pan, MD, Department of Cardiothoracic Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Ave., Wuhan 430030, PRC*

E-mail: *youmin-pan@hotmail.com*

Although cardiac myxoma is occasionally asymptomatic, 3 major categories of presentation are common: cardiac symptoms due to atrioventricular valve obstruction, neurologic manifestations caused by systemic embolization (peripheral or cerebral), and constitutional symptoms.[1,2] Cardiac symptoms, which occur in 60% to 90% of all patients, most often provoke diagnosis.[1-3] When neurologic complications—such as stroke or transient ischemic attack (TIA) due to cerebral embolism—present as the initial manifestation, this subset of patients is usually first treated by physicians other than cardiologists or cardiac surgeons. This can delay the diagnosis of myxoma and increase the risk of sequelae. In fact, central embolisms occur more often than expected in the setting of cardiac myxoma—in 10% to 30% of all cases.[1,2] Left atrial myxoma has been well documented in the medical literature, but few of those studies have focused on central nervous system manifestations attributed to myxoma. Are there any differences in clinical presentation between patients with embolic sequelae and those without? Does neurologic damage have an influence on the diagnostic process, the timing of surgery, and the long-term outcome? The above questions should all have common-sense answers that already are widely known. However, few papers from large clinical series (most of them case reports) explain this "old idea" with data. We now report what is, to the best of our knowledge, the largest clinical case series of cerebral manifestations of left atrial myxoma to come from a single institution.

Patients and Methods

In performing a search of hospital records at Tongji Hospital (a tertiary-care teaching hospital in central China), we identified 92 patients who had been diagnosed with cardiac myxoma from January 2000 through December 2012. Of these, 5 were ex-

cluded because their diagnoses of cardiac myxoma had been made on the basis of echocardiographic findings alone: they had not undergone tumor resection for histopathologic study. Another 9 patients were excluded because their myxomas were confined to the right atrium. We thoroughly reviewed the medical records of the remaining 78 patients. Our review was approved by our institutional committee of human research.

The following data were collected: each patient's age, sex, clinical presentation (including cardiac, embolic, and constitutional symptoms), the time from the first onset of symptoms to diagnosis, characteristics of the cardiac myxoma, perioperative death, and morbidity. In the embolism group, findings of neurologic imaging (computed tomographic or magnetic resonance imaging of the brain, or magnetic resonance angiography) were recorded as well.

There were 48 females (62%; age range, 30–65 yrs) and 30 males (38%; age range, 37–65 yrs). Cardiac symptoms (including dyspnea, palpitation, chest pain or discomfort, and syncope) were noted in 55 patients (71%), embolic symptoms (including headache, hemiparesis, ataxia, aphasia, and memory impairment) in 15 (19%), and constitutional symptoms (including fatigue, weight loss, fever, and myalgia) in 14 (18%). In accordance with the symptoms and neurologic imaging findings (as described below), study patients were classified into 2 groups: embolism (15 patients, 19%) and nonembolism (63 patients, 81%).

All patients were monitored in the outpatient center, with clinical visits and echocardiography performed on an annual basis during the first 3 years after surgery. After 3 years, patients were monitored irregularly by mail or telephone contact. The follow-up was complete. The mean time to the last follow-up contact was 45 ± 34 months (range, 4–156 mo).

Statistical Analysis

Statistical analysis was performed with SPSS 13.0 software (SPSS Inc., now part of IBM Corporation; Armonk, NY). Categorical variables are presented in frequencies and percentages and are compared between groups by means of the χ^2 test. Continuous variables are presented as mean ± SD and are compared by means of the Student *t* test. Results were considered statistically significant at a *P* value of less than 0.05.

Results

Preoperative Echocardiography. Transthoracic echocardiography indicated a diagnosis of myxoma in every patient and was a simple, noninvasive method of morphologic examination of the cardiac chambers. Transesophageal echocardiography was also performed in 38 patients. The mean size of the cardiac myxomas was 3 ± 3 cm (range, 1–7 cm). Most cardiac myxomas (75, or 96%) arose around the margin of the septal fossa ovalis, 2 (3%) arose from the posterior left atrial wall, and 1 (1%) arose from the base of the left atrium. The mean left ventricular ejection fraction (LVEF) was 0.56 ± 0.20 (range, 0.50–0.68). In addition to these findings, mild-to-moderate pulmonary hypertension was found in 22 patients, mild-to-moderate mitral insufficiency in 31 patients, and severe tricuspid insufficiency in 1 patient.

Neurologic Imaging. All 15 patients in the embolism group underwent cranial computed tomography; in addition, 10 underwent cranial magnetic resonance imaging and 5, magnetic resonance angiography. The neurologic imaging findings were consistent with ischemic cerebral infarction in 12 patients, but no intracerebral hemorrhage was observed. In the remaining 3 patients, no abnormality was detected by neurologic imaging. Transient ischemic attack was diagnosed by neurologists on the basis of characteristic symptoms and the neurologic imaging findings.

Surgical Resection. Surgical excision of tumors was performed through median sternotomy with cardiopulmonary bypass. The mean aortic cross-clamping time was 18 minutes (range, 15–48 min). Concomitant surgery was performed in 3 patients (4%): coronary artery bypass grafting in 2, and tricuspid valve repair in 1.

The myxomas were divided into 2 types, in accordance with the criteria described in previous clinicopathologic studies[4,5]: type 1, with an irregular or villous surface and a soft consistency; and type 2, with a smooth surface and a compact consistency (Figs. 1 and 2). There were 42 patients with type 1 myxoma and 36 with type 2.

Comparison between the Embolism and Nonembolism Groups

We compared the clinical features of the embolism and nonembolism groups (Table I). The duration of symptoms was significantly greater in the embolism group than in the nonembolism group. Type 1 myxoma was more frequently noted in the embolism group than was type 2. The difference was significant (P=0.04).

Short- and Long-Term Survival

There were 2 perioperative deaths, both in the nonembolism group. One patient had multiple-organ failure on the 5th postoperative day, and the other had respiratory failure on the 7th postoperative day. Early sequelae were observed in 4 patients, all in the nonembolism group, including arrhythmia in 2, low output cardiac syndrome requiring inotropic support in 1, and pneumonia in 1. No death or recurrence of cardiac myxoma was recorded in either group during the follow-up period.

No worsening of neurologic symptoms was observed in any patient during hospitalization. In the embolism group, neurologic symptoms were relieved by surgery, and no subsequent neurologic event was reported.

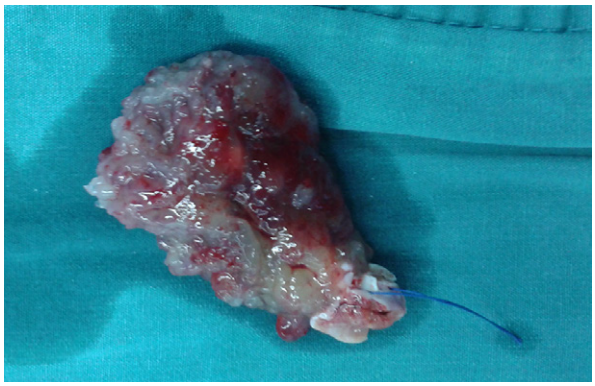

Fig. 1 *Photograph of a resected type 1 myxoma shows a villous surface and a soft consistency.*

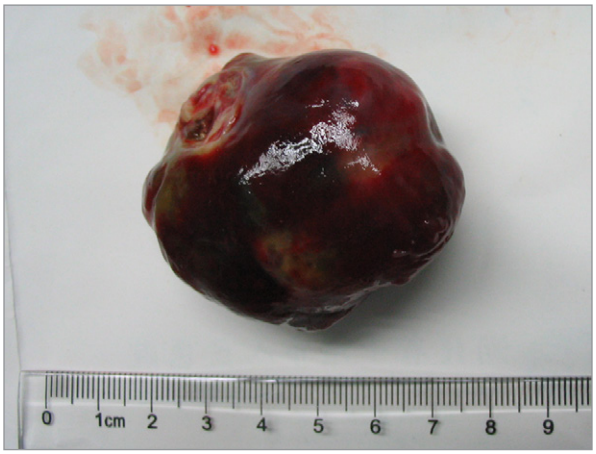

Fig. 2 *Photograph of a resected type 2 myxoma shows a smooth surface and a compact consistency.*

TABLE I. Comparisons between the Embolism and Nonembolism Groups

Variable	Embolism Group n=15	Nonembolism Group n=63	*P* Value
Age (yr)	49 ± 9	52 ± 6	0.16
Male	5	25	0.68
Duration of symptoms (d)	105 ± 190	23 ± 18	<0.01
Cardiac myxoma			
Type 1[a]	12	30	0.04[b]
Type 2[c]	3	33	0.04[b]
Number of tumors >1	0	4	—
Size of tumors >3 cm	5	32	0.22

[a]Type 1 is a cardiac myxoma with an irregular or villous surface and a soft consistency.
[b]Fisher's Exact Test
[c]Type 2 is a cardiac myxoma with a smooth surface and a compact consistency.

Data are presented as mean ± SD or as number. *P* <0.05 was considered statistically significant.

Discussion

In the literature, neurologic manifestations have been reported in 10% to 30% of left atrial myxoma patients, with embolic cerebral infarct the most frequently observed event.[1,2,6] According to previous studies, neurologic and embolic events were more often associated with type 1 myxoma.[7,8] This type generally has a friable or gelatinous texture, which gives rise to emboli by erosion and fragmentation of the neoplasm itself (cellular, stromal, or both), or by erosion of thrombus covering the surface. Type 2 myxoma, solid and ovoid, appears firm and smooth and usually can be removed in 1 piece during operation. Emboli from type 2 myxomas, although few in number, can result from cracking of the tumor's surface by turbulent blood flow.[4,7,8]

In 2 studies of central nervous system manifestations in cardiac myxoma, S.J. Lee[7] and V.H. Lee[8] and their respective colleagues showed that patients with cardiac myxoma who develop neurologic complications can lack concomitant cardiac symptoms. Accordingly, neurologic symptoms can present as the initial and only clinical manifestation. This subset of patients usually will be treated at onset by physicians other than cardiologists, which can delay diagnosis of myxoma and increase the risk of complications. Indeed this problem explains why, in our series, the time from onset of symptoms to diagnosis was much longer in the embolism group than in the nonembolism group.

The presence of cardiac symptoms actually directs diagnostic procedures to heart-imaging techniques, such as cardiac ultrasonography, and thereby accelerates diagnosis in this subset of patients. Although it has been suggested that some clinical examinations, such as auscultation, imply the presence of cardiac myxoma in a patient who has only neurologic manifestations, no series has yet confirmed this hypothesis. Neither could we, in our group, identify cardiac myxoma by auscultation. Whatever the case, if embolic stroke is suspected on the basis of neurologic symptoms, the possibility of cardiac myxoma must be borne in mind.[4,7,8]

Another interesting finding of our study is that recurrent cerebral infarction before surgical removal of tumor is not rare. One patient had 4 episodes of cerebral infarction during a period of 2 years, another had 2 in 8 months, and a 3rd patient had 2 in 6 months. In the embolism group, 4 patients had at least 1 onset of TIA before arrival at our institute with a final diagnosis of cardiac myxoma. Although peripheral embolism has occasionally been reported,[9-11] it was not observed in our series.

Limitations. Our study has 3 major limitations. First, it was a retrospective study in a single institution. Second, neurologic imaging was applied only to patients

with an embolic event as the initial manifestation, rather than to all patients. Consequently, patients who experienced asymptomatic cerebral infarctions would have been classified into the nonembolism group. Third, we could not directly confirm the relationship between cerebral embolism and cardiac myxoma, because we could not find any tumor-surface thrombus that could be related to embolism.

Conclusion

Once a definitive diagnosis has been established, the treatment of choice remains surgical excision. This should be performed as soon as possible, since the risk of further embolism and valve obstruction is high. The operative risk is relatively low in patients who have no neurologic damage. However, the timing of open-heart surgery in patients who have experienced a recent stroke remains a matter of debate. The concern is that extracorporeal circulation and anticoagulation can exacerbate the neurologic injury that exists preoperatively. There is no consensus on the issue of a safe interval from the onset of symptoms to surgery.[12]

Our experience has been that 2 to 3 weeks of post-diagnosis neurologic stabilization (with no new-onset cerebral embolism) might be optimal timing for surgery with low operative risk. However, optimal timing is also influenced by the patient's cardiac function, overall condition, and other factors. There was no perioperative death in our series. No sign of deterioration of neurologic symptoms was found in any patient during hospitalization. In fact, neurologic symptoms were relieved, or at least stabilized, by surgery. No late death, recurrence of myxoma, or delayed neurologic complication was recorded during the follow-up period. Our results showed favorable short- and long-term outcomes in patients with cerebral sequelae, similar to results described in previous studies.[7,11]

Because surgical resection is highly effective in treating left atrial myxoma, early diagnosis should be made to shorten the duration of symptoms and to avoid worse neurologic damage in patients who experience an embolic event as the initial manifestation.

References

1. Swartz MF, Lutz CJ, Chandan VS, Landas S, Fink GW. Atrial myxomas: pathologic types, tumor location, and presenting symptoms. J Card Surg 2006;21(4):435-40.
2. Vaideeswar P, Gupta R, Mishra P, Lanjewar C, Raut A. Atypical cardiac myxomas: a clinicopathologic analysis and their comparison to 64 typical myxomas. Cardiovasc Pathol 2012; 21(3):180-7.
3. Aggarwal SK, Barik R, Sarma TC, Iyer VR, Sai V, Mishra J, Voleti CD. Clinical presentation and investigation findings in cardiac myxomas: new insights from the developing world. Am Heart J 2007;154(6):1102-7.
4. Acebo E, Val-Bernal JF, Gomez-Roman JJ, Revuelta JM. Clinicopathologic study and DNA analysis of 37 cardiac myxomas: a 28-year experience. Chest 2003;123(5):1379-85.
5. Wang JG, Li YJ, Liu H, Li NN, Zhao J, Xing XM. Clinicopathologic analysis of cardiac myxomas: seven years' experience with 61 patients. J Thorac Dis 2012;4(3):272-83.
6. Alvarez-Sabin J, Lozano M, Sastre-Garriga J, Montoyo J, Murtra M, Abilleira S, Codina A. Transient ischaemic attack: a common initial manifestation of cardiac myxomas. Eur Neurol 2001;45(3):165-70.
7. Lee SJ, Kim JH, Na CY, Oh SS. Eleven years' experience with Korean cardiac myxoma patients: focus on embolic complications. Cerebrovasc Dis 2012;33(5):471-9.
8. Lee VH, Connolly HM, Brown RD Jr. Central nervous system manifestations of cardiac myxoma. Arch Neurol 2007;64 (8):1115-20.
9. Zhang T, Zhang X, Zhang X, Jiang J, Chen J, Zhou B. Management of multiple embolization arising from atrial myxoma. Ann Thorac Surg 2012;94(2):646-9.
10. Ekinci EI, Donnan GA. Neurological manifestations of cardiac myxoma: a review of the literature and report of cases. Intern Med J 2004;34(5):243-9.
11. Knepper LE, Biller J, Adams HP Jr, Bruno A. Neurologic manifestations of atrial myxoma. A 12-year experience and review. Stroke 1988;19(11):1435-40.
12. Sethi NK. Is it safe to proceed with thrombolytic therapy for acute ischemic stroke in a patient with cardiac myxoma? Eur Neurol 2013;69(2):67.