

Cardiac Myxoma: Sixteen-Year Experience in Central Chest Institute of Thailand

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Background: Among the rare diseases of primary cardiac tumor, myxoma is a leading pathology. A sixteen-year clinical experience and follow-up of patients with surgical removal of this particular mass is reported.

Material and Method: Medical records of intracardiac tumor patients between April 1995 and June 2012 were reviewed and only cardiac myxoma patients who underwent surgical resection were studied. The data of clinical presentations, investigations, operative details, and results were analyzed.

Results: Forty-five cardiac myxoma patients with a mean age of 52.6 ± 2.3 (14 to 82) years were operated during the sixteen-year period; of these, 76% were female. Dyspnea was the most common symptom accounting for approximately 78%, followed by heart failure 38%, and stroke 18%. Constitutional symptoms of weight loss, fatigue, and fever were found 33%, 13%, and 11%, respectively. Mean ejection fraction was 62% and the tumor size varied from 1.4 to 10 centimeters in diameter. Site distribution of tumors were left atrium (89%), right atrium (9%), and multiple site (2%), with the interatrial septum as the most frequent site of attachment (69%). Patients with irregular surface tumors had 29% greater chance of having stroke than those with smooth surface tumors ($p = 0.015$). There was no operative or post-operative mortality. The complete follow-up was 98% with 99.8 ± 52 months of mean follow-up. Ten and fifteen-year survival were 97%. A recurrence was found in one patient with multiple site tumors at eight-year follow-up.

Conclusion: Myxoma is a rare disease with a variety of clinical presentation. Surgical resection provides excellent operative and long-term survival. Despite a very insignificant chance of recurrence, long-term follow-up is still necessary.

Keywords: Cardiac myxoma, Clinical presentation, Surgical resection, Outcomes

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Primary cardiac tumors are uncommon lesions⁽¹⁾. Among these pathologies, myxoma is the most common cause accounting for approximately 70% of all cardiac tumors⁽²⁾. Clinical presentations may vary from constitutional symptoms to the hazards of systemic or cerebral embolism, intracardiac obstruction, and sudden death^(3,4). Tumors can be found in any of the heart chambers and can be attached to any part of the chamber⁽⁵⁻⁹⁾. The advancement of imaging technologies including echocardiography, cardiac MRI and CT scan have enabled early diagnosis and prompt surgical removal and thus have revealed the excellent early and late outcomes. To date, small case series from different centers without long-term clinical outcomes had been reported in Thai population⁽¹⁰⁻¹²⁾. The present study reports a sixteen-year clinical experience with

cardiac myxoma in the Central Chest Institute of Thailand (CCIT).

Material and Method

The present study was approved by the Central Chest Institute of Thailand Ethics Committee. Patients with intracardiac tumor were retrieved from patient records of the Central Chest Institute of Thailand between April 1995 and June 2012. Only cardiac myxoma patients who underwent surgery were studied. Clinical presentations, laboratory tests, tumor morphology, location, operative details, and results were obtained.

Preoperative diagnosis was done by transthoracic two-dimensional echocardiography (TTE). This imaging technique could determine size, location, and pedicle attachment of the tumors. Other structural heart abnormalities and heart function were also detected with this tool. Trans-esophageal echocardiography (TEE) was performed in patients with uncertain diagnosis. Coronary angiography was

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carried out in patients with symptom of chest pain or in patients who were over 40 years of age. Cardiac MRI was performed in patients when information obtained was still inconclusive.

Laboratory investigation criteria used were as follows; elevated erythrocyte sediment rate (ESR > 30), thrombocytosis (platelet count > 450,000 per micro liter), thrombocytopenia (platelet count < 150,000 per micro liter), leukocytosis (white blood cell counts > 15,000 per micro liter), and leucopenia (white blood cell counts < 3,500 per micro liter).

Surgical removal of the tumor was performed as soon as possible after the diagnosis under cardiopulmonary bypass, using aortic and bicaval cannulation with moderate hypothermia except for those presenting with large cerebral infarction at admission, which have to be postponed for another three weeks to minimize intracerebral hemorrhage from heparinization during surgery. For a tumor that was located in the right atrium, inferior vena cava was usually cannulated from a femoral vein. To prevent embolization, manipulation of the heart including vent sucker insertion before aortic clamp was kept at minimum. Antegrade cold blood cardioplegia and topical heart cold irrigation were used for myocardial protection. Entire tumor removal and resection of the attachment site together with a few more millimeters of the surrounding endocardium were the goal of the operation. Choice of surgical approaches depended on surgeon preference and location of the tumor. However, superior transseptal incision was the major technique used. The excised attachment sites were directly closed or by the use of a pericardial patch if the surgical excision site was more than 1.5 centimeters in diameter.

Morphology of the tumor was categorized into smooth regular surfaces and irregular surfaces that included lobulated and papillary tumors according to the gross pathological reports.

Follow-up information was derived from consecutive outpatient clinic visits, telephone interviews, or questionnaires mailed to patients or families.

Statistical analysis

Results are expressed as mean \pm SD. The X^2 test was used for categorical variable. Long-term cumulative survival was assessed with Kaplan-Meier analysis. Analysis was performed using SPSS (SPSS, Inc., Chicago, Illinois). A p-value less than 0.05 was considered statistically significant.

Results

Fifty-one intracardiac tumors were treated in the CCIT during the past sixteen years. Of these tumors, 8% were malignant, consisting of malignant rhabdomyosarcoma, non-Hodgkin lymphoma, metastatic synovial sarcoma, and metastatic mucinous carcinoma. Two patients who were suspected of cardiac myxoma from TTE denied surgical treatment. Both of them died at one and two months after diagnosis. Definite diagnosis of myxoma with surgical pathology was found in 45 patients (76% female) with a mean age of 52.6 ± 2.3 years (Table 1).

A summary of clinical profile and result of investigation of the patients is shown in Table 2. Dyspnea was the most common presentation (77.8%). Heart failure and stroke were found in approximately 37.8% and 17.8%, respectively. Constitutional symptoms consisting of weight loss, fatigue, fever, and rash were presented, approximating at 33.3%, 13.3%, 11.1%, and 2.2%, respectively. Sixty percent of the patients had elevated ESR. Thrombocytosis and leukocytosis were detected 6.7%, whereas thrombocytopenia and leukopenia were found 2.2%. Over all mean ejection fraction was $61.7 \pm 1.6\%$ with tumor size ranging from 1.4 cm to 10 cm in diameter.

As to the tumor location and pedicle, 88.8% of the tumors were located in the left atrium, followed by 8.8% in the right atrium and 2.2% in multiple lesions. The attachment site was identified at the interatrial septum 68.9%, atrial free wall 24.4%, and valve leaflet 6.7% (Table 3).

Concomitant procedures included mitral valve repair in four patients (8.9%), tricuspid valve repair in

Table 1. Types of tumor

Tumor types	Number of patients	Mean age \pm SD	Gender (male/female)
Myxoma	45	52.6 ± 2.3	11/34
Rhabdomyosarcoma	1	36	0/1
Lymphoma	1	76	1/0
Metastatic synovial sarcoma	1	29	1/0
Metastatic mucinous carcinoma	1	72	1/0

one patient (2.2%), and coronary artery bypass grafting in one patient (2.2%). Surgical approaches through right atrial incision were used in 8.7%, classical left atrial incision 6.5%, biatrial incision 2.2%, and superior transseptal incision 82.6% (Table 4).

Of these, the patient with smooth surface tumor was 37.8% and with irregular surface was 62.2%. There were no significant differences of clinical symptoms including dyspnea ($p = 0.36$), palpitation ($p = 0.27$), syncope ($p = 0.17$) and heart failure ($p = 0.07$) between the two groups. However, the central embolic

phenomenon was significantly higher in irregular surface tumor patients ($p = 0.015$) (Table 5).

There was no operative and post-operative mortality. Neither serious bleeding nor neurological deficit after the operation was found in this series. Two patients using superior transseptal approach and one patient using classical left atrial approach developed post-operative supraventricular arrhythmia during hospitalization. However, the arrhythmia spontaneously converted to normal sinus rhythm within five days in all cases. The follow-up was

Table 2. Clinical features and investigation results in 45 myxoma patients

	Percent
Clinical presentations	
Dyspnea	77.8
Heart failure	37.8
Palpitation	22.2
Syncope	20.0
Stroke	17.8
Constitutional symptoms	
Weight loss	33.3
Fatigue	13.3
Fever	11.1
Rash	2.2
Laboratory tests	
Elevated ESR	60.0
Thrombocytosis	6.7
Leukocytosis	6.7
Thrombocytopenia	2.2
Leukopenia	2.2
Echocardiographic parameters	
EF	61.7 ± 1.6
LA size (mm)	41.9 ± 1.2
TRPG (mmHg)	41.9 ± 3.6
Tumor size (in maximal diameter, cm)	1.4-10

EF = ejection fraction; LA size = left atrial size; TRPG = tricuspid regurgitation pressure gradient

Table 3. Tumor locations and attachment sites (n = 45)

	n (%)
Locations	
Left atrium	40 (88.8)
Right atrium	4 (8.8)
Multiple sites	1 (2.2)
Attachment sites	
Interatrial septum	31 (68.9)
Atrial free wall	11 (24.4)
Valve leaflet	3 (6.7)

Table 4. Operative characteristics

	n (%)
Operation	
Remove LA myxoma	40 (86.9)
Remove RA myxoma	4 (8.7)
Remove LA, RA, RV myxoma	1 (2.2)
Redo remove RA, RV myxoma	1 (2.2)
Concomitant operation	
Mitral valve repair	4 (8.9)
Tricuspid valve repair	1 (2.2)
Coronary bypass graft	1 (2.2)
Surgical approach	
Superior transseptal incision	38 (82.6)
Right atrial incision	4 (8.7)
Left atrial incision	3 (6.5)
Biatrial incision	1 (2.2)

Table 5. Tumor morphology and clinical features

Clinical features	Tumor morphology		p-value
	Smooth surface (n = 17)	Irregular surface (n = 28)	
Dyspnea	12 (70.5%)	23 (82.1%)	0.36
Palpitation	4 (23.5%)	6 (21.4%)	0.27
Syncope	3 (17.6%)	6 (21.4%)	0.17
Heart failure	8 (47.0%)	9 (32.1%)	0.07
Stroke	0	8 (28.5%)	0.015

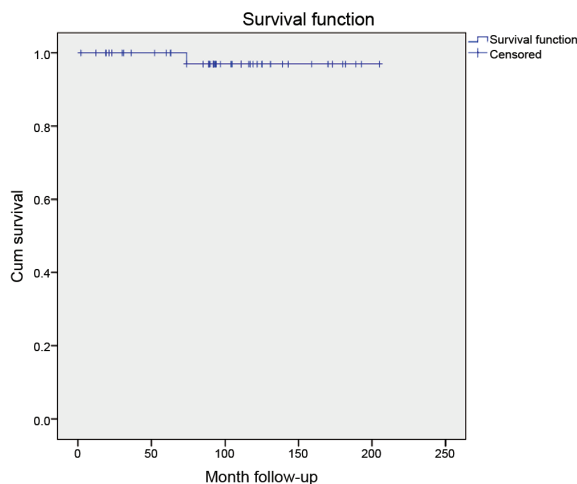


Fig. 1 Actuarial survival curve

98% completed and mean time to last follow-up was 99.8 ± 52 months (median, 93.5 months). A patient died of non-cardiac cause at 74 months after surgery. Actuarial survival was 97% at 10 and 15 years (Fig. 1). One patient with multiple tumors in right ventricle and both atria had a recurrence in right heart chambers at eight-year follow-up.

Discussion

Tumors of the heart are uncommon disorders. In particular, primary cardiac tumors are very rare with an incidence of 0.001 to 0.28% in autopsy series⁽¹³⁾. Among these masses, myxoma shares the major role accounting for 42 to 77%. The exact incidence in Thailand is not known. However, the present study revealed that the proportion of myxoma removal was 0.003% of the 11,397 cardiac operations performed in CCIT during the 16-year time period. In harmony with other series, range age of myxoma patients varied from 15 to 80 years, with a mean age of 50 years and predominantly found in females^(14,15).

Approximately 75% of myxoma was found in left atrium, followed by right atrium 18%, right ventricle 4% and left ventricle 4%⁽¹³⁾. In the present study, there were 89% in left atrium, 9% in right atrium. Multiple myxoma was found in one case (2%). In the literatures⁽¹⁶⁻¹⁸⁾, it was reviewed that these multiple tumors occurred around 10% and were associated with familial history or syndrome including spotty skin pigmentation, peripheral or endocrine neoplasm. This particular group of patients were usually young of age (mean age of 20 years) and more likely to develop recurrences (66%). A multiple

myxoma patient aged 45 years in the present series had a recurrence at 8 years after the operation; however, she did not have other criteria that matched the familial type. She was doing well without another recurrence for 9 years after the second operation.

Clinical symptoms in cardiac myxoma patients are quite variable ranging from mild forms of constitutional symptoms including fever, malaise, weight loss and rash to hazard forms of cardiac obstruction and embolism⁽¹⁶⁾. Interleukin 6, an inflammatory cytokine produced from the tumor, is believed to be involved in acute phase response associated with the constitutional symptoms, elevated erythrocyte sedimentation rate (ESR), thrombocytosis, thrombocytopenia and leukocytosis⁽¹⁹⁻²¹⁾. Obstructive symptoms are related to tumor location and mobility that interfere ventricular filling phase. Thus, left atrial myxoma can cause mitral valve obstruction mimicking rheumatic mitral stenosis^(4,14,22). Approximately 60 to 88% of cases may present with clinical of mitral obstruction^(14,23). The authors found that 78%, 38%, 22%, and 20% of myxoma patients in the study had symptoms of dyspnea, heart failure, palpitation, and syncope, respectively. However, these manifestations can occur paroxysmally in correlation with a particular body position which results in occasional prolapse of the mobile tumor through atrioventricular valve into the ventricle^(4,16). Systemic and pulmonary embolization were reported in approximately 30% and 10% in left and right sided myxoma patients, respectively^(14,16). Eighteen percent of the patients in the present study presented with cerebral infarction, whereas pulmonary and peripheral emboli were not found. Tumor morphology has been reported to associate with the embolic events. Risk of embolism increased if the tumor were polypoid or multilobulated⁽²⁴⁾. The authors found that less emboli occurred in patients with smooth surface tumors (0% vs. 29%, $p = 0.015$).

Echocardiography is generally used to diagnose an intracardiac mass. This technique can approximate the size and shape; moreover, it can locate the attachment site and identify the mobility of the tumor⁽²⁵⁾. Nevertheless, patients with poor transthoracic echocardiographic window, transesophageal echocardiography will provide a more superior imaging⁽²⁶⁾. Care must be taken to differentiate intracardiac tumors from thrombus, which are more common. Left atrial thrombus is usually associated with mitral valve stenosis or atrial fibrillation and more likely to be attached at the posterior and lateral wall or extend from left atrial appendage, meanwhile left

ventricular thrombi occupy in dyskinetic or aneurysmal part of the ventricles⁽²⁷⁻²⁹⁾. However, cardiac CT scan can demonstrate filling defects within a contrast material-filled cardiac chamber. Nevertheless, this technique does not give a precise point of the tumor attachment⁽¹⁴⁾. Cardiac MRI can give more details when echocardiographic findings are not conclusive. Attachment sites can be identified in most cases with this tool except those with a huge mass that occupied the entire cavity. Although both thrombi and myxoma can give heterogenous signal intensity by using MRI, the differentiation of non-enhancement thrombi from myxoma can be done by using gadolinium enhancement technique^(30,31).

Tumor attachment sites are varied. They can be attached to left atrial free wall, mitral annulus and even mitral valve itself but most are usually found at the fossa ovalis of interatrial septum⁽¹³⁾. The authors found that the originating sites are at the atrial septum, atrial free wall and valve leaflet, 69%, 24% and 7%, respectively. To prevent tumor from recurring it is recommended to perform adequate resection and special attention is given to the attachment sites. Nevertheless, full thickness and only endocardial resection of the attachment of the tumor were not different in recurrent rate in recent studies^(32,33). The endocardial resection of the attachment sites was considered acceptable if the origin was near the conduction tissue, atrioventricular groove or in the ventricles^(18,26). In case of mitral valve leaflets in origin, mitral valve replacement may be needed. In this review, there were three cases with tumors arising from mitral leaflets and the pericardial patch reconstruction of the valve leaflets were performed successfully with good results.

The optimal operative approach to the tumors is to be individualized depending on the location and size. However, it is necessary to have adequate exposure for complete resection and less tumor manipulation simultaneously^(34,35). Some literatures^(18,34,35) advocated inspecting all four cardiac chambers for removal of remaining tumor tissues to prevent postoperative embolism and recurrence. Transseptal approach can be used in case of a small left atrial myxoma with a stalk at the fossa ovalis^(18,35). For larger left atrial tumors originating from the septum, it is better to approach with separated incision in both atria, which is called biatrial approach⁽³⁴⁾. With this technique, the tumor pedicle can be localized clearly from left atriotomy and the septal resection with tumor removal can be carried out through the

right atriotomy^(18,35). As for left atrial myxoma with attachment site other than the atrial septum, the tumor can be approached via a classical left atrial incision posterior to the interatrial groove^(18,34). In the authors' experience, a superior transseptal incision was preferred as it allowed a more clearly defined tumor pedicle at any sites with less manipulation of the tumor. The right atrial incision was extended vertically to the left atrial roof then the attachment at the atrial septum was evaluated deliberately through the roof incision before cutting the septum. Moreover, this approach could give an excellent exposure of the mitral valve and all four cardiac chambers^(36,37). The superior transseptal incision has been criticized for a high incidence of postoperative arrhythmia^(38,39). However, the authors did not find other serious problems with the postoperative rhythm disturbance, which is in agreement with several studies⁽⁴⁰⁻⁴²⁾.

Surgical resection of cardiac myxoma has an excellent result with operative mortality of less than 1%^(16,18). Recurrent rate in sporadic cardiac myxoma was 1-3%⁽¹⁸⁾. The mechanisms of recurrence may be associated with incomplete removal, intraoperative embolization, and multifocal sites⁽²⁶⁾. In the present series, a patient with multiple site tumors had recurrence tumor at eight-year follow-up after the first surgery. For this reason, long-term follow-up after surgery of cardiac myxoma patients is recommended, in particular those with multiple lesions.

Conclusion

Myxoma is the most common primary tumor of the heart. Clinical features vary from mild form of constitutional symptoms to life threatening form of cardiac obstruction and cerebral embolism. Echocardiography is the first choice of investigation. However, cardiac MRI is also helpful in doubtful cases. Surgical removal shows an excellent result. Although recurrence is likely to happen albeit very small, long-term follow-up is still necessary.

Limitations

There are some limitations in the study. Since this was a retrospective review which required medical record retrieval, some helpful data were not available due to the incomplete recording of medical details. Furthermore, during the follow-up period, echocardiography was not performed routinely in all patients to detect for recurrent tumors. Therefore, the exact incidence of recurrence, especially those without clinical manifestation might be missed.

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Potential conflicts of interest

None.

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เนื้องอกมิกโซมาในหัวใจ: ประสบการณ์ในระยะสิบหกปีของสถาบันโรคทรวงอก

ปราโมทย์ ปรปักษ์ขาม, พรวิไล ปรปักษ์ขาม, พรหมพร เพชรรงทอง

ภูมิหลัง: มิกโซมา เป็นเนื้องอกที่พบได้บ่อยที่สุดในจำนวนโรคเนื้องอกของหัวใจชนิดที่มีต้นกำเนิดในหัวใจ ซึ่งเป็นโรคที่พบบได้น้อยมาก บทนิพนธ์นี้ ได้นำเสนอประสบการณ์ในการดูแลรักษาผู้ป่วย และติดตามผู้ป่วยที่ได้รับการผ่าตัดเนื้องอกมิกโซมาของสถาบันโรคทรวงอก ในระยะสิบหกปีที่ผ่านมา

วัสดุและวิธีการ: ได้มีการศึกษาข้อมูลจากเวชระเบียนของผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นโรคเนื้องอกของหัวใจชนิดที่มีต้นกำเนิดในหัวใจที่ได้รับการรักษาที่สถาบันโรคทรวงอก ในระยะเวลาระหว่างเดือนเมษายน พ.ศ. 2532 ถึงเดือนมิถุนายน พ.ศ. 2555 โดยรวบรวมเฉพาะผู้ป่วยที่ได้รับการรักษาโดยการผ่าตัด และมีผลชิ้นเนื้อยืนยันว่าเป็นเนื้องอกมิกโซมาของหัวใจ และได้นำข้อมูลทั้งในเรื่องของอาการแสดงนำ การตรวจวินิจฉัย รายละเอียดของการผ่าตัด และผลลัพธ์ของการรักษาการศึกษา

ผลการศึกษา: ผู้ป่วยที่ได้รับการผ่าตัดเนื้องอกมิกโซมาของหัวใจในระยะเวลา 16 ปี มีจำนวนทั้งสิ้น 45 ราย โดยมีอายุเฉลี่ย 52.6 ± 2.3 (14-82) ปี เป็นเพศหญิงร้อยละ 76 อาการนำที่พบบ่อยที่สุดคือ อาการเหนื่อย ร้อยละ 78 อาการหัวใจล้มเหลวและภาวะอัมพฤกษ์อัมพาต พบได้ร้อยละ 38 และ 18 ส่วนอาการร่วมอื่นๆ เช่น ไข้ต่ำๆ น้ำหนักลด และอาการอ่อนเพลีย พบได้ร้อยละ 11, 33 และ 13 ตามลำดับ การบีบตัวของหัวใจห้องล่างซ้ายเฉลี่ยร้อยละ 62 เนื้องอกมีขนาดตั้งแต่ 1.4 ถึง 10 เซนติเมตร ตำแหน่งของเนื้องอกพบที่หัวใจห้องบนซ้ายร้อยละ 89 หัวใจห้องบนขวา ร้อยละ 9 และร้อยละ 2 พบได้หลายตำแหน่ง ผันกั้ระหว่างหัวใจห้องบนเป็นตำแหน่งที่ก้านของเนื้องอกยึดติดมากที่สุด โดยพบได้ร้อยละ 69 ผู้ป่วยที่มีเนื้องอกชนิดที่ผิวไม่เรียบมีโอกาสเกิดอัมพฤกษ์อัมพาตได้มากกว่าผู้ป่วยที่มีเนื้องอกชนิดผิวเรียบได้ร้อยละ 29 ($p = 0.015$) ไม่พบอัตราการตายจากการผ่าตัดและอัตราการตายระยะต้นในผู้ป่วยกลุ่มนี้ ผู้ป่วยจำนวนร้อยละ 98 ได้รับการติดตามการรักษาโดยมีระยะเวลาเฉลี่ยอยู่ที่ 99.8 ± 52 เดือน โดยมีอัตราการรอดชีวิตระยะยาวที่ 10 และ 15 ปี เท่ากับร้อยละ 97 พบการกลับมาเป็นซ้ำในผู้ป่วยหนึ่งรายที่มีเนื้องอกมิกโซมาในหัวใจมากกว่าหนึ่งตำแหน่ง ในช่วงระยะเวลา 8 ปีที่มีการติดตามการรักษา

สรุป: เนื้องอกมิกโซมาเป็นโรคที่พบบได้น้อยมาก มีอาการแสดงทางคลินิกที่หลากหลาย การผ่าตัดให้ผลลัพธ์ในการรักษา และอัตราการรอดชีวิตระยะยาวได้อย่างดีเยี่ยม การติดตามผู้ป่วยระยะยาวมีความจำเป็นถึงแม้ว่าอัตราการกลับมาเป็นซ้ำของโรคจะต่ำมากก็ตาม
