Review article

Atrial Myxoma: Trends in Management

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Abstract

Myxomas are the most common type of cardiac tumours in all age groups accounting for one-third to one-half of cases at postmortum and for about three quarter of tumours treated surgically. Most atrial myxomas, whether left or right, arise from the atrial septum. About 10% have other sites of origin, particularly posterior wall, anterior wall and the appendages (in order of frequency). Myxomas are frequently located in left atrium and produce symptoms when they fragment and cause systemic emboli or when they interfere with cardiac valvular function and cause pulmonary congestion. Careful surgical management of these lesions should be curative with minimal early and late morbidity and mortality. Recurrence of atrial myxomas can occur most likely in about 3% of patients. However, extensive resection of the myxoma attached to atrial septum or atrial wall can reduce the likelihood of recurrence to a greater extent. Long term clinical and echocardiographic follow-up is mandatory.

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Introduction

Despite De-Senac's assertion in 1783 that "the heart is an organ too noble to be attacked by a primary tumour" the heart has no specific immunity from neoplasia and cardiac tumours have become increasingly recognized. Though cardiac tumours can be primary or metastatic, later group is more common. Among primary cardiac tumours, three quarters are benign and

remainders are malignant.

Myxomas are the most common type of cardiac tumours in all age groups accounting for one-third to one-half of cases at postmortum and for about three quarter of tumours treated surgically. (1) Most atrial myxomas, whether left or right, arise from the atrial septum, usually from the region of the limbus of fossa ovalis. About 10% have other sites of origin, particularly posterior wall, anterior wall and the appendages (in order of frequency). (2)

Review of Literature

First recognition of a heart tumour is attributed to Columbus in 1559 (3), followed by Malpighi, who in 1666 wrote a dissertation entitled "De polypo cordis". (4)

Bahnson and Newman (1953) reported(5) the earliest surgical approaches to myxomas by removing a myxoma from the right atrium via right anterior thoracotomy using a short period of caval obstruction at normothermia. Craford (1955) [6] successfully excised a myxoma from left atrium using cardiopulmonary bypass whereas Coates et al (1958) [7] reported a successful excision of a right atrial myxoma.

Firror WB (1966) [8] in a follow-up study of 3 patients, who had undergone removal of left atrial myxoma five to ten year previously, concluded that it would appear that simple excision of left atrial myxomas without removal of the atrial wall from which it has arisen is an adequate operation and is not associated with any evidence of recurrence.

James V. Richardson et al (1979) [9] conducted a study on 11 patients who underwent surgical excision of atrial myxoma during a 15 years' period, with no hospital deaths. The operation consisted of excision of tumour with a generous portion of atiral septum or wall. Patch reconstruction of atrial septum was required in most patients. There were 2 late deaths.

Late recurrences have been reported in other series but no recurrences were diagnosed in any of the patients in the series re-examined by echocardiography 7 to 156 months after operation.

Late functional results were excellent. It was concluded that excision of atrial myxoma can be accomplished safely with good results. Recurrence of atrial myxoma can be as many as 14% patients, but most likely in 5%. It appeared that extensive resection of the myxoma attachment to

atrial septum, or atrial wall can reduce likelihood of recuurence. Re-recurrence can be noted several years postoperatively.

Larrieu AJ et al (1982) [10] in their experience of 25 cases of primary cardiac tumours reported that malignant primary cardiac neoplasms are mostly sarcomas and usually follow a rapid lethal course. However, they may simulate benign disease, usually a benign myxoma, and therefore, close preoperative and postoperative scrutiny of all patients with cardiac tumours is recommended. Surgical resection, when possible, is the treatment of choice for all primary cardiac tumours, since with benign tumours, it is curative and with malignant tumours, it may prolong life for up to a year.

David C. Cleveland et al (1983) [11] observed that intracavitary tumours of right atrium are rare, generally diagnosed as myxoma. Once identified by echocardiography, right atrial lesions should be evaluated further by good quality inferior vanacavagram. The pattern of recurrence after surgical resection of atrial myxoma would suggest a minimum of five years of follow up by echocardiography. Myxoma can be malignant; thus complete surgical excision encompassing full thickness of normal surrounding tissue should be the goal in every case.

Henson EC (1985) [12], in his clinical experience and late results of 33 patients of atrial myxomas, 24 patients have been studied by two-dimensional echocardiography upto 20 years after operation (mean 4 years) with no recurrence. Excellent results were obtained by simple excision of the tumours with or without the margin of normal atrial septum. Long-term clinical and echocardiographic follow-up is recommended since late recurrence, although rare, has been reported.

Uberto Bortolotti et al (1990) [13], 54 patients underwent excision of an intracardiac myxoma, which was located in the left atrium in 46 (85%), right atrium 6 (11%) and right ventricle in 2 (4%). Extended follow-up of patients with intracardiac myxoma revealed that excision of such tumours is curative and long term outcome is excellent. Regardless of their location, cardiac myxomas should always be approached, at least initially, through the intra-atrial septum. This route provides adequate exposure of the mass in most intances, allowed radical excision, and is associated with a low incidence of late postoperative arrythmias.

Selke FW(1990) [14] in his series of 22 patients who underwent 24 operations for cardiac myxomas, 2 patients had complex myxoma syndrome. Mitral valve replacement was required in 2 patients. The long-term prognosis of these relatively large group patients with cardiac myxomas has been good. Patients without complex myxoma syndrome had no recurrence. Long term disability and a chronic arrythmias have been infrequent and functional status and employability of these patients had been very good.

Meyns B et al (1993) [15], in a series of 32 consecutive patients undergoing resection of a cardiac myxoma over 20 years period (1971-1991) reported a mean age of patients as 57±11 years. All the myxomas were located in the left atrium and were resected. Follow up showed excellent results with no recurrence and concluded that recurrence is mainly confined to patients with familial presentation and/or myxoma complex.

Castells E (1993),(16) in his series of 27 operated cases, with a follow up of 22 years (mean 6.5 years) reported satisfactory long-term results without recurrence. Hospital mortality was 7.3% and long-term mortality 7%. The postoperative life expectancy of these patients seems similar to that of normal population, except in cases of recurrence and mitral valve replacement. Recurrence is very low except in case of young patients and recurrent, familial, multiple or complex myxomas. The multigrowth potential of the tumour seems more important than inadequate surgical resection.

Kabbani SS et al (1994) (17) used biatrial approach for atrial myxoma in 23 patients. Diagnosis was established preoperatively in all patients by echocardiography with or without angiocardiography. Twenty one patients had left atrial myxoma and 2 had right atrial myxoma. All tumours were excised with wide margin of full thickness septum. Four patients had concomitant mitral valve reconstruction. He suggested that the advantage of dual incisions is: complete tumour removal, mitral valve visualization and the operative ease, especially with large tumours.

Kamili and Ahangar (1997) (18) reported a giant right atrial myxoma weighing 100gms, about 8x8cms in size and recommended prompt diagnosis, location of tumour by 2D echocardiography and subjecting patients to surgery as soon as possible as there is ever lasting danger of embolism.

Staffan Bjessmo et al (1997) [19] in their experience of 63 patients over 40 years, concluded that surgical resection of a single myxoma is safe and effective treatment, with a low risk of recurrence. After uncomplicated resection, the frequency with which postoperative echocardiography is performed, should be limited, except for patients with multiple, atypical, or familial myxomas, a few transthoracic echocardiographic examinations performed at 5 years' intervals should be adequate if there has been no recurrence in the first few years.

Laurent Pinede (2001)[20] in his series of 112 consecutive cases of clinical presentation of left atrial cardiac myxoma, illustrated that this benign tumour may cause a wide range of clinical symptoms not only such as cardiac disease, but also infective, immunologic, or neurloogic diseases. Diagnosis is rarely made only on clinical grounds, because there are no specific physical signs or symptoms. Myxomas usually occur sporadically, but familial or recurrent cases have been reported. Two-dimensional echocardiography including the transesophageal approach is the technique of choice for diagnosis and follow-up of this tumour. An embolic event in young adults, in the absence of signs of symptoms of endocarditis or arrhythmia must lead to a primary consideration of myxoma as embolic source.

Elvira Acebo et al (2003)[21] in their series of clinicopathologic study and DNA analysis of 37 cardiac myxomas over 28 years showed that villous surface of myxomas predispose to embolism, and large left atrial tumours are related to atrial fibrillation. Echocardiography is reliable method with which to predict tumour size and morphology. Myxoma cells usually express IL-6 and some tumours have abnormal cellular DNA content. Surgical excision of the tumour is safe and effective treatment.

Pathophysiology

Most myxomas (80-90%) are in the left atrium. Right atrial myxomas tend to be more solid and sessile than left atrial myxomas, with a wider attachment to the atrial wall or septum.[22] They can be multicentric (within a single chamber) or biatrial. The most common arrangement (75%) of biatrial tumours involves attachment of two stalks to the opposite side of the same area of the septum. [23] Most cases are sporadic, approximately 10% are familial and are transmitted in an autosomal dominant mode. Multiple tumours occur in approximately 50% of familial cases

and are more frequently located in the ventricle. Myxomas can be polypoid, round or oval. They are gelatinous with a smooth or lobulated surface and usually are whitish, yellowish, or brown in colour. The mobility of tumour depends upon the extent of attachment to the inter-atrial septum and the length of the stalk.

Although atrial myxomas are typically benign, local recurrence due to inadequate resection or malignant change has been reported. Occasionally, atrial myxomas recur at a distant site because of intravascular tumour embolization. The risk of recurrence is higher in the familial myxoma syndrome.

Symptoms are produced by mechanical interference with cardiac function or embolization. Being intra-vascular and friable, myxomas account for most cases of tumour embolism. Embolism occurs in 30-40% of patients. The site of embolism is dependent upon the location (left or right atrium) and the presence of an intracardiac shunt.

Jong-Won Ha and associates [(24)] reported a more frequent occurrence of systemic embolism in polypoid tumours as compared to round (50% to 60%). Also, polypoid tumours more frequently prolapse into the ventricle. Prolapse of tumour through the mitral or tricuspid valve may result in the destruction of the annulus or valve leaflets also. Left atrial myxomas produce symptoms when they reach a weight of about 70gms, right atrial myxomas grow to approximately twice this size before becoming symptomatic. Tumours vary in size, ranging from 1-15cms in diameter.

Gender

Approximately 75% of sporadic myxomas occur in females. Female sex predominance is less pronounced in familial atrial myxomas.

Clinical features

Symptoms range from non-specific to constitutional to sudden cardiac death. In about 20% cases, myxomas are asymptomatic and are discovered as an incidental finding. Signs and symptoms of mitral stenosis, endocarditis, mitral regurgitation and collagen vascular disease can simulate those of atrial myxomas. A high index of suspicion aids in diagnosis.

Symptoms of left-sided heart failure

- Dyspnea on exertion that may progress to orthopnea, paroxysmal nocturnal dyspnea and pulmonary edema is observed.
- Symptoms are caused by obstruction at mitral valve orifice. Valve damage may result in mitral regurgitation.

Symptoms of right-sided heart failur

- Patients experience fatigue and peripheral edema.
- Abdominal distension due to ascites is rare; however, it is more common in slowly growing right sided tumours.
- These symptoms are also observed in later stage of progressive heart failure associated with left atrial myxomas.

Severe dizziness/syncope

- This is experienced by approximately 20% of patients.
- The most frequent cause in patients with left atrial myxomas is obstruction of mitral valve
- Symptoms may change as the patient changes position.

Symptoms related to embolization

- Systemic or pulmonary embolization may occur from left or right sided tumours.
- Left sided symptoms are produced from the infarction or hemorrhage of viscerae.
- Embolization to central nervous system may result in transient ischemic attack, stroke, or seizure.
- Involvement of retinal arteries may result in vision loss
- Systemic embolization that causes occlusion of any artery, including coronary, aortic, renal, visceral or peripheral, may result in the infarction or ischemia of the corresponding organ.
- On the right side, embolization results in pulmonary embolism and infarction.
- Multiple, recurrent small emboli may result in pulmonary hypertension and cor-pulmonale.
- Presence of an intra-cardiac shunt (atrial septal defect or patent foramen ovale) may result in paradoxical embolism.

Constitutional symptoms

- These include fever, weight loss, arthralgias, and Raynaud's phenomenon are observed in 50% of patients. These symptoms may be related to overproduction of interleukin-6.
- Hemoptysis due to pulmonary edema or infarction is observed in up to 15% of patients.
- Chest pain is infrequent, if it occurs, it may be due to coronary embolization.

Physical symptoms

- Jugular venous pressure may be elevated, and a prominent A-wave may be present.

- A loud S_1 caused by delay in mitral valve closure due to prolapse of the tumour into mitral valve orifice (Mimicking mitral stenosis).
- P_2 may be delayed. Its intensity may be normal or increased, depending on presence of pulmonary hypertension.
- In many patients, early diastolic sound, called a tumour plop is heard. This sound is produced by the impact of the tumour against the endocardial wall or when its excursion is halted.
- An S_3 or S_4 may be audible.
- A diastolic atrial rumble may be heard if the tumour is obstructing mitral valve.
- If there is valve damage from tumour, mitral regurgitation may cause systolic murmur at apex.
- Right atrial tumour may cause a diastolic rumble or holosystolic murmur due to tricuspid regurgitation.

General physical examination

May reveal fever, cyanosis, digital clubbing, rash or Petechiae.

Associated spotty pigmentation, myxomas in breast, skin, thyroid gland or neural tissue may be present (Carney syndrome).

Laboratory Studies

Laboratory Studies are non-specific and non-diagnostic. If present, abnormalities may include the following:-

- Elevated erythrocyte sedimentation rate (ESR) and elevated C-reactive protein and serum globulin levels.
- Leucocytosis.
- Anaemia may be normochromic or hypochromic. Hemolytic anaemia may occur because of the mechanical destruction of erythrocytes by the tumour.
- Serum interleukin-6 level may be raised and can be used as a marker of recurrence.

Imaging studies

Chest radiography may show

- Cardiomegaly
- Abnormal cardiac silhouette, mimicking mitral stenosis.
- Unusual intracardiac tumour calcification.
- Pulmonary edema
- Biventricular hypertrophy with or without LA enlargement.

Echocardiography

Although transesophageal echocardiography is more sensitive, 2-dimensional echocardiography is usually adequate for diagnosis.

All four chambers should be visualized because of multicentricity of tumour.

Transesophageal echocardiography

- It has better specificity and 100% sensitivity compared to transthoracic echocardiography.
- Has good resolution of both atria and atrial septum and better anatomic details.
- Reveals smaller (1-3mm in diameter) vegetations or tumour and detects shunting.
- **Imaging (MRI)**
- It provides useful information about size, shape and surface characteristics.
- Information about tissue composition can be used to differentiate a tumour and a thrombus.

Other tests

ECG may show left atrial enlargement, atrial fibrillation, atrial flutter or conduction disturbances.

Cardiac catheterization

Used in selected patients in case non-invasive evaluation is inadequate.

Used to exclude co-existing coronary artery disease in patients of over 40 years of age.

Histological studies: are characterized by the presence of lipidic cells embedded in myxoid stoma.

Treatment

No known medical treatment exists for atrial myxomia, drug therapy is used only for complications such as Congestive Heart Failure or cardiac arrhythmias. Surgical resection of the myxoma is the treatment of choice, surgery being safe with low morbidity and mortality. Pericardial/PTFE patch can be used to close the surgical defect caused by excision of tumour. The risk of tumour fragmentation and embolization, vigorous palpation or manipulation is avoided or performed only after cardioplegia. Damaged valve may require repair or replacement. Recurrence is usually attributable to incomplete excision of tumour, growth from second focus or intracardiac implantation from primary tumour.

Conclusion

Myxomas are the most common tumour of the heart. They are frequently located in left atrium and produce symptoms when they fragment and cause systemic emboli or when they interfere with cardiac valvular function and cause pulmonary congestion. Careful surgical management of these lesions should be curative with minimal early and late morbidity and mortality. Optimal operative technique emphasized minimal manipulation of the heart before institution of cardiopulmonary bypass and aortic cross-clamping and careful examination of intracardiac chambers with meticulous removal of myxomatous debris. Recurrence of atrial myxomas can occur most likely in about 3% of patients. However, extensive resection of the myxoma attached to atrial septum or atrial wall can reduce the likelihood of recurrence to a greater extent. Thus, long term clinical and echocardiographic follow-up is mandatory.

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