A Look at Cardiac Myxoma

Ahraaz Wyne, Medicine 2010
Reviewed by Dr. David Massel

Cardiac Myxoma is the most common primary cardiac tumor. It arises from the endocardium as a lipidic cell mass embedded in a vascular myxoid stroma. Most myxomas are sporadic and the cause is largely unknown. Familial variants with an autosomal dominant inheritance exist. Myxomas typically develop in females between the second to sixth decades of life. Clinical manifestations can mimic many cardiac conditions and depend on the natural behaviour of the tumor and its location within the heart, ranging from completely asymptomatic to causing sudden death. Establishing an early diagnosis is essential and requires imaging techniques. 2D-Echocardiography is the diagnostic modality of choice however, ultrafast CT or MRI may be required. The preferred treatment is surgical resection which is curative and should be performed as early as possible to avoid systemic complications such as emboli. Patients with cardiac myxoma generally have an excellent prognosis. Following surgical resection, screening for recurrence is prudent, especially among the familial variants, where the recurrence rates may be as high as 20%. Myxomas, although rare, present a varied clinical picture and represent a diagnostic challenge. Consequently, physicians must have a high index of suspicion, since prompt surgical removal improves quality of life and extends survival.

Introduction
The first description of a left atrial myxoma is accredited to King in 1845. A recent review of Carl Rokitansky’s collection has revealed a 170-year old perfectly conserved myxoma of the pulmonary valve; the patient died in 1833. Prior to 1951 the diagnosis was made primarily at postmortem examinations; in that year, an intracavitary left atrial tumor was diagnosed by angiography. The first successful excision of a left atrial myxoma was performed in 1955. Primary tumors of the heart are rare clinical entities and studies estimate the incidence as being between 0.0017% and 0.19% at autopsy, among unselected patients. Cardiac myxomas are the most common of the primary cardiac tumors comprising about 30-50%. Approximately 75% are located in the left atrial cavity, 23% in the right atrial cavity, and about 2% in a ventricular cavity. While extremely rare, tumors may be found in multiple cavities. Cardiac myxomas have varied clinical presentations which primarily depend on the cardiac chamber where they occur and thus present a challenge for early diagnosis.

Epidemiology and Clinical Practice
Epidemiology: Myxomas occur in all age groups but are particularly frequent between the third and sixth decades of life. The youngest known patient was a stillborn infant, and the oldest a 95-year-old woman. The majority of myxomas are sporadic and tend to be single, atrial, and more typically in women. Approximately 10% are familial, with an autosomal dominant inheritance. At present, the Carney complex is used to describe an autosomal dominant trait that includes cardiac myxomas, cutaneous myxomas, spotty pigmentations on the skin, endocrinopathy, and both endocrine and non-endocrine tumors. These patients are considerably younger at the time of diagnosis when compared to patients with sporadic myxomas.

Pathology: Histological examination shows atrial myxomas arising from the endocardium, commonly attached at the border of the fossa ovalis in the left atrium. The cells arise from multipotential mesenchymal cells and are characterized as lipidic cells embedded in a vascular myxoid stroma. Tumors vary in shape from round-oval to polygonal, and often show calcification, necrosis and/or hemorrhage (see Figure 1). The expression of interleukin-6 (IL-6) by atrial myxomas has been widely reported in the literature and is believed to aid tumor-cell proliferation and differentiation. In one series of 37 cases of myxoma, 74% showed expression of IL-6. The malignant potential of cardiac...
myxoma remains doubtful, although there have been reports of remote myxomatous growth that has embolized.18 Clinical Presentation: While small myxomas can be asymptomatic, the majority present with one or more of the triad of intracardiac obstruction, cardioembolism, and/or nonspecific constitutional manifestations; The clinical presentation will vary depending upon the physical behaviour of the tumor and its location within the heart.

A. Physical Behaviour: Obstruction of the circulation through the heart or heart valves commonly gives rise to symptoms of left- (dyspnea, recurrent pulmonary edema, paroxysmal nocturnal dyspnea, orthopnea) or right-sided (peripheral edema, ascites, fatigue, hepatomegaly) heart-failure, often mimicking mitral or tricuspid stenosis. The severity of symptoms will depend upon the extent of obstruction and can vary with body position. If the tumor is large, easily deformable and has a long stalk, then temporary complete obstruction of the mitral or tricuspid valve orifices can occur, resulting in syncope, dizziness (20% of patients) or sudden death.4 Interference of the tumor with heart valve function may produce symptoms of valvular insufficiency. This occurs due to movement of the mass back and forth between the atrium and ventricle ("wrecking ball" effect), hampering proper valve closure or damaging the AV-valve apparatus (e.g. chordal rupture).4 Invasion of the myocardium can cause impaired contractility, supraventricular arrhythmias, heart block or pericardial effusion. If the myxoma invades adjacent lung tissue, pulmonary symptoms can manifest, often mimicking bronchogenic carcinoma.

Embolization, which occurs in 30-40% of myxomas, is usually systemic4 but may also be pulmonary; it will depend on the tumor’s chamber of origin. It is for this reason that myxoma should always be on the differential for pulmonary embolism, pulmonary hypertension, and embolic strokes. Constitutional or systemic symptoms such as fatigue, fever, rashes, joint pains and weight loss can also be seen. Laboratory abnormalities are usually seen as elevated inflammatory markers (erythrocyte sedimentation rate, serum C-reactive proteins and globulin levels) as well as anemia, and high serum interleukin-6 levels.4,11 Sometimes, low grade but long-standing fever can be the only symptom.9 B. Location: The majority (75%) of atrial myxomas arise in the left atrium and up to 23% percent in the right atrium. Most arise from the inter-atrial septum at the border of the fossa ovalis, but they can also originate, in descending order of frequency, from the posterior atrial wall, the anterior atrial wall, and the atrial appendage.1,4 Tumors can also grow into the atrial lumen and cause symptoms of blood flow obstruction or create mitral insufficiency, which are symptoms often associated with commoner conditions such as mitral valve disease, heart failure and/or secondary pulmonary hypertension. If the tumor moves within the atrium, depending on the length of its stalk and extent of attachment to the septum, symptomatic alterations can occur with changes in body position. Myxomas can also embolize producing serious pulmonary and neurologic sequelae.

Physical Examination: Physical signs are highly variable and depend upon the clinical presentation and the originating chamber of the myxoma. For example, right atrial myxomas may manifest as elevated jugular venous pressure or a prominent a wave. If the myxoma leads to valvular damage (stenosis/regurgitation), then systolic or diastolic murmurs may be auscultated. A loud S1 will be heard if there is a delay in mitral valve closure due to tumor prolapse into the valve orifice (mimicking mitral
stenosis). The intensity of P2 may also be normal or increased, depending upon the presence of pulmonary hypertension. In many cases, an early diastolic sound called a ‘tumor plop’ is heard, as the tumor impacts against the endocardial wall in left and right sided myxomas. Upon general examination, systemic signs could include fever, cyanosis, clubbing, rash, or petechiae. Patients with familial or syndromic forms of myxoma may also have features including skin pigmations or endocrine abnormalities such as Cushing’s Syndrome.

**Diagnosis**

The goals of diagnosis are three-fold: to ascertain whether a tumor exists, determine its location, and to characterize it. Diagnosis of myxoma requires a high index of suspicion and, because of the non-specific nature of laboratory testing, requires various imaging studies. Echocardiography first successfully showed a left atrial myxoma in 1959. Today, because of its wide availability and simplicity, 2D-echocardiography is an excellent noninvasive tool for initial evaluation. It typically shows unimpeded images of the atria, septae and ventricles making it helpful in detecting tumor location (see Figure 2) and morphology (cysts, calcifications, necrotic foci, and hemorrhage). Doppler techniques aid in determining degree of cardiac obstruction or valvular damage. In many situations a transesophageal echocardiogram (TEE) is preferred as it provides superior images showing characteristics of the tumor and location in relation to the interatrial septum.

Sometimes, newer imaging techniques such as cardiac MRI and ultrafast-CT may be required; both provide noninvasive, high resolution cross-sectional views of cardiac structures. Cardiac MRI is generally preferred because of its higher resolution (Figure 3) and ability to reflect chemical microenvironments within a tumor by differential T1- and T2-weighting; however tumors must measure at least 0.5 cm before they are detectable. CT scanning is useful when MRI is unavailable or contraindicated. Finally, contrast angiography has also been used in the diagnosis of myxoma however catheterization is more invasive and runs the risk of embolizing tumor fragments. A study by Agostini et al. showed that positron emission tomography (PET) could also be used in the diagnosis of myxoma, however PET remains widely unavailable in Canada and may not offer resolutions comparable to MRI or CT.

**Treatment**

The treatment of choice for myxoma is curative surgical resection. After a review of the literature, there appears to be no known medical therapy for shrinking or preventing recurrence of myxoma and drugs are primarily used to manage symptoms, such as heart failure, or when trying to differentiate tumor from thrombus (e.g. anticoagulants). Furthermore, there are no recommended dietary modifications and lifestyle activities are permitted as tolerated. Once a presumptive diagnosis has been made, most surgeons recommend prompt resection to avoid embolic complications such as sudden death. This includes asymptomatic patients.
who have had incidental findings of myxoma during routine echocardiography. Surgery entails performing a median sternotomy and subsequent tumor excision with the use of mild general and deep topical hypothermia, cardioplegic cardiac arrest, and cardiopulmonary bypass. Care is taken to avoid intraoperative fragmentation as all chambers of the heart are inspected for multifocal disease. If there is associated valvular damage, then this is corrected with annuloplasty, repair or replacement. The results of surgical resection are generally very good with most series reporting operative mortality rates under 5 percent. Major complications of the surgery include tumor embolization, supraventricular arrhythmias and requirement of permanent cardiac pacing due to conduction disturbances. Alternative surgical approaches using endoscopic tumor resection have also been used for their cosmetic advantage and faster recovery. Recurrence is low, close to 5% in patients with sporadic myxomas but can be as high as 20% with the familial variants. As such, there is a need for careful follow-up and biannual 2-D echocardiograms would be reasonable. In rare cases of frequent recurrences, cardiac transplantation has also been performed.

Conclusion
Although rare, myxoma is the most common type of primary cardiac tumor and requires a high index of suspicion. For the patient’s illness experience, myxoma ranges from being completely asymptomatic to causing severe morbidity and sudden death, with symptoms suggestive of many cardiac causes. Surgical removal offers curative treatment with excellent prognosis and recurrences are rare. This paper has briefly provided an overview of cardiac myxomas as probably presenting the most varied clinical picture of all cardiac tumors.

References