Is the heart truly noble?

"The heart is an organ too noble to be attacked by a primary tumor" - De-Senac (1783). We now know for certain that the heart has no specific immunity from neoplasm.

Primary cardiac tumors are extremely rare with the most common being atrial myxomas.[1,2] Columbus from Venice, Italy was the first to recognize a myxoma in 1559.[3] Other primary cardiac tumors are papillary fibroelastomas, rhabdomyomas, fibromas, hemangiomas, teratomas, lipomas, and paragangliomas. The cavity of the left atrium harbors 75% of myxomas and the rest in the right atrium. Multiple tumors, wherepresent, maybe located in the ventricle as well.

Atrial myxoma, is a masquerader, mimicking thrombus or vegetation in the heart. Most cases are sporadic. Approximately 10% are familial and are transmitted in an autosomal dominant mode. Myxomas originate from the endocardium and are polypoid, round, or oval. They are gelatinous with a smooth or lobulated surface and usually are white, yellowish, or brown. These can range in size from 1 to 15 cm in diameter, although most measure approximately 5-6 cm across. The most common site of attachment is at the border of the fossa ovalis in the left atrium. They may have a stalk, which makes them mobile.

Although they are histologically benign, cardiac myxomas by virtue of their location, size, and potential to embolize (30-40%) can be a source of significant morbidity and mortality. Ha *et al*.[4] reported a more frequent occurrence of systemic embolism in polypoid tumors (58%). Prolapse of a polypoid tumor through the mitral or tricuspid valve may result in the destruction of the annulus or valve leaflets from repetitive "wrecking ball" effect.

Myxomas have been demonstrated to produce numerous growth factors and cytokines, including, vascular endothelial growth factor, resulting in angiogenesis, and tumor growth and an increased expression of the inflammatory cytokine, interleukin-6.[5,6] Cardiac myxomas rarely metasasize, although should they do so, their common sites are the brain, sternum, vertebrae, pelvis, and scapula.

Approximately 75% of sporadic myxomas occur in females. The mean age for sporadic cases is 56 years and for familial cases 25 years. In a retrospective review of 171 patients from India, the mean age of the presentation was 37.1 years. Most of these patients were symptomatic; dyspnea was the most common symptom.[7]

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Signs and symptoms of mitral stenosis, endocarditis, mitral regurgitation, and collagen vascular disease can simulate those of atrial myxoma. Symptoms of left-sided heart failure such as dyspnea on exertion orthopnea, paroxysmal nocturnal dyspnea, and pulmonary edema are observed. Fatigue and peripheral edema suggest symptoms of right-sided heart failure. Severe dizziness or syncope raise the suspicion of myxomas obstructing the mitral valve.

Systemic embolization that causes occlusion of any artery including, coronary, aortic, renal, visceral, or peripheral, may result in 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 intracardiac shunt (atrial septal defect or patent foramen ovale) may result in a paradoxical embolism.Embolization to the central nervous system may result in transient ischemic attack, stroke, or seizure. Other complications include, myxoma-induced cerebral aneurysm and myxomatous metastasis that can mimic vasculitis or endocarditis. Involvement of the retinal arteries may result in vision loss.

Palpitations, cough, hemoptysis, and stenocardia (angina pectoris) may be noticed. Constitutional symptoms that include fever, cachexia, arthralgias, malaise, and Raynaud phenomenon are observed in half of the patients. These symptoms may be related to overproduction of interleukin-6. One recent case report of 5-year history of visual loss, vertigo, ataxia, tinnitus, and bone lesions that resolved after diagnosis and resection of the atrial myxoma has raised a possibility of it causing a paraneoplastic syndrome.[8] Atrial myxoma can get infected when vegetations may be seen attached to its surface.[9]

The physical signs depend on the location of the myxoma, jugular venous pressure (JVP) t may be elevated, S_1 could be loud, P_2 may be delayed, and in many cases, an early diastolic sound called a tumor plop is heard. Mitral or tricuspidregurgitant (holosystolic) murmurs suggest destruction of the valves.

Syndromes namely Carney (5.6%), and to a lesser extent NAME (nevi, atrial myxoma, myxoid neurofibromata and ephelides) and LAMB (lentigines, atrial myxoma, mucocutaneous myoma, blue nevus) have been associated with the myxomas. Carney syndrome features myxomas in the breast, skin, thyroid gland, or neural tissue, spotty pigmentation such as lentigines (i.e., flat brown discoloration of skin), pigmented nevi, endocrine hyperactivity, and multiple cerebral fusiform aneurysms may be seen.[10]

Laboratory studies are nonspecific and nondiagnostic. Patients tend to show elevated total globulin, erythrocyte

sedimentation ratet, and C-reactive protein levels. Hemolytic anemia occurs in approximately 33% of cases due to the mechanical effects of the tumor on the formed elements of the blood.

Straightening of left heart border and intracardiac tumor calcification (5-10% of cases) may be seen on chest skiagram. Electrocardiography may show left atrial enlargement, atrial fibrillation, atrial flutter, or conduction disturbances. Two-dimensional echocardiography is usually adequate for diagnosis. Tumor location, size, attachment, and mobility can be assessed with this technique. Transesophageal echocardiography has better specificity and 100% sensitivity compared to transthoracic echocardiography and is to be considered only when an ambiguity arises.

Magnetic resonance imaging (MRI) also provides useful information about size, shape, and surface characteristics on T1- and T2-weighted images. Information about tissue composition can be used to differentiate a tumor and a thrombus. Ultrafast computed tomography scan can be used when MRI is contraindicated or unavailable. Angiographic imaging of the coronary arteries is indicated in patients older than 40 years to exclude co-existent disease and also to establish whether or not tumor vessels are supplied from the branches of the left or right coronary arteries. Because myxomas may embolize, transvenous biopsy is not warranted.

Surgical resection is the only curative treatment modality for cardiac myxoma and should be performed at the earliest after the diagnosis is made to prevent sudden death. Bahnson and Newman (John Hopkins, USA,1953) t reported 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.[11] Crafoord (1954) successfully excised a myxoma from left atrium using cardiopulmonary bypass in Sweden.[12]

Khan *et al*. have in their article extensively described the standard approach for excision of atrial myxoma along with its histology. The surgeon while removing the tumor must also ensure that fragments are not dislodged and both atria and ventricles are free of other foci. Complete resection involves the removal of the root of the pedicle and consequently a full-thickness removal of the attached inter-atrial septum where appropriate. This in turn creates an atrial septal defect that can be closed primarily with a pericardial or cloth patch (Dacron, PTFE - Polytetrafluoroethylene). Some centers advocate the destruction of pre-tumorous cells around the stalk by laser photocoagulation. This obviates the need for a wide surgical resection. In cases where the tumor has affected the valve, a concomitant valve repair, with or without annuloplasty, or, where this is impossible, a valve replacement using an artificial prosthesis is performed.

Surgery for sporadic atrial myxoma is usually curative. Long-term prognosis is excellent. In a series of 112 patients from Baltimore, USA only four deaths occurred over a median follow-up of 3 years.[13] In another single-center study from India, of 62 patients with the cardiac myxoma, actuarial survival was 96.8 ± 1.8% at 10 years.[14] A study from Pakistan finds agreement with these observations.[15]

Advances in optics and instrumentation with the da Vinci S Surgical System have facilitated minimally invasive and robotic cardiac procedures for atrial myxoma excision as demonstrated by Schilling *et al*. Cincinnati, USA.[16] Totally thoracoscopic surgical resection of cardiac myxoma has been performed in Xian, China.[17] Studies from the different centers and long-term results are required before considering it a valid oncologic approach.

Reports from Germany show the recurrence rate is 1-5% and after 4 years is uncommon. However, the recurrence rate of familial patients is 20%.[18] Recurrence is usually attributed to incomplete excision of tumor, growth from a second focus, or intracardiac implantation from the primary tumor. Annual transthoracic echocardiography along with the monitoring of serum interleukin-6 level help to assess for recurrence.

Atrial myxomas despite being benign is lethal and therefore, mandates urgent excision as it is most often curative and carries minimal risk. Further, patients need to be educated about the risk of recurrence in familial myxoma and the necessity for family screening with the transthoracic echocardiography.

The findings of Khan *et al*. are in general agreement with the reviewed literature with comparable surgical outcomes. Their series of 38 cases of atrial myxoma in less than a decade reflects a higher incidence (0.6%) as compared to most centers (0.40-0.50%) for all cardiac surgeries. Furthermore, it is of interest to note that there is a male preponderance.

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