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BENIGN CARDIAC TUMORS: A REVIEW

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Introduction

Tumors of the heart are very uncommon and can occur as primary or secondary metastatic tumors. Metastatic tumors are over 40 times more common than primary cardiac tumors. Primary tumors of the heart are benign in 75% of cases and malignant in 25%.[1, 2] We first reported our institutional experience with all primary cardiac tumors in 2003.[3] Of the 85 patients seen, 17 had malignant tumors (20%) and 68 had benign tumors (80%). These benign tumors and our subsequent experience form the basis of this report.

Historical Review of Cardiac Tumors

In 1559, Realdo Colombo became the first physician to report a primary benign cardiac tumor.[4-6] An atrial tumor that was thought to cause valvular obstruction was described in 1809 by Alden Allen Burns of England.[7] The first series of cardiac tumors that matched what we now recognize as myxoma was noted in 1845 by King.[8] In 1931, Yates reported on 9 cases of primary cardiac tumor and established a classification system similar to today's.[9] All of these tumors were postmortem reports, with the first antemortem diagnosis reported in 1934 of a cardiac sarcoma with abnormal electrocardiogram and a metastatic lymph node that allowed tissue diagnosis.[10] Surgical intervention with excision of cardiac tumors was uncommon; the first reported success, described by Beck in 1936, involved removal of a teratoma external to the right ventricle.[11] In 1951, Mauer reported the successful removal of a left ventricular lipoma.[12]

This paucity of surgical success changed because of 2 events: 1) the introduction of cardiopulmonary bypass (CPB) in 1953 by John Gibbon, allowing a safe and reproducible entry into the cardiac chambers, and 2) the introduction of echocardiography, allowing easy, noninvasive imaging of intracardiac structures and masses. Bhanson made an early attempt at removing an intracardiac right atrial myxoma in 1952 by using caval inflow occlusion, but the patient expired 24 days later.[13] The first successful removal of an intracardiac tumor is generally credited to Crafoord of Sweden, who in 1954 removed a left atrial myxoma using CPB.[14] Progress from this point was rapid; by 1960, 60 successful cases of atrial myxoma removal had been reported, with increasing use of echocardiography for detection and CPB for removal.[15] Today, operation for benign cardiac tumors, although still uncommon, is not rare and is generally carried out with low morbidity and mortality. Even in our last reported series containing 68 patients with benign primary cardiac tumors, we

No.	Type of benign primary cardiac tumor
73	Myxomas
11	Fibroelastoma
6	Paragangliomas
3	Hemangioma
1	Lipoma
1	Fibroma
1	Castleman's tumor

Table 1. Number and types of benign primary cardiac tumors treated at the Methodist DeBakey Heart & Vascular Center.

had no hospital deaths, local recurrence or late death from tumor.[3] Benign primary cardiac tumors have been categorized in the Atlas of Tumor Pathology by McAllister,[1] with myxoma being most common (49%), followed by lipoma (19%), and papillary fibroelastoma (17%). Table 1 describes our current institutional experience, which includes 73 myxomas, 11 fibroelastomas, 6 paragangliomas, 3 hemangiomas, 1 lipoma, 1 fibroma, and 1 Castleman's tumor.

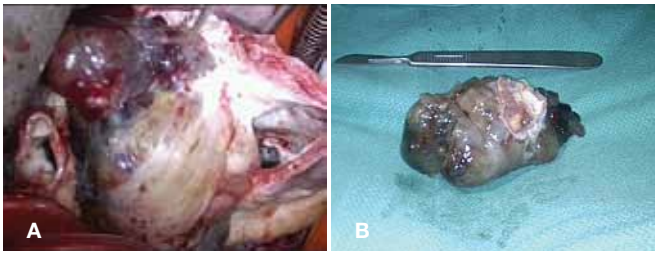

Figure 1. (A) Large left atrial myxoma removed intraoperatively using autotransplant technique; (B) explanted tumor.

Types of Benign Tumors

Myxoma

Myxoma is by far the most common benign primary cardiac tumor. The peak incidence for myxoma is between the third and sixth decades of life, and 94% of these tumors are solitary.[16] Although they can occur in any of the cardiac chambers, about three-quarters of these myxomas occur in the left atrium,[17] 10%–20% in the right atrium, and the rest equally divided between left and right ventricles. These tumors tend not to be associated with other abnormalities and rarely recur.[16] There is a familial occurrence of myxoma in about 5% of patients that exhibits an autosomal dominance pattern of inheritance.[18] These familial or complex myxomas tend to occur in younger patients, are more often multicentric (22%), and have a recurrence of 21%–67%.[19-21] Carney's complex is an autosomal X-linked inheritance characterized by cardiac myxoma, cutaneous pigmentous lentigines and primary pigmented adrenocortical disease with hypercortisolism.[22]

Myxomas are usually round or oval tumors with a smooth or slightly lobulated surface that tend to be on short stalks and mobile. Myxomas arise from the endocardium and are derived from a subendocardial multipotential cell. The classic triad of clinical presentation is congestive heart failure (CHF) from intracardiac obstruction of blood flow, embolization, and constitutional symptoms of fever and weight loss. In our series, patients with benign tumors presented with CHF (29%), chest pain (16%), palpitations (15%), central nervous system embolus (12%), peripheral embolus (7%) and constitutional symptoms (13%).[3] All tumors were diagnosed with transthoracic echocardiography. We routinely use intraoperative transesophageal echocardiography, which we believe eliminates the need for multicardiac chamber exploration, to detect additional myxomas as has been suggested by some. We have had no hospital deaths or late-tumor recurrences in our series. Most myxomas can be approached through standard and often minimally invasive techniques, but some are so large or complex that more advanced approaches are necessary for success. One patient with a giant left atrial myxoma required cardiac autotransplant for removal because of its size and increased likelihood of malignancy (Figure 1A, intraoperative photo; Figure 1B, explanted tumor).[23]

Another patient had a large left ventricular tumor that presented with right renal artery embolism and involved the ventricular side of the mitral valve and the left ventricular wall. This tumor also required a cardiac autotransplant technique for complete removal (Figure 2). Two months later, a right nephrectomy was performed, revealing viable myxoma tissue in the renal artery and infracted kidney.[24] Both of these patients did well and are currently free of disease.

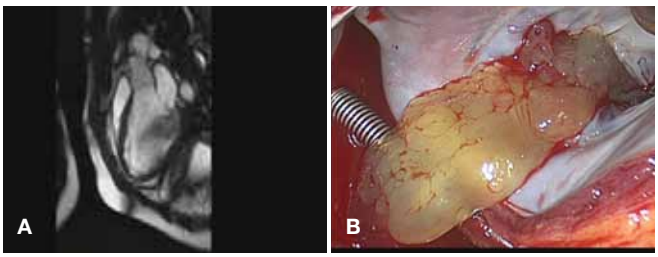

Figure 2. (A) MRI scan of left atrial tumor involving the mitral valve and left ventricular wall; (B) Intraoperative photo of tumor and its relationship to the left ventricle and mitral valve.

Papillary Fibroelastoma

The next most common primary benign cardiac tumor is the papillary fibroelastoma (PF), which most often arises from the cardiac valves or the endocardium immediately adjacent to the valve.[25] The most common location is the aortic valve, followed by the mitral valve. Atrioventricular and ventricular-arterial valves are equally involved. These tumors are usually asymptomatic but can embolize to the coronaries, causing a myocardial infarction, or to the brain, causing a stroke. It is difficult to accurately estimate the risk of embolism since the true denominator of patients with asymptomatic PF is not known. The classic description

of a papillary fibroelastoma is a tumor with frond-like projections that, when dropped into a basin of water, resembles a sea anemone. These tumors are generally single and solitary.[26] Multiple tumors occur in about 7%–10% of cases.[27] Cases with numerous multiple tumors numbering between 35 and 40 tumors in a single case have rarely been described.[28]

Hypertrophic cardiomyopathy and previous cardiac surgery have been suggested to be associated with the occurrence of papillary fibroelastoma,[27] yet the etiology of fibroelastoma is neither clear nor agreed upon. Some suggest that PF is a reactive lesion and not a true tumor,[27] others have suggested a virus as the inciting factor in tumor growth,[29] and still others suggest these may be hamartomas or organizing thrombi. It is our opinion that these represent true tumors, but their origin remains unclear. We have operated on 11 patients with PF with no hospital mortality. In these cases, all valves were spared, no valve replacement was necessary, and no patients have had a recurrence of tumor to our knowledge.

Most cases are approached through the wall of the atrium or across the ventricular arterial valve using standard techniques. One of our recent patients, who presented with repetitive transient ischemic attacks, had a PF in the intracavitary apex of his left ventricle (Figure 3A). Visualization and surgical approach to this tumor in the left ventricular apex was with thoracoscopic-assisted resection through the aortic valve orifice (Figure 3B). The patient did well and has had no further problems.[30]

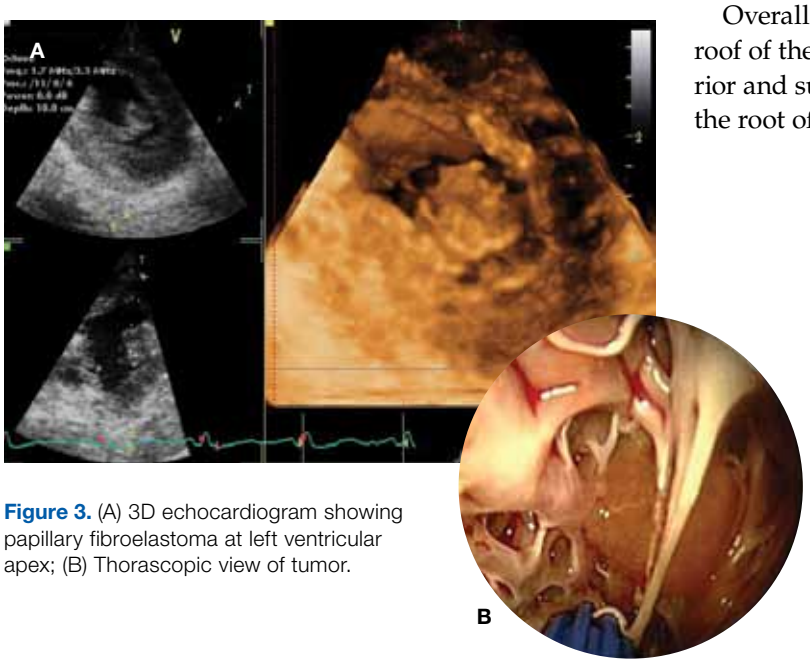

Figure 3. (A) 3D echocardiogram showing papillary fibroelastoma at left ventricular apex; (B) Thorascopic view of tumor.

Cardiac paraganglioma

The next most common benign cardiac tumor in our experience has been the paraganglioma. We have operated on 6 cardiac paragangliomas, and this high incidence likely represents a referral pattern to our cardiac tumor center, rather than a true incidence of these uncommon tumors in the general population. Paragangliomas are rare tumors of neural crest origin. Cardiac paragangliomas account for only about 0.3% of all mediastinal neoplasms, and less than 50 cases were reported in the world literature as recently as 1992.[31] Cardiac paragangliomas are highly vascular tumors that usually involve the roof of the left atrium[32] but can occur around the intrapericardial aorta, or the right atrium and ventricle. They tend to parasitize the coronary blood flow, which gives them a soft, brownish appearance at surgery, and major hemorrhage is a substantial risk of biopsy or resection.[31] The biologic activity that is usually seen in adrenal pheochromocytomas is rarely seen in cardiac paragangliomas. Clinical presentation can be incidental, or these tumors can present with heart failure due to obstruction of intracardiac or coronary blood flow. Coronary ostial obstruction can also lead to ischemia or conduction abnormalities, which also can occur if there is tumor encroachment on AV nodal tissue. "Hormonally active cardiac paraganglioma" is the terminology for biologically active cardiac paragangliomas rather than pheochromocytoma, which is confined to hormonally active adrenal paragangliomas. Of our 6 patients with cardiac paraganglioma, none of them had a hormonally active tumor. All tumors were very large and extremely vascular in nature, as seen in 1 patient's angiogram depicted in Figure 4.

Overall in our series, 5 of the tumors occurred in the roof of the left atrium and involved most of the posterior and superior left atrial wall. One tumor involved the root of the aorta (Figure 5A, CT scan; Figure 5B,

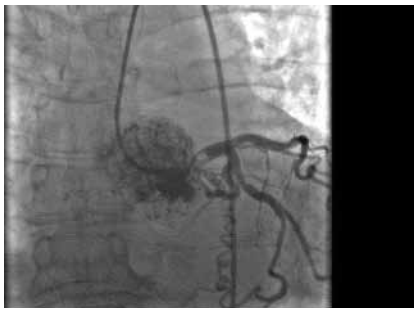

Figure 4. Coronary angiogram with vascular blush from left coronary artery in a left atrial paraganglioma.

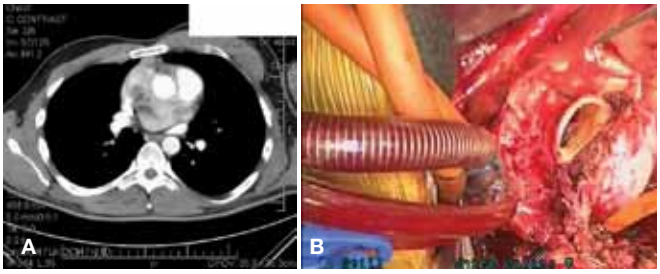

Figure 5. (A) CT scan showing aortic root paraganglioma; (B) surgical view after resection and aortic root reconstruction.

intraoperative photo) and was resected, which involved replacing the root with an allograft.[33] The patient did well and has had no return of tumor or other problems. Of the 5 left atrial paragangliomas, 3 were large tumors involving the entire posterior left atrial wall and required cardiac autotransplantation for complete resection. All of these patients did well and have not had any subsequent problems. Two of the cases required transection of the aorta and pulmonary artery in order to achieve surgical resection. Of these 2 patients, 1 did well and the second, which was a third-time redo for recurrence, developed severe right heart failure and died, putting the overall mortality in our paraganglioma group at 16%.

Hemangioma

Cardiac hemangiomas are extremely rare primary tumors of the heart. They comprise 2%–5% of benign tumors and can arise from all layers of the heart, including endocardium, myocardium and epicardium. Most common locations in the heart include ventricles, atria and tricuspid valve. They can also arise from the pericardium, as we have described in 1 patient (TEE), (Figure 6).[34] Although these tumors are extremely rare, they can cause outflow tract obstruction, valvular regurgitation, dysrhythmia and embolization. Diagnosis is made by TEE, CT scan, MRI or cardiac catheterization, which demonstrates a tumor blush. The natural history ranges from dormancy, accelerated growth or spontaneous regression. The mainstay of treatment includes operative intervention with resection or close observation, depending on symptomatology.

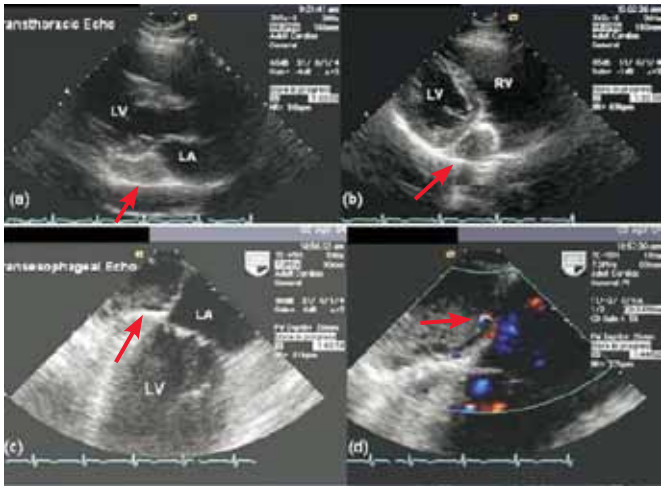

Figure 6. Hemangioma arising from pericardium.

Lipoma

Lipoma is usually the third most common benign cardiac tumor seen, although we have only operated on 1 cardiac lipoma in our experience. Most of these do not cause symptoms, and have been resected in the past because of the uncertainty of the diagnosis and risk of leaving a malignant tumor. These tumors have a typical T1 and T2 signal on cardiac MRI that readily classifies them as a lipoma, and they are usually followed.[35, 36] If surgical resection is required (i.e., obstructive physiology), then routine cardiac surgical techniques can be employed with relatively low risk.

Fibroma

Fibromas are more common in children and are the second most common benign primary cardiac tumor in children, with most diagnosed by 2 years of age. Only about 100 of these unusual tumors have been reported in the literature. They are not inherited or associated with other disease. They are firm, nodular, gray-white tumors that tend to be large in size. When symptomatic, it is usually because the tumor impairs normal cardiac function by interfering with valve function or cardiac blood flow. Successful, complete surgical excision is curative, but can be difficult due to the large tumor size.[37] Cardiac orthotopic transplantation has been used, but carries all the attendant problems and risks of heart transplantation.[38]

Our 1 case was a 35-year-old female with a large left ventricular tumor that was resected, and the left ventricle was reconstructed with bovine pericardium (Figure 7). The patient did well for 4 days and then developed severe mitral regurgitation. She was

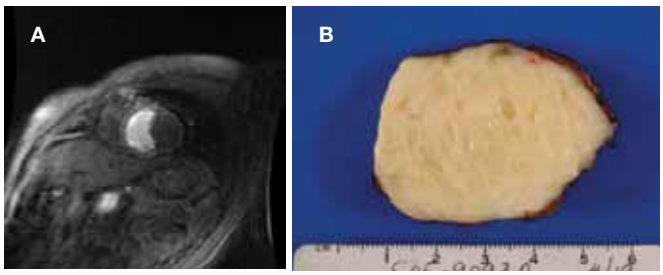

Figure 7. (A) Patient with a large left ventricular fibroma; (B) resected specimen.

returned to surgery and found to have disruption of her antero-lateral papillary muscle, which was close to the tumor resection margin. Mitral valve replacement was performed, and the patient has done well for the last 5 years without further problems.

Castleman's disease

Castleman's disease is a poorly understood, benign lymphoproliferative disease that may behave in a malignant fashion, depending on the structures it invades. Our 1 case was a patient whose tumor invaded the left ventricle and obstructed the proximal left anterior descending coronary artery. A coronary stent was placed, but a fistula later developed in communication with the tumor, leading to a large anterior-wall myocardial infarction. Due to the patient's progressive heart failure, heart transplant was considered but rejected by the outside institution due to the possibility of the tumor being malignant. The patient was referred to our institution for tumor removal and possible heart transplant. The patient underwent tumor removal, which required CPB and bypass to the distal left anterior descending artery (Figure 8A). The degree of LV dysfunction eventually required placement of a Thoratec LVAD, and the patient actually recovered (Figure 8B). He received a heart transplant 2 months later and fully recovered. He is now 3 years post transplant and doing well.[39]

Conclusion

Benign cardiac tumors will continue to be present and will require standard cardiac surgery resection techniques. With the advancement in imaging technologies including MRI, patients will benefit from more focused surgical and diagnostic interventions. Those tumors with unusually aggressive behavior and large size may need more invasive strategies, including cardiac autotransplantation techniques. In summary, our significant experience with benign cardiac tumors would suggest that this condition is highly treatable, and surgical intervention is often necessary for cure.

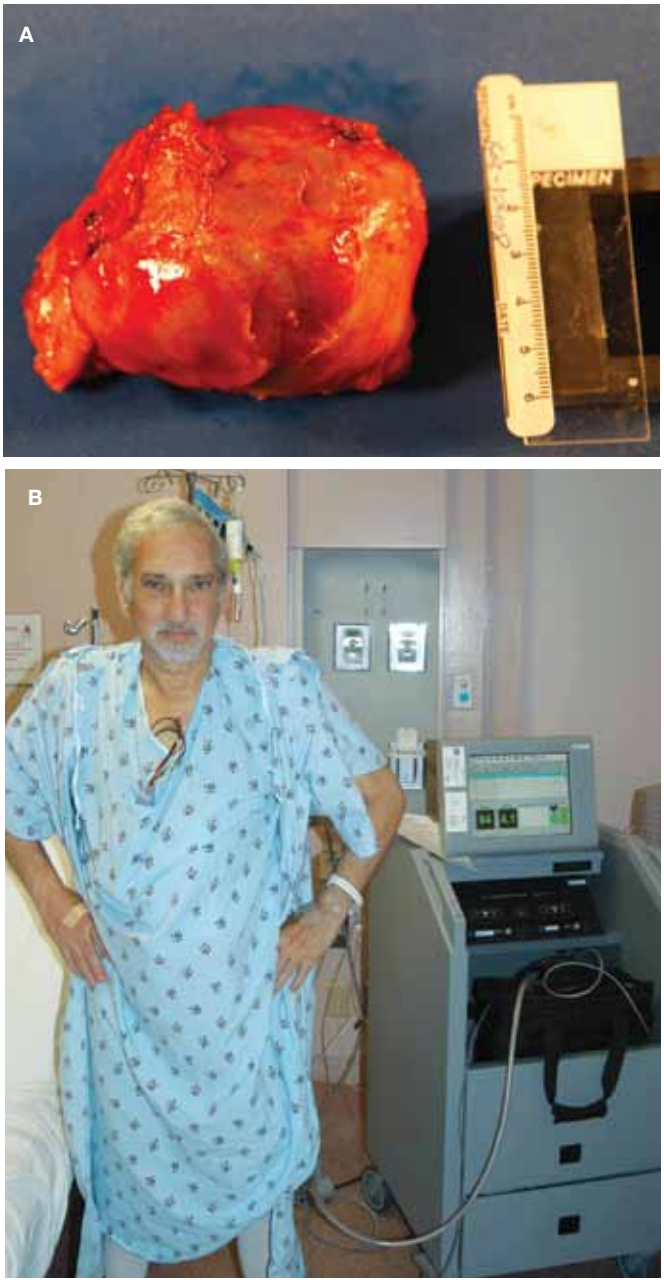

Figure 8. (A) Explanted surgical specimen from patient with Castleman's disease; (B) patient with Thoratec LVAD awaiting cardiac transplant.

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