

THE GREAT SIMULATOR

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ABSTRACT

Cardiac myxoma often simulates multisystem disease and initially defies diagnosis. In this paper, we present three cases of cardiac myxoma in adults. Their clinical features and differential diagnosis will be reviewed, with special emphasis on their insidiousness and suspicion necessary for correct and prompt diagnosis. The role of echocardiography in diagnosis and treatment will be discussed, and finally, the surgical management and prognosis is briefly outlined.

INTRODUCTION

Tumours of the heart, while uncommon, present in protean ways and have challenged the acumen of physicians since the seventeenth century. Antemortem diagnosis however, was rare before 1950 (1). This situation has changed with the advent of angiography and especially with non-invasive cardiac imaging techniques.

Primary tumours of the heart are less common than secondary involvement by metastatic growth. Cardiac myxoma is the most frequent primary tumour and occurs with an incidence of 1-5 per 10,000 autopsies or 2 per 100,000 of the general population. They are commoner in females and usually originate from the mural endocardium in the region of the fossa ovalis within the atria. Over 75% of them are located within the left atrium, 18% within the right atrium, 4% within the left ventricle and another 4% within the right ventricle. Although they are common between the ages of 30 and 60, myxomas have been described in neonates, children and the elderly. Familial occurrence has been reported but cardiac myxomas are typically sporadic.

Other benign primary cardiac tumours include: rhabdomyomas and fibromas (common in children and infants), papillary fibroelastomas, lipomas, mesotheliomas of the atrioventricular node (which can cause

sudden death from complete heart block or ventricular fibrillation), and, vasoformative tumours such as haemangiomas or lymphangiomas. Almost all primary malignant cardiac tumours are sarcomas, most frequently angiosarcomas.

CASE PRESENTATION

The three cases to be presented had come to the attention of the Medical Department of St. Luke's Hospital between April 1990 and March 1991.

Case 1 (Fig. I and II) A.M. was a previously perfectly healthy 40 year old female. She presented with a one month history of dyspnoea on mild exertion, palpitations, anorexia and weight loss but no orthopnoea, paroxysmal nocturnal dyspnoea or ankle oedema. On examination she was found to be tachycardic, with a pulse rate of 120 beats/min, regular in rhythm and volume. Precordial auscultation revealed a loud first sound with a rumbling mid-diastolic murmur of grade 2/6 intensity at the apex. Clinical impression: mitral stenosis.

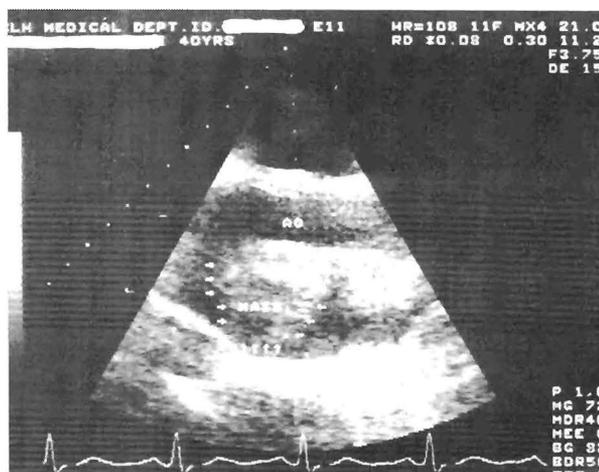


FIG.I Long-axis parasternal view of case 1. The myxoma lies within the left atrium and can be seen to almost obstruct the mitral valve orifice.

TABLE 1

	CASE 1	CASE 2	CASE 3
a) Routine			
ESR (mm 1st hr)	110	?	140
Hgb (g/l)	11.3	14.5	10.1 (indices normal)
WBC (X 10 exp9/l)	11.5	8.1	6.8
CXR	Minimal cardiomegaly	Cardiomegaly Pulmonary venous congestion	Moderate cardiomegaly Perihilar venous congestion Left lower zone shadow No pleural effusion
ECG	Sinus bradycardia P Mitrale	Sinus rhythm P mitrale	New T Wave inversion in limb lead III
b) Echocardiography			
Site	Left atrium	Left atrium	Right atrium
Size (mm)	33 x 35	45 x 45	60 x 45
Character	Pedunculated Slightly lobulated	Pedunculated Calcified borders	Pedunculated Grossly lobulated
Other features	Right atrial enlargement Moderate mitral and tricuspid regurgitation Pulmonary hypertension (Peak RV pressure = 85 mmHg)	Slight left ventricular hypertrophy	Minimal, intermittent mitral regurgitation No pericardial effusion
c) Duration of symptoms from onset to diagnosis	1 month	9 months	2 months
d) Outcome	Operated 5 days after diagnosis - Excision of myxoma - Tricuspid valvuloplasty Patient is alive and well	Operated - Excision of myxoma Patient is alive and well	Developed axillary vein thrombosis and anticoagulated Operated 5 days post-diagnosis Succumbed from massive pulmonary embolism post-op.

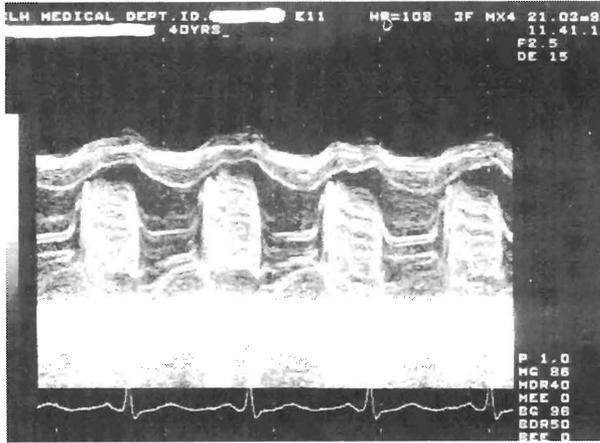


FIG. II M-mode view through the mitral valve orifice of case 1. The short echo-free space between the mitral valve opening and the tumour can be seen. The cloud of tumour echoes behind the anterior mitral valve leaflet almost completely fills the mitral valve in diastole.

Case 2 (Fig. III and IV) P.D. was a 64 year old female with a past history of hypercholesterolaemia, but no hypertension, diabetes mellitus or rheumatic fever, and no previous hospital admissions. She presented with two attacks of pulmonary oedema following retrosternal pain and a choking sensation in the neck over a nine month period. Clinical impression: left ventricular failure secondary to coronary artery disease.

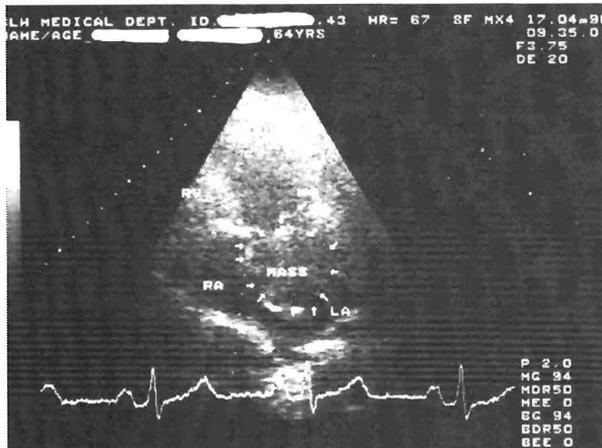


FIG. III Apical 4-chamber view of case 2. The left atrial myxoma lying at the mitral valve orifice.

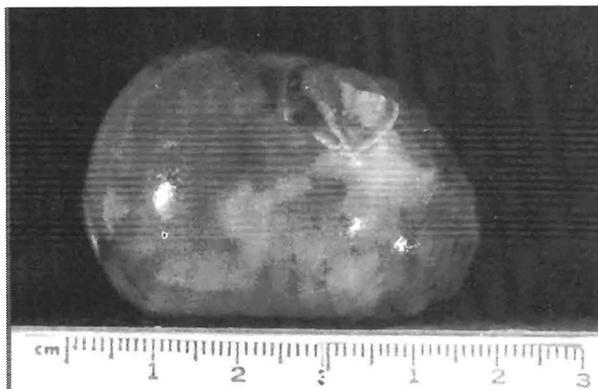


FIG. IV Gross pathological appearance of the left atrial myxoma excised from Case 2. Note the pedicle which was connecting the mass with the left atrium.

Case 3 (Fig.V) P.M. was a 61 year old female with a past history of rheumatic fever in childhood and a right hydronephrosis due to pelvi-ureteric junction obstruction. She presented with a two month history of pyrexia (100-102F) and a dry hacking cough associated with left-sided pleuritic chest pain. On examination she was noted to be pale and showed signs of right-sided heart failure: elevated jugular venous pressure, tender hepatomegaly and gross lower limb oedema. A pericardial rub was heard on precordial auscultation. Clinical impression: recurrent pulmonary embolism.

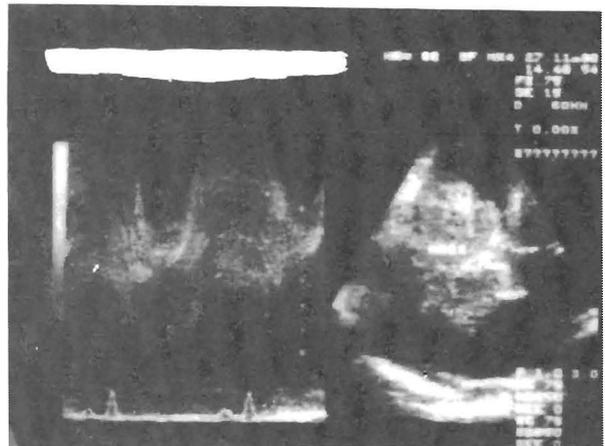


FIG. V Apical 4-chamber view of case 3 with annotated diagram on the extreme right. The tumour mass is seen to move vigorously in and out of the tricuspid valve orifice and can be seen to be multilobulated.

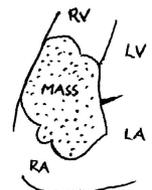


Table 1 indicates the results of the relevant investigations carried out on these patients as well as their clinical outcome. In all three cases, the diagnosis was clinched by echocardiography after a time interval of between one and nine months. Figures 1 through 5, illustrate the gross pathological and echocardiographic appearance of the myxomas in these three cases.

DISCUSSION

a) Clinical features

Intra-cavitary myxomas are characterized by a triad of clinical features: haemodynamic, embolic and constitutional.

The haemodynamic consequences derive from their propensity to obstruct the valvular orifice with resultant mitral or tricuspid stenosis, or, pulmonary vein obstruction. The patient may present with recent onset of cardiac murmurs which progress rapidly without an obvious cause. Prolapse of the tumour through the valve orifice may transiently obstruct the blood flow to such an extent that the cardiac output falls and syncope or even sudden death occurs. Other common presenting features are exertional dyspnoea or palpitations. Frequently, the diagnosis of atrial myxoma comes as a surprise in a patient suspected clinically to have rheumatic mitral stenosis, as was the case in the first patient presented. It is reported that intra-cavitary myxomas continue to be seen in a

ratio of approximately 1 per 100 patients presenting for mitral valve surgery (2). Characteristically, the clinical course is relatively recent in origin, as was the case in our patient. This may help to distinguish atrial myxoma from rheumatic valve disease.

Sometimes, the continual to-and-fro motion of a mobile tumour mass, especially if calcified, results in valvular leaflet damage with mitral or tricuspid regurgitation. This is known as the "wrecking ball" effect and may be severe enough to cause total destruction of the leaflets and require valve repair or even replacement (3).

In none of our cases was a "tumour plop" specifically heard. This early diastolic sound resembles an opening snap and is produced by the impact of the mass on the ventricular wall. Occurrence of the plop requires a large enough mass or a long enough stalk to permit such an impact (4). Classically, the tumour plop varies with posture.

Up to 40 or 50% of patients with atrial myxomas develop embolism of tumour fragments or surface clots. Systemic emboli lodge in the arteries of the brain (5), kidneys or extremities, or even at the aortic bifurcation (6), retinal (7) or coronary arteries with resultant ischaemia or infarction. Indeed the second case presented might have been suffering from coronary artery embolization with angina and left ventricular failure. Emboli to the skin may mimic vasculitis and this may be the reason why the patient presents, often to a dermatologist (8, 9). Right-sided myxomas may embolize to the lungs, with resultant pulmonary infarction and/or pulmonary hypertension. Case 3 was probably suffering from recurrent pulmonary emboli with pulmonary infarction and overlying pleural irritation. Paradoxical embolism may also occur to the systemic circulation via an atrial septal defect. All these emboli may be or become septic.

The third element of the triad concerns the constitutional manifestations which occur in up to 90% of patients with cardiac myxomas, hence their reputation of being "the great simulators" of connective tissue disease. This systemic upset occurs more frequently if the myxoma lies within the right atrium. However the presumed proteinaceous substances released by the tumour into the circulation are removed or inactivated by the lungs.

Interleukin-6 has been detected in the serum of patients with cardiac myxomas if they are accompanied by systemic features. The levels were higher than those found in patients with active rheumatoid arthritis and dropped down to undetectable values when the myxomas were excised (10). This may be one of the agents responsible for the immunologic features similar to those observed in true autoimmune diseases.

Patients may suffer from pyrexia, weight loss, myalgia, arthralgia or fatigue. Typically, there is an accelerated sedimentation rate with elevated levels of IgG, with an anaemia (often haemolytic) or polycythaemia. There

may also be leucocytosis, thrombocytopenia, clubbing and Raynaud's phenomenon. Generalized amyloidosis of the AA-type protein has been described (11). Auto-antibodies with immune complex formation have also been found (12).

Some of these features of multisystem involvement were present in all the cases presented above, especially in the third patient who had very florid features of a systemic illness. Her pericardial rub suggested pericarditis which was not associated with a pericardial effusion.

Recently, a subset of patients with "syndrome myxoma" (13) or "Carney's complex" (14), has been distinguished from the larger group of patients with the commoner sporadic myxoma. This subset is characterized by the presence of multiple pigmented cutaneous lesions, non-cardiac myxoid tumours or neurofibromas and multiple endocrine neoplasms (adrenal, testicular or pituitary). These patients are usually younger and often have affected family members.

b) Differential diagnosis

Cardiac myxomas can simulate many other diseases and must therefore be considered in their differential diagnosis. Special care must be taken to exclude it in all cases of multisystem disease, vasculitis, pyrexia of unknown origin, mitral or tricuspid valvular disease, as well as infective endocarditis or ischaemic heart disease. The correct diagnosis will be made if a high index of clinical suspicion is maintained in patients with diverse and protean features, especially when cardiac, embolic and constitutional manifestations co-exist.

c) Diagnostic methods

Echocardiography can evaluate the exact size, shape, location and attachment site of the tumour, as well as the valvular integrity and myocardial function. Indeed, for many years, this was one of its most central roles. It is also used serially in patient follow-up. 2-D mode echo in real time is sufficiently reliable to permit immediate operative intervention without the need for additional invasive studies. It is now also being performed intra-operatively via the trans-oesophageal route to provide guidance in the selection of the most appropriate surgical approach (15). In addition, trans-oesophageal echocardiography can better detect myxomas that are bi-atrial or multiple or in the presence of chest deformity.

Echocardiographic diagnosis is not always easy, as it can be very difficult to distinguish a myxoma from a ball thrombus. However, even in this latter case, surgical exploration is necessary. Doppler studies demonstrate the haemodynamic consequences by detecting the flow velocity patterns across the valvular orifices.

Once a diagnosis of myxoma is made, a second concurrent tumour should always be carefully sought as multiple tumours within the same heart are common (16). If

multi-centric tumours are in fact found, then all other members of the family should be screened echocardiographically.

The diagnosis may be confirmed by gated radio-nucleide imaging techniques and/or by magnetic resonance imaging.

If coronary artery disease is suspected, coronary angiography should be carried out. This may reveal neovascularisation (through branches of the coronary arteries) and outline the presence of shunts: left-to-left through the tumour (17) or right-to-left through a patent foramen ovale (18). Significant and operable coronary artery disease may be found, especially in the more elderly population (19). Unfortunately, we lack details of the coronary angiography performed on case 2.

d) Other investigations

Possible clues to the diagnosis may be provided by the electrocardiogram and chest X-ray. The former may show evidence of atrial enlargement and pulmonary hypertension; the latter may reveal unusual bulges in the cardiac silhouette or normal sized heart in the presence of severe cardiac failure.

e) Management and prognosis

Surgical excision is the only acceptable form of treatment that prevents tumour emboli and sudden death. Referral for excision becomes urgent when there is evidence of prior embolic events, when there have been syncopal attacks and when there is echocardiographic

evidence of a multilobulated mass. The third patient had this latter feature on her echocardiogram. She was in fact operated promptly, but succumbed shortly afterwards from pulmonary embolism which is a recognized complication after surgery for right atrial myxomas.

The prognosis of myxomas is good, as these tumours are invariably benign and have a 20-year survival of over 90% (20). Local invasion is unknown but tumour recurrence is common, reaching even 5% in 5 years, hence the need for regular post-operative echocardiography. Recurrence may be explained either by incomplete excision of the base or by a truly multi-centric growth pattern. In fact, the risk of recurrence is much higher when the myxoma is of the familial type (21). The DNA ploidy pattern of the myxoma seems to be sensitive for detecting biologically unusual tumours with a high risk of recurrence (22). Metastatic growth is exceptional, though it may occur by embolic spread to the brain or skin. All patients presenting with myxomas in unusual locations of the body should have complete cardiac evaluation to exclude the presence of a primary cardiac myxoma (23).

CONCLUSION

Cardiac myxomas, although rare, are great simulators of other diseases and often present insidiously. A high index of clinical suspicion should be maintained to ensure that the diagnosis is made promptly, before complications arise. Echocardiography will usually confirm the diagnosis and guide further management.

REFERENCES

- Hall RJ, Cooley DA, McAllister HA, Frazier OH: Neoplastic Heart Disease in Hurst JW (Ed): *The Heart*. McGraw Hill 1990; p.1382-1389.
- Peters MN, Hall RJ, Cooley DA, et al: The clinical syndrome of atrial myxoma. *JAMA* 1974; 230:694.
- Turlapati RV, Jacobs LE, Kotler MN: Right atrial myxoma causing total destruction of the tricuspid valve leaflets. *Am Heart J* 1990; 120: 1227-1231.
- Keren A, Chenzbruna A, Schuger L, Milgarter E, Tzivoni D: The aetiology of tumour plop in a patient with huge right atrial myxoma. *Chest* 1989; 95: 1147-1149.
- Marazuela M, Garcia Merino A, Yebra M, Brasa JM, Diego J, Durantez A: Magnetic resonance imaging and angiography of the brain in embolic left atrial myxoma. *Neuroradiology* 1989; 31: 137-139.
- Weerasena NA, Groome D, Pollock JG, Pollock JC: Atrial myxoma as the cause of acute lower limb ischaemia in a teenager. *Scott Med J* 1989; 34: 440-441.
- Yasuma F, Tsuzuki M, Yasuma T: Retinal embolism from left atrial myxoma. *Jpn Heart J* 1989; 30: 527-532.
- Feldman AR, Keeling JH: Cutaneous manifestations of atrial myxoma. *J Am Acad Dermatol* 1989; 21: 1080-1084.
- Reed RJ, Utz MP, Terezakis N: Embolic and metastatic cardiac myxoma. *Am J Dermatopathol* 1989; 11: 157-165.
- Jourdan M, Bataille R, Segiun J, Zhang XG, Chaptal PA, Klein B: Constitutive production of interleukin-6 and immunologic features in cardiac myxomas. *Arthritis Rheum* 1990; 33: 398-402.
- Wens R, Goffin Y, Pepys MB, Kutnowski M, Van Beers D, Decodt P, Verbanck M: Left atrial myxoma associated with systemic AA amyloidosis. *Arch Intern Med* 1989; 149: 453-454.
- Maisch B: Immunology of cardiac tumours. *Thorac Cardiovasc Surg* 1990; 38 Suppl 2: 157-163.
- Vidaillet HJ, Seward JB, Fyke FE, Su WPD, Tajik AJ: "Syndrome myxoma": a subset of patients with cardiac myxoma associated with pigmented skin lesions and peripheral and endocrine neoplasms. *Br Heart J* 1987; 57: 247-255.
- Cheung PS, Thompson NW: Carney's complex

- of primary pigmented nodular adrenocortical disease and pigmentous and myxomatous lesions. *Surg Gynecol Obstet* 1989; 168: 413-416.
15. Milano A, Dan M, Bortolotti U: Left atrial myxoma: excision guided by transoesophageal cross-sectional echocardiography. *Int J Cardiol* 1990; 27: 125-127
 16. Nass PC, Niemeyer MG, Brutel De La Riviere A, Brune DF, Plokker HW: Left atrial and right ventricular cardiac myxoma. A case report. *Eur J Cardiothorac Surg* 1989; 3: 468-470.
 17. Jorens PG, Van Del Heuvel PA, Van Cauwelaert PA, Parizel GA: Myxoma with a left-to-left shunt and fistula. *Chest* 1989; 96: 945-946.
 18. Lee JJ, McKenzie FN, Novick R: Right atrial myxoma with cyanosis due to right-to-left shunting. *Can J Cardiol* 1990; 6: 262-264.
 19. Fueredi GA, Knechtges TE, Czarnecki DJ: Coronary angiography in atrial myxoma; findings in 9 cases. *Am J Roentgenol* 1989; 152: 737-738.
 20. Bortolotti U, Maraglino G, Rubino M, Santini F, Mazzucco A, Milano A, Fasoli G, Livi U, Thiene G, Gallucci V: Surgical excision of intracardiac myxomas: a twenty-year follow-up. *Ann Thorac Surg* 1990; 49: 449-453.
 21. Larsson S, Lepore V, Kennergren C: Atrial myxomas: results of 25 years' experience and review of the literature. *Surgery* 1989; 105: 695-698.
 22. McCarthy PM, Schaff HV, Winkler HZ, Lieber MM, Carney JA: Deoxyribonucleic acid ploidy pattern of cardiac myxomas. Another predictor of biologically unusual myxomas. *J Thorac Cardiovasc Surg* 1989; 98: 1083-1086.
 23. Rupp GM, Heyman RA, Martinez AJ, Jungreis CA: The pathology of metastatic cardiac myxoma. *Am J Clin Pathol* 1989; 91: 221-227.
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