MYXOMA OF THE LEFT ATRIUM*

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With the recent very great advances in cardiac surgery, myxoma of the left atrium is no longer just a pathological curiosity. If the diagnosis is made, a dramatic cure may now be attained by surgical removal of the tumour.[1-5] It is thus thought that the following case, where the correct diagnosis was seriously entertained, but unfortunately not pursued, is of sufficient interest to warrant description and discussion. Prichard[6] has stated that myxoma is the com-

* Paper presented at a meeting of the Transvaal Branch of the Southern African Cardiac Society, 21 May 1959, and submitted for publication on 28 March 1960.

monest primary tumour of the heart and constitutes nearly 50% of primary cardiac tumours.

CASE REPORT

The patient, a 62-year-old White miner, was admitted to the Johannesburg General Hospital on 8 January 1959. He stated that for nearly 2 years he had been mildly breathless on exertion, but that over the last 2 months this had rapidly increased in severity and was now present after walking only a few yards. Seven weeks before admission, he was awakened at night by a severe constricting retrosternal pain, which lasted about 3 hours and was associated with sweating and marked breathlessness. This attack was followed by other short episodes of similar retrosternal pain, occurring mainly on exertion and relieved by trinitrin given him by his general practitioner. Systematic questioning by the house physician (Dr. R. Stephenson) brought out that, for 1 year, the patient had often felt giddy when standing erect.

On examination on admission to the hospital (Dr. R. Gollach and Dr. R. Stephenson) the patient was not in congestive heart failure, no bruits were heard, but a gallop rhythm was audible over the precordium. The chest and abdomen were clinically normal. Ten days later dependent oedema developed, the liver was enlarged 2 fingers below the costal margin, the jugular venous pressure was elevated, and the patient was considered to be in congestive cardiac failure. Soft apical presystolic and mid-diastolic murmurs were subsequently heard on several occasions by both observers. The usual treatment for congestive cardiac failure, including digitalis and a mercurial diuretic, was started on 18 January. On 12 February the patient was referred to the Cardiac Clinic for assessment for mitral valvotomy with the provisional diagnosis of congestive heart failure due to mitral stenosis.

On examination in the Clinic the patient was dyspnoeic and orthopnoeic. Peripheral cyanosis plus sacral and ankle oedema were present. The pulse was 80 per minute, regular, and of small volume. The blood pressure was 80/60 mm.Hg. The jugular venous pressure was raised 10 cm. with a large 'a' wave followed by the systolic wave of tricuspid incompetence. The apex beat was in the 5th left intercostal space on the mid-clavicular line. There was a prominent right ventricular heave at the sternal area. A quadruple rhythm was audible at the apex and lower sternum. Both the intensity of the atrial sound and the time interval between this atrial sound and the first heart sound increased significantly with deep inspiration, thus confirming that the atrial sound was arising from the right side of the heart.[7] A grade 2[8] regurgitant systolic murmur of tricuspid incompetence was audible on inspiration near the xiphisternum. The second heart sound was narrowly split, unaffected by respiration, and there was some increase in the intensity of the pulmonary component. No diastolic murmurs were heard. Chest movement was good and, except for a few crepitations at the right base, the lungs were clinically clear. The liver was enlarged 3 fingers below the right costal margin but no direct pulsation of this organ was detected.

An ECG (Fig. 1) showed right axis deviation, marked clockwise rotation, and some right ventricular hypertrophy. Chest X-rays (Figs. 2 and 3) showed some cardiomegaly (cardiothoracic ratio 55%) with right ventricular enlargement, a prominent pulmonary artery, and a straightened left heart border. Slight enlargement of the left atrium was detected in the right oblique view (Fig. 3). The lungs were congested, with prominence of the superior pulmonary veins. No Kerley 'B' lines were seen.

The blood count showed a mild normochromic anaemia (Hb. 12 g.%). The sedimentation rate, performed on several occasions, varied between 20 and 50 mm. per hour (Wintrobe). The blood urea was 45 mg. % on admission and 94 mg. % 6 weeks later; the urine was normal. These figures were regarded as compatible with congestive heart failure. There was an occasional pyrexia of 99·5°F during the hospital course.

The patient therefore had the physical signs of severe right ventricular failure with pulmonary hypertension and functional tricuspid incompetence. Recurrent pulmonary embolism was regarded as the possible cause, with a left atrial myxoma as the most likely alternative. Significant mitral stenosis was thought to be unlikely.

It was decided to treat the patient with anticoagulant therapy and to observe progress. Unfortunately, he died suddenly 3 weeks later.

At necropsy a large myxoma was found filling the left atrium. The mitral valve was normal. The right ventricle was hypertrophied and dilated, with functional incompetence of the tricuspid valve. There was passive venous congestion of systemic organs and some congestion of the pulmonary veins. On histological examination of the lungs, the pulmonary arterial system was 'remarkably normal' and no evidence of intimal proliferation or medial hyperplasia was observed.

CLINICAL FEATURES OF LEFT ATRIAL MYXOMA

A review of some of the reported cases of left atrial myxoma indicates that the clinical course follows a fairly typical pattern. The clinical features can be divided into 3 main groups as follows:

1. *Features dependent on intermittent obstruction of the mitral valve orifice (sometimes precipitated by postural changes)*

Attacks of *dizziness or fainting* are common.[6,9-14] Episodes of *sudden acute breathlessness* occur,[9-13,15-19] and these are sometimes associated with *chest pain* indistinguishable from that of myocardial ischaemia.[6,9,11,12,14,16,20] *Cardiac arrhythmias*, which may be initiated by a postural change, have also been reported[9] but generally seem to be rare. *Systolic and diastolic murmurs*, usually associated with the diagnosis of mitral incompetence or stenosis, are commonly but not invariably present at some period of the clinical course. These murmurs may vary in intensity and character, sometimes depending on the position of the

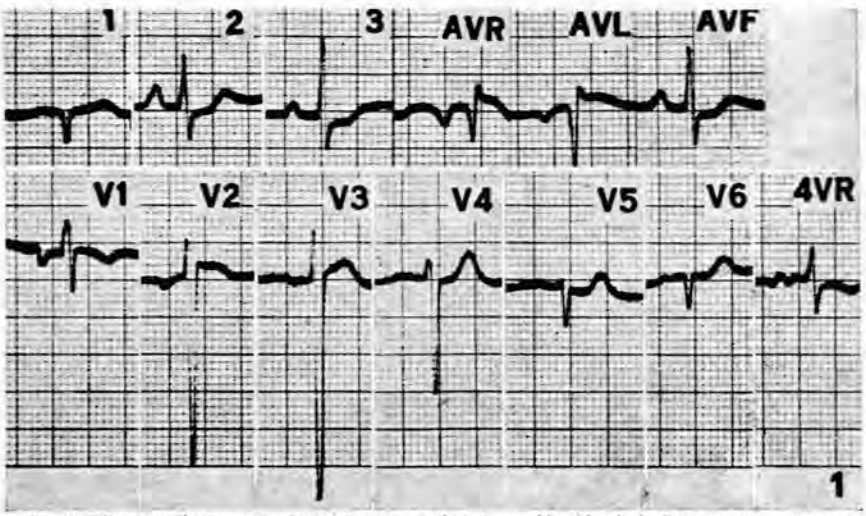

Fig. 1. Electrocardiogram showing right axis deviation, considerable clockwise rotation, and some right ventricular hypertrophy.

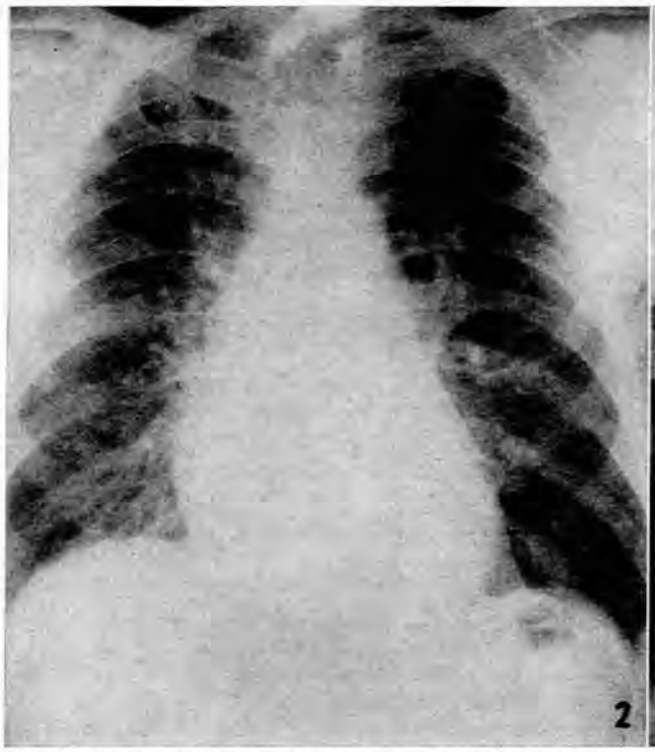

Fig. 2. Postero-anterior radiograph showing cardiomegaly, 'mitralized' heart, prominent superior pulmonary veins, and 'congested' lung fields.

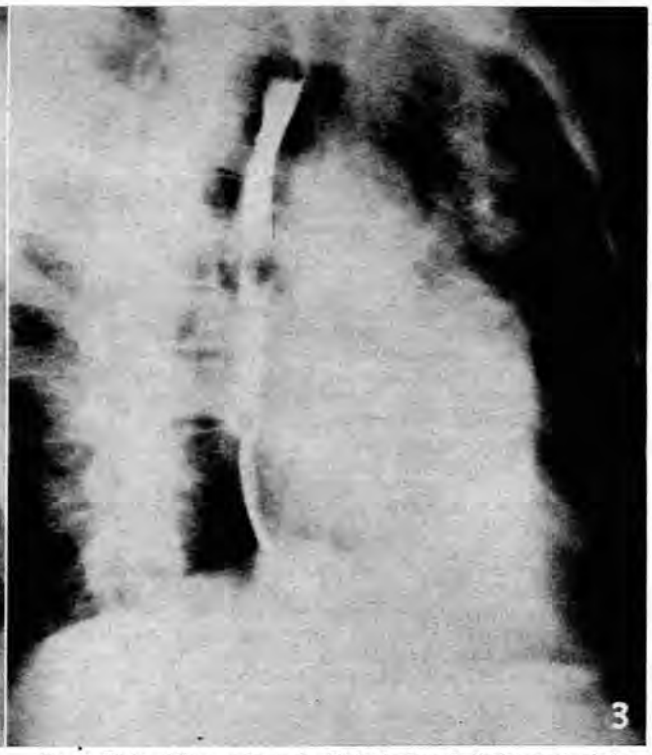

Fig. 3. Right oblique radiograph. Slight backward displacement of the barium-filled oesophagus is seen in the region of the left atrium.

patient.[11,18,21,22] *Sudden death* is usual[12,13] and is reputed to occur occasionally without any preceding symptoms.[4,9]

2. *Features due to gradual left atrial or mitral valve orifice obstruction*

Although several other signs and symptoms of left atrial myxoma usually precede it, progressive and intractable *right ventricular failure* will sooner or later always occur.[3,4,10-15,18,20,21,23-26]

The congestive heart failure may show temporary improvement with diuretic and digitalis therapy, but deterioration inevitably follows soon unless the tumour is surgically removed.

As already mentioned, perhaps the commonest feature of reported cases has been the presence of murmurs simulating mitral valve disease.[1-5,10,13,14,17,18,20,24,25] These have, in fact, often resulted in the diagnosis of rheumatic mitral valvular disease and not infrequently the correct diagnosis has been established at operation intended for mitral valvotomy.[1,2,4,5,17]

Obstruction by a myxoma to blood flow, either in the left atrium or at the mitral valve orifice, results in some *left atrial enlargement*, which may be detected on the X-ray[1,3-5,10,17,18,20,26] or the electrocardiogram.[1,2,20] *Pulmonary venous hypertension* will also occur and might be detected radiologically by the presence of distended superior pulmonary veins and possibly Kerley 'B' lines. Chest X-rays in reported cases have often shown 'pulmonary congestion',[10,13,16,18] but there has been little comment on whether it was known to be venous in origin. Kerley 'B' lines have seldom been mentioned.

3. *The 'subacute bacterial endocarditis syndrome'*

The association of *anaemia, intermittent mild pyrexia, malaise* and a *raised sedimentation rate* in many patients with left atrial myxoma creates a clinical picture similar to that of subacute bacterial endocarditis.[11,13,14] The varying mitral murmurs might also suggest this diagnosis. *Systemic emboli*, sometimes causing transient or permanent neurological signs, have been frequently encountered[2,3,10,15,18-20,23] and are again compatible with the diagnosis of subacute bacterial endocarditis.

DIAGNOSIS OF LEFT ATRIAL MYXOMA

A study of the relevant features of this and previously reported cases suggests that the following conditions should be considered in the differential diagnosis:

1. *Mitral Stenosis or Incompetence*

The presence of an apical mid-diastolic murmur in a patient in right ventricular failure is suggestive of mitral stenosis and this is the diagnosis which has usually been made. A bifid P wave sometimes present on the EGG, plus the radiological appearances of a dilated left atrium, pulmonary venous congestion, and an enlarged right ventricle and pulmonary artery, might seem compatible with this diagnosis; so might any associated features of the 'subacute bacterial endocarditis syndrome'.

It would be most unusual, however, for any case of mitral stenosis, provided that uncontrolled atrial fibrillation or other arrhythmia was not present, to develop right heart failure unless the pulmonary vascular resistance was considerably increased.[27] An increased pulmonary vascular resistance in such cases can be detected on the ECG in

that evidence of marked right ventricular hypertrophy is seen.[27,28] Such evidence is lacking both in this patient (Fig. 1) and in all the reported cases that have been encountered. Unfortunately, the actual ECGs have seldom been reproduced, but the interpretation commonly given by the various authors has been that of right axis deviation, clockwise rotation, and sometimes associated right ventricular strain.[4,11,13,16,18,26] Recently Evans,[29] in his description of 2 cases who died from left atrial myxoma, made the point that the 'ECG showed only right ventricular duress short of ventricular preponderance'. Both of his patients had been in heart failure and the one ECG illustrated (p. 203 of his article[29]) does not show the degree of right ventricular hypertrophy that would be expected in a case of mitral stenosis causing right ventricular failure.

It seems that it is this absence of appreciable right ventricular hypertrophy on the ECG which is the most important factor in excluding the diagnosis of mitral stenosis in this and other cases of left atrial myxoma. In a recent paper Rodriguez Torres *et al.*[28] have accepted an R/S or R′/S ratio in lead VI greater than 1·0 mv., with R or R′ greater than 0·5 mv., as the commonest ECG sign of right ventricular hypertrophy in mitral stenosis with a raised pulmonary vascular resistance. When, however, the pulmonary vascular resistance is great enough to cause right ventricular failure, it is probably fair to say that the ECG shows very marked right ventricular hypertrophy, with a large dominant R or R′ in VI and a very small or even absent S wave. T waves over the right precordial leads are usually deeply inverted.

Another feature which helped to exclude significant mitral stenosis in the present patient was the absence of a bifid P wave on the ECG and the minimal left atrial enlargement seen radiologically. Some ECG evidence of left atrial enlargement is probably always present in patients with sinus rhythm in right ventricular failure from mitral stenosis, but P-wave enlargement has been absent or inconspicuous in many cases of myxoma.[4,10-12,14,18,20,25,26] Left atrial enlargement on X-ray has also sometimes been absent or only slight in other patients with myxoma,[5,11,12,16-19] and this again would be unusual in significant mitral stenosis. Here, however, it must be remembered that radiological signs of left atrial enlargement are often not great in mitral stenosis if the pulmonary vascular resistance is raised.[27]

There was no mid-diastolic murmur on the several occasions that I examined this patient and that again would have been most atypical for significant mitral stenosis. It is appreciated that patients with tight mitral stenosis may have a very soft murmur, or perhaps even no audible murmur,[30] but patients in that group have a greatly increased pulmonary vascular resistance with consequent ECG evidence of marked right ventricular hypertrophy. In some patients with left atrial myxoma no mid-diastolic murmur was heard at any stage[11,12,16,19] and in others the murmur was variable.[3,4,13,18] Provided no tachycardia is present, it is probably exceedingly rare for any case of tight mitral stenosis to have no mid-diastolic murmur on careful auscultation. An absent or variable mid-diastolic murmur should always cause the diagnosis of mitral stenosis to be questioned.

There has been much emphasis in the literature on the symptoms and signs resulting from intermittent complete or almost complete obstruction of the mitral orifice by the tumour. It is agreed that when such features are present in a case of apparent mitral stenosis they should arouse suspicion of the possibility of a myxoma. It should, however, perhaps be remembered that attacks of breathlessness, angina, syncope and paroxysmal arrhythmias may all occur in patients with mitral stenosis with or without a ball-valve thrombus in the left atrium.

The question of whether an opening snap can ever be produced by a normal valve still remains uncertain. Leatham[31] has stated that an opening snap of the normal tricuspid valve can be recorded with the phonocardiograph (PCG) in atrial septal defect. This sound, however, could not be demonstrated in recent PCG observations on 20 cases of atrial septal defect, and an opening snap has not yet, in fact, been encountered in any condition where both mitral and tricuspid valves were normal.[32] There have been several cases of left atrial myxoma where the authors considered that an opening snap was audible and autopsy or operation later confirmed that the mitral valve was normal.[1,2,17,33] In only one of these[17] is a PCG published and that, though technically not good, shows a loud sound varying in time between 0·08 and 0·10 seconds after closure of the aortic valve, but also varying very greatly in intensity from beat to beat. The PCG appearances of this sound seem to be unusual for an opening snap of the mitral valve. It seems possible that the sound is due to a movement of the tumour just after the mitral valve has opened. In any event, the presence of an opening snap, or a sound similar in character and timing to an opening snap, is rare in left atrial myxoma; it has even been stated[3] that the absence of an opening snap in a patient with 'mitral stenosis' should, in fact, suggest the possibility of a myxoma. Since it is not uncommon, especially when the mitral valve is calcified, for cases of tight mitral stenosis to have no opening snap, that argument also loses some importance.

The patient reported here had a quadruple rhythm, and the atrial sound was clearly shown on a PCG (Fig. 4).

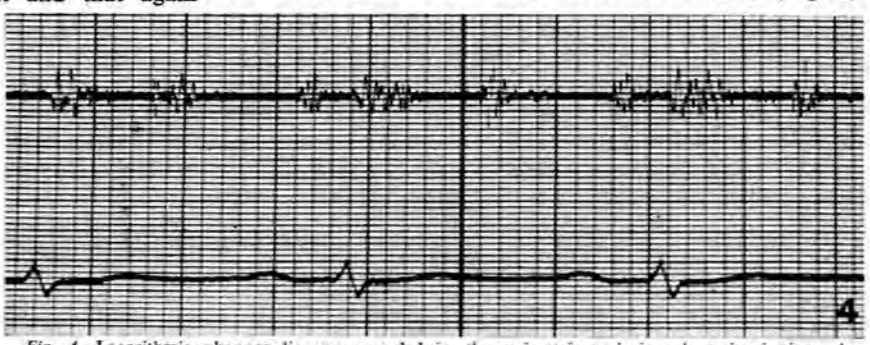

Fig. 4. Logarithmic phonocardiogram recorded in the epigastrium during deep inspiration. A loud atrial sound is clearly seen

A right atrial gallop is not uncommon in cases of cor pulmonale, but is rarely heard in patients with mitral stenosis.[32] This was yet another feature against that diagnosis. Other reports on left atrial myxoma have sometimes mentioned gallop rhythm, but either the type of gallop was not specified or else it was thought to be protodiastolic (i.e. 'third heart sound gallop').[10,26,29]

Apical systolic murmurs are not infrequent in cases of left atrial myxoma and have often been attributed to mitral incompetence. These systolic murmurs, like the mid-diastolic murmurs, may sometimes vary with positional changes[3,4,12,14,18,20] and this sign should always be sought where a myxoma is suspected. There was no apical systolic murmur in the present patient. The regurgitant systolic murmur, audible in the epigastrium and lower sternal area, increased markedly with inspiration and was almost certainly caused by functional tricuspid incompetence. It is not unusual for a systolic murmur of tricuspid incompetence to be heard near the apex, and it seems possible that some of the systolic murmurs in other cases of left atrial myxoma were due to this cause. When, however, a systolic murmur does arise at the mitral valve it possibly results because the partially protruding tumour does not allow the mitral valve cusps to close completely.[1] A diagnosis of significant organic mitral incompetence is unlikely to be confused with that of left atrial myxoma in view of the absence of left ventricular enlargement in the latter condition.

It has been suggested that the relatively short period, often from 18 months to 2 years, between the onset of symptoms and the development of right ventricular failure in cases of myxoma would be atypical for mitral stenosis.[9,13,14,26] This may generally be true, but longer histories, ranging from 4 to 23 years, have also been encountered.[4,10,20,26]

Some authors state that left atrial myxoma should be considered in any patient showing features of mitral stenosis but with no history of rheumatic fever.[3,5,9,14,26] The absence of such a history in patients with mitral stenosis, however, is surely far too common for this to be of much value. Wood[27] has estimated that a history of rheumatic fever, subacute rheumatism, or chorea, is obtained in only 60% of cases of mitral stenosis.

2. *Cor Pulmonale*

It has already been mentioned that intractable right ventricular failure will develop sooner or later in all patients with left atrial myxoma except in those rare instances where sudden death occurs early in the course of the illness. It is thus understandable that lung disease or pulmonary vascular obstruction should be entertained as the cause of the right heart failure. The present patient was, in fact, thought to be a case of cor pulmonale with (since there was no clinical or radiological evidence of primary lung disease) multiple small pulmonary emboli as the likely aetiological factor. In Lekisch's case,[11] however, where the chest X-ray showed a diffuse mottling of both lung fields, the diagnosis of metastatic carcinoma of the lungs and Hamman-Rich syndrome had been considered.

When there is no apical mid-diastolic murmur, as is sometimes the case in patients with left atrial myxoma, the differentiation of right ventricular failure due to left atrial myxoma from that following pulmonary arterial obstruction or lung disease, must depend largely on the presence or absence of evidence of pulmonary venous hypertension and left atrial enlargement on the X-ray, and of large bifid P waves on the ECG. This differentiation may be difficult, but the present patient's X-rays did show distended superior pulmonary veins and a slightly enlarged left atrium. These radiological appearances should, in retrospect, have resulted in left atrial myxoma being even more strongly suspected than it was at the time.

3. *Occlusion of Pulmonary Vein*

A chronic granulomatous lesion of the mediastinum, usually of unknown aetiology, may cause constriction of the main pulmonary veins.[26,29,34] Pulmonary venous hypertension ensues and is followed by a raised pulmonary arterial pressure, right ventricular failure, and death. The course of the illness ranges from 4 to 10 years and the predominant symptoms are dyspnoea, haemoptysis, and finally those of intractable right ventricular failure.[34] Chest X-ray seldom shows the mediastinal mass but pulmonary venous congestion is apparent.

This rare condition understandably has many features similar to those of left atrial myxoma.[26,34] Absence either of left atrial enlargement or of a mitral diastolic murmur might favour constriction of the pulmonary veins, but angiocardiography should always be performed in doubtful cases.

4. *Ischaemic Heart Disease*

A history of episodes of constricting precordial pain, often associated with sweating, breathlessness or syncope, and later followed by congestive heart failure, is clearly compatible with ischaemic heart disease. This diagnosis seemed unlikely in the present patient in view of the severe right ventricular failure without evidence of left ventricular dilitation or definite ECG signs of myocardial ischaemia or infarction. It seems strange, however, that though anginal pain has been a common symptom in many cases of left atrial myxoma, ischaemic heart disease has seldom been mentioned in the literature in discussion of the differential diagnosis.

5. *Cardiomyopathy*

This term was used by Brigden[35] to embrace the relatively rare group of conditions which cause serious non-coronary myocardial disease without significant disease elsewhere. It includes such conditions as familial cardiomegaly, alcoholic cardiomyopathy, cardiac amyloidosis, and the various forms of non-specific 'myocarditis'. Symptoms include angina pectoris, syncope, paroxysmal dyspnoea, and those related to the onset of heart failure. Clinical examination often reveals gross cardiomegaly, gallop or quadruple rhythm, regurgitant systolic murmurs of functional atrioventricular valve incompetence, small pulse pressure and intractable congestive cardiac failure.[35] Sudden death is not unusual, sometimes occurring in patients who had previously had no cardiac symptoms.[35] It will be apparent that these clinical features have some similarity to those described in left atrial myxoma. The radiological appearances of generalized chamber enlargement, however, and the diffuse pathological changes on the ECG, comprising abnormal T waves, low voltage QRS

complexes, intraventricular conduction defects, and abnormal Q waves, are unlike left atrial myxoma and should help to distinguish the cardiomyopathy group.

CONCLUSIONS

The case discussed in this paper showed, in retrospect, many of the classical features of a left atrial myxoma and this diagnosis should probably have been made with confidence. The relatively short history of increasing dyspnoea and orthopnoea, giddiness on standing, and intermittent anginal pain, associated with the signs of intractable right ventricular failure, a varying apical mid-diastolic murmur, several features of the so-called 'subacute bacterial endocarditis syndrome', right axis deviation and extreme clockwise rotation with some right ventricular hypertrophy shown on the ECG, and radiological signs of some left atrial enlargement with pulmonary venous hypertension, were all typical of a left atrial myxoma.

Significant mitral stenosis could be excluded by the absence of electrocardiographic signs of the degree of right ventricular hypertrophy and left atrial enlargement which would be expected in a case of congestive cardiac failure due to this cause. The prominent right-sided quadruple rhythm, the absence of an opening snap, the but slightly enlarged left atrium as seen radiologically, and the complete absence, at times, of an apical mid-diastolic murmur, were all features which also failed to support a diagnosis of mitral stenosis.

In any patient in severe right ventricular failure, with no clinical or radiological evidence of lung disease, it is probably reasonable to suspect recurrent pulmonary emboli as the underlying cause. Attacks of anginal pain and breathlessness are also compatible with that diagnosis. However, this patient had other features, mentioned above, which suggested left atrial obstruction without significant mitral stenosis, and consequently the possibility of a left atrial myxoma arose. It is unfortunate that this possibility was not quickly pursued since an angiogram would almost certainly have shown a large filling defect in the left atrium.[3,4,20,21,23,24,36] Surgery might then not only have saved the patient's life, but also have attained a complete cure.

SUMMARY

A case of left atrial myxoma is described. In retrospect it is realized that the patient showed many typical features of this condition, and the correct diagnosis, which had been seriously considered, should have been made.

The clinical, ECG, and radiological features of cases of left atrial myxoma are described and discussed. It is appreciated that it may be difficult to differentiate cases of left atrial myxoma from those of mitral stenosis, but it is suggested that important differences exist particularly on the ECG. The differential diagnosis of left atrial myxoma is discussed in some detail.

I am grateful to Dr. R. Gollach for permission to present this case to the Transvaal Branch of the Southern African Cardiac Society. My thanks are due to Prof. B. J. P. Becker for the postmortem findings, and to Prof. G. A. Elliott and Dr. B. van Lingen for permission to publish this report.

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