Clinico-Pathological Conference

A male with rheumatic mitral stenosis

THE POSTGRADUATE INSTITUTE OF MEDICAL EDUCATION AND RESEARCH, CHANDIGARH

THE CASE

A 45-year-old man was admitted to the Postgraduate Institute of Medical Education and Research (PGI), Chandigarh in 1980 and diagnosed to have rheumatic heart disease. He was put on digoxin, lasix and potassium supplements, his salt intake was restricted and he was prescribed prophylactic penicillin. His condition deteriorated to class III (by the New York Heart Association classification). Subsequently, he was advised a mitral valve replacement in 1981, but he did not comply.

In December 1988 he was admitted for cardiac catheterization and angiography. By this time he had progressed to class IV symptoms and had episodic streaky haemoptysis and paroxysmal nocturnal dyspnoea. The catheterization procedure was uneventful except that he developed a mild hypersensitivity reaction to the injected radiological contrast. After this he was given a date for operation.

He was admitted on 23 March 1989, for surgery. Soon after admission he developed left-sided pleuritic chest pain, fever, cough and mucoid expectoration.

Examination at admission revealed a middle-aged man of average build and nourishment. There was no pallor, cyanosis, clubbing, pedal oedema or jaundice. The pulse rate was 100/minute and it was irregular. The jugular venous pressure was 4 cm above the clavicle with a sharp v-y collapse and the blood pressure 100/70 mm Hg. There were no peripheral signs of rheumatic activity or infective endocarditis. The precordium was pulsatile and the apex beat felt in the left 6th intercostal space in the axillary line. It was left ventricular in type with a moderate left parasternal heave. The P2 and the main pulmonary artery pulsations were palpable and S2 was loud and variable. The S2 was loud and P2 louder than A2. An opening snap and a mid-diastolic murmur were present at the apex. A grade III/VI pan-systolic murmur was heard at the apex radiating to the axilla. There was a short systolic murmur in the tricuspid area increasing with inspiration. On auscultation of the lungs there were vesicular breath sounds with bilateral basal crepitations. The results of investigations over his three admissions are in Table I.

At admission he was being treated with digoxin, frusemide, potassium chloride and isoptin for congestive cardiac failure and control of the ventricular rate. He was also given co-trimoxazole and deriphylline. During his hospital stay his dyspnoea worsened and he developed a left-sided chest pain without haemoptysis and there was tachypnoea of 56/minute. He was thought to have pulmonary embolism and was started on heparin. However, his condition continued to deteriorate and he developed hypotension and died.

CLINICAL DIAGNOSIS

Chronic rheumatic heart disease with mitral stenosis and regurgitation, pulmonary venous and arterial hypertension, atrial fibrillation (fast ventricular rate). Congestive cardiac failure (partially controlled) and possibly pulmonary embolism.

DIFFERENTIAL DIAGNOSIS

Dr Ramesh Kumar: This patient had heart disease and renal failure. I will start by discussing each of these problems and then speculate on the terminal events.

He had classical physical signs of dominant mitral stenosis (MS), regurgitation (MR) and congestive cardiac failure (CCF). The echocardiogram showed a thickened mitral valve with paradoxical motion of the posterior leaflet, a large left atrium and a mitral valve orifice of 1.0 cm². Cardiac catheterization revealed an end-diastolic gradient between the left atrium and ventricle of 18-20 mm Hg. These findings confirm the diagnosis of severe MS. The left ventricular angiogram showed opacification of the left atrium during ventricular systole, thus establishing the presence of MR as well. The doppler study excluded any associated aortic regurgitation. The aortic root angiogram could not be done as the patient developed hypersensitivity to the contrast.

The pulmonary artery pressure was 43/30 mm Hg with a mean of 36 mm Hg, confirming the diagnosis of severe pulmonary arterial hypertension (PAH). In view of the mitral valve thickening, paradoxical movement of the posterior leaflet and a past history of rheumatic fever, the aetiology was probably rheumatic.

In addition to rheumatic valvular heart disease this patient also had azotaemia with a good urine output. Since his serum creatinine was normal in December 1988 his renal failure was probably of recent origin. In the absence of a urine examination and other relevant investigations I would consider the first possibility to be infective endocarditis. The patient had fever, CCF and renal involvement and the diagnosis of infective endocarditis should be considered in every patient with fever and a heart murmur. So, I strongly suspect it in this patient. The glomerulonephritis in infective endocarditis is of three types.
**Table I. Results of clinical tests**

<table>
<thead>
<tr>
<th>Clinical tests</th>
<th>November 1980</th>
<th>December 1988</th>
<th>March 1989</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/100ml)</td>
<td>14.0</td>
<td>14.6</td>
<td>16.0</td>
</tr>
<tr>
<td>Total white cell count (cmm)</td>
<td>9800</td>
<td>7200</td>
<td>5050</td>
</tr>
<tr>
<td>Differential white cell count</td>
<td>P70, L26, E3, M1</td>
<td>P79, L20, E2</td>
<td>P68, L32</td>
</tr>
<tr>
<td>ESR (first hour)</td>
<td>32</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Urine</td>
<td>Normal</td>
<td>RBC 5–6 HPF</td>
<td>Not done</td>
</tr>
<tr>
<td>Serum Na+/K+ (mEq/L)</td>
<td>132/4.2</td>
<td>138/3.6</td>
<td>137/4.9</td>
</tr>
<tr>
<td>Urea/creatinine (mg/dl)</td>
<td>51/1.2</td>
<td>63/1.3</td>
<td>120/4.0</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Chest X-ray (Fig. 1)</td>
<td>–</td>
<td>Cardiomegaly, left atrial appendage enlarged. Left and right atrium enlarged. Prominent main pulmonary artery and upper lobar veins.</td>
<td>–</td>
</tr>
</tbody>
</table>

**Electrocardiogram (Fig. 2)**

- 20 December 1988
  - 5.0
  - 3.1
  - 2.3
  - 6.5

- 22 December 1988
  - Same as on 20 December 1988 except mitral valve subvalvular apparatus thick. Mitral valve area = 1.0 cm². Doppler showed mitral regurgitation and no aortic regurgitation.

1. Focal and segmental proliferative glomerulonephritis which presents as mild proteinuria, microscopic haematuria with or without azotaemia.
2. Diffuse proliferative glomerulonephritis with azotaemia.
3. Crescentic glomerulonephritis manifests as rapidly progressive renal failure with severe azotaemia and oliguria.

In addition to these lesions, one may also encounter mild to severe endarteritis on renal histology. In this patient, I expect to see diffuse proliferative glomerulonephritis with or without crescents.

A low cardiac output state secondary to CCF may cause mild prerenal azotaemia but this patient never had hypotension or oliguria except terminally. Alternatively, the kidneys may have been involved by multiple renal infarcts secondary to embolization from the heart. A thrombus in the left atrium in one of the echocardiographic studies suggests this possibility. Since the serum creatinine was 4 mg/dl, it would be expected that this patient had large bilateral renal infarcts. However, the total absence of gross haematuria in such a situation is unusual. Hence I will not consider this possibility seriously.

Coming to the terminal event, this patient had chest pain, tachypnoea and hypotension—symptoms which suggest pulmonary thromboembolism in a bed-ridden patient with CCF.

**DR RAMESH KUMAR’S DIAGNOSIS**
- Chronic rheumatic heart disease, mitral stenosis (severe), mitral regurgitation (moderate), atrial fibrillation, pulmonary arterial hypertension and congestive cardiac failure.
- ? Infective endocarditis with diffuse proliferative glomerulonephritis.
- ? Pulmonary thromboembolism.

**CLINICAL DISCUSSION**

Dr K. S. Chugh: This is a very thoroughly investigated and followed up case and there seems to be no doubt about the cardiac condition.

Dr H. N. Khattar: There are two aspects of this case that need to be discussed. The patient had severe mitral stenosis, mitral regurgitation, fast ventricular response
atrial fibrillation and was in congestive heart failure for 6 to 7 years. What was the cause of his sudden deterioration when he developed tachypnoea with worsening of the congestive cardiac failure? Did he have a pulmonary thromboembolism? I think he had. The left atrium was reported to contain a large thrombus, but a repeat echocardiogram two days later showed no such thrombus. Did he develop multiple renal thromboemboli leading to multiple renal infarcts which caused acute renal failure and worsening of his condition?

**Dr Harjinder Singh:** This patient came for surgery very late. We did not seriously think of infective endocarditis. We were planning a closed mitral valvotomy but he went into hypotension and we strongly suspected that he had had a pulmonary thromboembolism.

**Dr R. Dhand:** I would like to reinforce the comments made by Dr Khattri. I think the pulmonary thromboembolism was not the only final episode but there is evidence of repeated emboli since November 1988.

**Dr H. N. Khattri:** I do not think that would be correct. The catheter data of December 1988 showed elevation of the pulmonary artery diastolic and wedge pressures. There was no evidence of pulmonary thromboembolism at that time.

**Dr B. K. Sharma:** Dr Ramesh Kumar has suggested the diagnosis of multiple renal infarcts to explain the renal failure. However, even in December 1988, there was some borderline elevation of the blood urea and serum creatinine and there were red cells in the urine. A small embolization to the kidney even at that time cannot be ruled out. My main suggestion is that there is no way to exclude the possibility of prerenal factors being responsible for this kind of renal failure. A patient with congestive cardiac failure who is receiving a lot of diuretics can easily show this degree of azotaemia.

**Dr K. L. Gupta:** I feel that the possibility of multiple thromboemboli to the kidney as suggested by Dr Sharma on the basis of a few red blood cells in the urine is not really tenable and cannot explain the present renal insufficiency since there is no history of frank haematuria. This patient is more likely to have had a glomerulonephritis due to infective endocarditis.

**Dr K. S. Chugh:** I also do not think that the renal picture
is one of thromboembolism. The puzzling aspect of this case is the left atrial thrombus. Are we dealing with a thrombus that has disintegrated and disappeared?

**DR P. L. WAHI:** Dr Chugh's question is clearly a loaded one. It is certainly possible to have systemic thromboembolism and no thrombus visible in the left ventricle on echocardiography (this may have moved into the systemic vascular circulation) or alternatively one may visualize the thrombus in the left atrium but there may not be systemic emboli. However, the situation is a peculiar one. A thrombus was seen but two days later it had disappeared. I find that some doubt has been expressed in both the reports and we should keep these doubts in mind.

**DR RAMESHKUMAR:** Actually on the basis of the first echocardiographic visualization of the thrombus the patient was put on heparin. Two days later, after a repeat examination, heparin was withdrawn as the cardiologists were not quite certain whether or not the thrombus was present and the patient was being prepared for a surgical operation.

**DR K. S. CHUGH:** This patient therefore had rheumatic heart disease with mitral stenosis and regurgitation and no aortic regurgitation. We are handicapped as far as the kidney lesion is concerned due to a lack of urine examination. There is a possibility of glomerulonephritis but I do not think there was a terminal thromboembolism. I now request Dr C. K. Banerjee to present the autopsy findings.

**PATHOLOGICAL DISCUSSION**

**DR C. K. BANERJEE:** A partial autopsy was performed. The brain was not examined. The serous cavities did not contain any excess of free fluid. As the heart was the main concern of the treating consultants as well as the topic of discussion now, I will start there. It was overweight (500 g) and enlarged. Both atria were hugely dilated and the mitral valve cusps were thickened. The edges were rolled and commissures fused (Fig. 4). The chordae tendinae were also thickened and only marginally shortened. The left ventricle was not very dilated and showed only borderline hypertrophy. The aortic valve cusps, tricuspid valve and pulmonary valve were all normal. The right ventricle was dilated and its wall was hypertrophied. Histologically a section from the mitral valve showed vascularization and the myocardium showed many Aschoff bodies (Fig. 5). There were no morphological features of pulmonary hypertension in the lung vessels and the liver showed no features of passive venous congestion.

The second pathology, which was responsible for his fatal outcome was in the lungs. The two lungs were massive, weighing more than 1 kg each. The pleura were mildly thickened. The cut surface showed almost total replacement of the lung parenchyma with miliary tubercles which were diffusely present in both lungs (Fig. 6). A small hilar lymph node also showed caseation. Histologically the lung showed features of confluent caseous bronchopneumonia. Granulomas were scanty (Fig. 7). Ziehl-Nielsen staining showed a large number of acid-fast bacilli in areas of acute inflammation in the lungs. Miliary tuberculosis was present in the myocardium (Fig. 8), liver (Fig. 9), spleen (Fig. 10), kidneys, adrenals and pancreas. The small and large...
Fig 7. Miliary tubercles with Langhans giant cell in the lung (H&E, ×120)

Fig 8. Miliary tubercle in the epicardium (H&E, ×120)

Fig 9. Tubercles in the liver (H&E, ×120)

Fig 10. Miliary tubercles in the spleen with a large area of caseation

Fig 11. Stress ulcers in the stomach and large linear ulcers in the duodenum

Fig 12. Hyphae of candida in one of the gastric ulcers (PAS, ×480)
intestines also showed miliary tuberculosis. The stomach and duodenum showed superficial ulcers (Fig. 11). Histologically these were acute ulcers with necrosis of the mucosa and a mild inflammatory cell infiltrate. One of the duodenal ulcers had perforated, the base of the ulcer being formed by the pancreas. The gastric ulcer and the duodenal ulcers showed superadded Candida infection (Fig. 12).

**AUTOPSY DIAGNOSIS**

—Chronic rheumatic heart disease with mitral valvulitis producing predominantly mitral stenosis and mild mitral regurgitation.
—Disseminated tuberculosis involving the lungs, hilar lymph nodes, heart, liver, spleen, kidneys, gastrointestinal tract, adrenals and pancreas.
—Stress ulcers in the stomach and duodenum with superadded candidiasis. Sealed perforation of duodenal ulcer.

**CONCLUDING DISCUSSION**

**Dr K. S. Chugh:** We have a surprise element which was not at all suspected during the life of the patient and I notice that everybody is trying to re-read the old chest X-rays to see if miliary tuberculosis was really missed.

**Dr P. L. Wahl:** This case illustrates that even in an apparently open and shut case the pathologist may still find something unsuspected. This highlights the importance and need for more autopsies in this country. Even close scrutiny of the chest X-ray done in December 1988 does not show any tuberculosis. A more recent X-ray is not available and it seems no X-ray was done in April 1989. Regarding the left atrial thrombus suspected on echocardiographic examination, one should note that the angiography carried out soon after this examination in April does not show any space-occupying lesion in the left atrium. At times in a large left atrium a whirlpooling of blood may be mistaken for a thrombus.

**Dr K. S. Chugh:** Dr Ramesh Kumar confirms that no chest X-ray was done during the second admission. Could the pathologist tell us if the lesions of tuberculosis can be dated? We know of course that these must have developed between December 1988 and April 1989.

**Dr S. Suri:** I would also like to record my surprise that even though the patient had fever, expectoration and was due to have surgery no chest X-ray was done. Tuberculosis could certainly have developed in the 4 months between December 1988 and his death in April 1989.

**Dr B. K. Sharma:** We thought his fever might be due to infective endocarditis but the tests excluded this possibility. If you read the clinical protocol it says ‘fever occurred during the last few days’.

**Dr S. K. Jindal:** Tuberculous granulomas can form in 3 weeks. In this case the miliary spread may have originated from a tuberculous mediastinal lymph node which was perhaps present for a longer period.

**Dr N. K. Ganguly:** I would like to make a comment regarding the laboratory diagnosis of infective endocarditis. Not only should the bacterial culture be done but bacterial teichoic acid and anti-teichoic acid antibodies should also be looked for. Also the levels of serum complement are raised in rheumatic heart disease as well as in tuberculosis but fall as infective endocarditis develops. This is particularly useful when there is renal involvement and one has to choose between embolism and an immune complex mediated renal lesion.

**Dr C. K. Banerjee:** The duration of onset of tuberculosis has probably been the 4 months between December 1988 and March 1989. Granulomas take about three weeks to develop and massive caseation may occur in 6 weeks. Therefore, in this case, I think, the tuberculous lesions look about 6 to 8 weeks old. I agree that the initial lesion was in a hilar lymph node.

**Dr B. N. Datta:** In the non-sensitized host a tubercle may take 3 to 6 weeks to develop but in a sensitized patient caseation and a tuberculous reaction develop very quickly, sometimes within days. The Aschoff bodies in the heart are usually a part of rheumatic heart disease but these can be stimulated by any toxic condition such as infective endocarditis or even, as in this case, by generalized and myocardial tuberculosis.

**Dr K. S. Chugh:** In conclusion, this case once again proves that because of the milieu in which we live, tuberculosis should be suspected in any patient with a history of fever, cough and expectoration and that a chest X-ray is still very important.

---

**Compiled by Dr B. N. Datta**

**Participants**

C. K. Banerjee: Department of Pathology
K. S. Chugh: Department of Nephrology
B. N. Datta: Department of Pathology
N. K. Ganguly: Department of Experimental Medicine
K. L. Gupta: Department of Nephrology
S. K. Jindal: Department of Chest Diseases
H. N. Khattar: Department of Cardiology
Ramesh Kumar: Department of Internal Medicine
B. K. Sharma: Department of Internal Medicine
Harjinder Singh: Department of Cardiothoracic Surgery
S. Suri: Department of Radiodiagnosis
P. L. Wahl: Department of Cardiology