JUVENILE MITRAL STENOSIS IN INDIA*

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Rheumatic heart-disease is well known to be the main cardiac problem in India (Basu 1925, Hughes and Yusuf 1930, Devichand 1959, Mathur 1960), but the unusual features of juvenile mitral stenosis in India are not so well known (Banerjea 1935, Kurumbiah 1935, Vaishnava et al. 1960). We describe here the clinical and physiopathological findings in 108 patients with mitral stenosis who were below the age of 20 years.

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Material and Method

In the past four years, 2383 patients with heart-disease were seen at the cardiac clinic of this institute, 754, of whom 171 were below the age of 20 years, had rheumatic heart-disease. Of these 171 patients, 108 had pure or predominant mitral stenosis, and they form the clinical material of this report. Mitral-stenosis patients who had significant mitral regurgitation or associated aortic-valve disease were not included in the study. There were 66 boys and 42 girls.

The right heart was catheterised in 62 of these patients. The baseline for all pressure measurements was taken as half the chest thickness at the second costal cartilage with the patient supine (Roy et al. 1957). 23 of these patients had operations on the mitral valve. Tissue for microscopic examination was taken at operation from the left atrial appendage, the parietal pericardium, and the lower lobe of the left lung and an additional 8 patients came to necropsy. The tissues were fixed in neutral buffered 10% formalin, sectioned in paraffin, and stained routinely as follows: (1) with haematoxylin and eosin, and selectively with Perl's reaction for iron; (2) with Verhoeff's stain counterstained with van Gieson's stain for differentiating between elastic and collagenous elements; (3) with Masson's trichrome stain for differentiating between muscular and collagenous elements; and (4) with Gomori's reticulin stain (Armed Forces Institute of Pathology 1957).

Results

Rheumatic Fever

A history of at least one attack of rheumatic fever was obtained in 71 (66%), and of more than one attack in 30 (28%) patients. The diagnosis of rheumatic fever was based on a history of migratory polyarthritis (more often polyarthralgia), fever, and manifestations of carditis. Chorea and subcutaneous nodules appeared infrequently (3%), and erythema marginatum was conspicuously absent (Roy 1960). The interval between the first attack of rheumatic fever and the onset of symptoms varied from a few weeks to several years, but 50 (70%) of the 71 patients with a history of rheumatic fever had symptoms within five years of the first attack.

Table I—Clinical Features in 108 Patients with Juvenile Mitral Stenosis

<table>
<thead>
<tr>
<th>Feature</th>
<th>No. of males (66)</th>
<th>No. of females (42)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of rheumatic fever</td>
<td>45</td>
<td>26</td>
<td>71</td>
</tr>
<tr>
<td>Dyspnoea:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>7</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Moderate</td>
<td>26</td>
<td>20</td>
<td>46</td>
</tr>
<tr>
<td>Severe</td>
<td>26</td>
<td>13</td>
<td>39</td>
</tr>
<tr>
<td>Paroxysmal nocturnal dyspnoea</td>
<td>10</td>
<td>7</td>
<td>17</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>15</td>
<td>14</td>
<td>29</td>
</tr>
<tr>
<td>Angina</td>
<td>7</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>Embolism</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Congestive heart-failure</td>
<td>32</td>
<td>17</td>
<td>49</td>
</tr>
<tr>
<td>Rheumatic activity</td>
<td>12</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>7</td>
<td>3</td>
<td>10</td>
</tr>
</tbody>
</table>

Symptoms

Although 9% of the patients were asymptomatic, over 78% had significant exertional dyspnoea (table I). The high prevalence of congestive heart-failure (45%) and the low prevalence of atrial fibrillation (6%) in these patients are of particular interest. 12% had angina.

Valvular Disease

Table II shows that isolated mitral stenosis was the commonest single lesion, being present in 40%. Predominant mitral stenosis with or without some regurgitation was present in 63% of the 171 patients with juvenile rheumatic heart-disease.

Table II—Valvular Disease in 171 Patients with Juvenile Rheumatic Heart-disease

<table>
<thead>
<tr>
<th>Valvular lesion</th>
<th>No. of patients affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral stenosis</td>
<td>69 (40%)</td>
</tr>
<tr>
<td>Mitral stenosis with slight regurgitation</td>
<td>39 (33%)</td>
</tr>
<tr>
<td>Mitral stenosis with moderate regurgitation</td>
<td>14 (8%)</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>12 (7%)</td>
</tr>
<tr>
<td>Mitral and aortic-valve disease</td>
<td>31 (18%)</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>6 (3%)</td>
</tr>
</tbody>
</table>

Electrocardiograms and X-rays

Routine 12-lead electrocardiograms showed moderate right ventricular hypertrophy (R/S ratio in lead V1 greater than 1) in 38 patients and severe (R/S ratio in lead V1 greater than 5) in 26 patients. The prime R in lead V1 exceeded 12 mm. in 13 patients. Radiological changes consistent with moderate to severe degrees of pulmonary hypertension were observed in 68 patients. Our criteria for radiological assessment have been reported elsewhere (Subba et al. 1960).

Rheumatic Activity

Rheumatic disease was active in 24 patients, as judged by one or more of the following features: peri-carditis, chorea, subcutaneous nodules, polyarthritis, prolongation of the PR interval, a triad of raised erythrocyte-sedimentation rate and C.R.P., high anti-streptolysin-O titre and positive throat culture, and fever and leucocytosis. But if congestive heart-failure by itself in this age-group indicates carditis (and hence active rheumatic disease) then the total number of patients with active rheumatic disease was 49.

Haemodynamic Data

Fig. 1 shows that in over two-thirds of the catheterised patients the resting mean pulmonary arterial pressures were considerably raised, occasionally even exceeding the systemic arterial pressures. In 60% of the patients the resting pulmonary arterial wedge pressures exceeded 20 mm. Hg, reaching almost oedema level in a quarter of the patients. The cardiac output, on the other hand, was normal in 80% of the patients. The pulmonary vascular resistance (gradient resistance) was grossly abnormal.
Surgical Findings

At operation, in 17 of the 23 patients, the pulmonary arterial trunk was large and turgid, and the aorta was relatively small. Calcification and mural thrombi were detected in only 1 patient, but in 18 of the 23 patients the mitral valve was stenosed enough to obstruct the passage of the tip of the surgeon’s index finger.

Histopathological Changes

Abnormal changes in the pulmonary vessels, haemosiderin, and septal oedema were evaluated and graded in the lung sections; subendocardial Aschoff systems were present in the atrial appendages. Broadly, the most striking change was in the small muscular branches of the pulmonary artery accompanying the terminal and respiratory bronchioles and in the pulmonary arterioles and venules. There was pronounced medial muscular hypertrophy in all these vessels together with either concentric or eccentric thickening of the intima (figs. 2 and 3). Severe narrowing of the lumen was the rule. Rigidity and sclerosis of the alveolar capillaries with thickening and duplication of their reticular framework were prominent features (fig. 4). Epithelialisation of alveoli was unusual.

Haemosiderosis and septal oedema were inconstant. Vasculitis was not encountered.

Besides the medial hypertrophy of vessels, we were greatly impressed by smooth-muscle proliferation in the distal air passages—namely, the bronchiolo-alveolar system. Normally, smooth muscle extends in interlacing bundles and strands for a varying distance from the respiratory bronchiole into the alveolar ducts and sacs. The smooth muscle was greatly hypertrophied in the lungs examined, and occasionally even extended into the alveolar septa (fig. 5). This picture is apparently what was described in earlier reports as “musculare lungencirrhose” of mitral stenosis (Davidsohn 1905).
Discussion

Isolated mitral stenosis in patients below the age of 20 with rheumatic heart-disease is common in India. Boys are affected oftener than girls. Vaishnava et al. (1960), working in South India, gave the prevalence in 133 patients below the age of 13 with rheumatic heart-disease as 26%, and the male to female ratio as 1.6 to 1. On the other hand, Bland (1963), who reviewed 709 consecutive patients below the age of 22 with rheumatic heart-disease, found only 12 (1.7%) with isolated mitral stenosis and 304 (42.9%) with mitral stenosis and regurgitation. Cowan and Ritchie (1935) noted that the frequency of chronic mitral-valve disease was 2% in the first decade, and 19% in the second decade, the frequency of stenosis and regurgitation being the same. Wood (1954), on the other hand, found that mitral stenosis with or without unimportant leak was four times as common as pure mitral regurgitation, and twice as common as combined stenosis and regurgitation in his series of 300 unselected adult cases of mitral-valve disease. The male to female ratio was 1:4 in mitral stenosis, 1:1 in mixed lesions, and 3:2 in pure regurgitation. In the present series, males predominated in all the types of valvular disease.

The clinical features of rheumatic fever in India seem also to be different, since erythema marginatum is not seen, and chorea and subcutaneous nodules are uncommon. Although congestive heart-failure is a frequent finding in this age-group, atrial fibrillation is not. But in another review (unpublished) of 1000 patients with rheumatic heart-disease the frequency of atrial fibrillation was found to increase with each decade, reaching 40% in patients over the age of 40. Congestive heart-failure in patients with mitral stenosis below the age of 20 need not necessarily indicate rheumatic activity. The youth of our patients seems to negative the assumption that in mitral stenosis angina may be due to coincidental coronary arterial disease. Haemodynamic data in 6 of the 13 patients, revealing moderately severe pulmonary vascular obstruction and significant stenosis of the mitral valve, support Wood’s (1954) view that in such patients angina is due to functional impairment of the coronary flow caused by limitation of the cardiac output.

The high prevalence of severe pulmonary hypertension with gross pulmonary vascular changes as seen in this group of young patients could suggest a hypersensitive reaction of the pulmonary vasculature to a fulminating rheumatic process, or a tissue response to multiple overt attacks of rheumatic fever, since chemoprophylaxis is generally unknown in India. Moreover, because of the youth of the patients, the possibility of continued smouldering rheumatic activity cannot be completely ruled out. Nevertheless, the ability of the heart to maintain adequate cardiac output indicates a good functioning ventricular myocardium in most of the patients.

The findings at operation confirmed the physiological observations. The absence of calcification in the mitral valve and of thrombi could be due to the youth of the patients. The severe anatomical disturbances in the pulmonary vasculature conform with the data on
pulmonary vascular pressure and resistance. Although the muscular hypertrophy of the blood-vessels may be due partly to vasospastic influences, and may thus be reversible, the extent to which the intimal fibrosis and the reticular sclerosis in the alveolar capillaries is reversible after surgical correction is problematical. Smooth-muscle bands in the distal air-passages do not seem to have received much attention lately, and their significance remains obscure. Rodbard (1953) suggested that they may be related to "contraction atelectasis". We believe that the prominent musculature is a response of the lung to high vascular pressures reached within a short time in a young person. Its precise significance is unknown to us.

Summary

Physiological studies revealed that a majority of 108 patients below the age of 20 with mitral stenosis following rheumatic fever had severe pulmonary hypertension with gross pulmonary vascular obstruction, fairly normal cardiac output, but critical stenosis of the mitral valve.

Isolated mitral stenosis was the commonest single valvular lesion, and boys were affected more commonly than girls. Significant exertional dyspnoea was present in 78%, and congestive heart-failure in 45%, but atrial fibrillation was found in only 6% of the patients.

Operation revealed large turgid pulmonary arteries with relatively small aortas, absence of calcification, and tight stenosis of the mitral orifice.

Prominent features in lung biopsy specimens were: pronounced medial hypertrophy and intimal thickening of small muscular pulmonary arteries, arterioles, and venules; alveolar capillary sclerosis; and hypertrophic smooth-muscle bands in the distal respiratory passages.

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Juvenile Mitral Stenosis: An entity indeed

Till 1930, it was believed that rheumatic fever (RF) was a disease of ‘temperate climates’ and did not exist in tropical countries like India. The first report of the existence of RF in India was by Hughes and Yusuf in 1930. 1 The first Indian study of RF was published by Dr Wig in 1935. 2 This was followed by numerous case reports and articles establishing that rheumatic heart disease (RHD) was rampant in India. 3 Various articles appeared which identified the profile of RF and the pattern of cardiac involvement.

The House of the Good Samaritan in Boston, Massachusetts, USA, was one of the first major centres devoted almost exclusively to the care of patients with RF and RHD. Drs. T. Duckett Jones, of the Jones criteria fame, Benedict Massell and Edward Bland were associated with the House of the Good Samaritan. Dr Sujoy B. Roy worked with Dr Massell at the House of the Good Samaritan during his training in Cardiology in the USA. He joined the All India Institute of Medical Sciences (AIIMS) in 1958 and, because of his interest in RF/RHD, immediately got involved in studying the profile of RF and the pattern of RHD in patients attending the cardiac clinic at AIIMS. He published a paper on the profile of RF, emphasizing the absence of erythema marginatum and low frequency of occurrence of chorea and subcutaneous nodules as compared with the Boston experience. 3

At the same time, he identified the peculiar and very early occurrence of severe rheumatic mitral valve obstruction in patients with RHD and coined the term ‘juvenile mitral stenosis’. One of the bibles of cardiology at that time, the Textbook of Cardiology by Paul Wood, specifically stated that: (i) the presence of congestive failure in paediatric and adolescent patients of RHD indicated active carditis and (ii) it took almost 2 decades after RF for patients to become symptomatic from mitral stenosis (MS).

This landmark publication by Roy et al. in The Lancet 4 identified that:

1. Rheumatic MS in the Indian subcontinent does not take over 2 decades to become symptomatic;
2. It is not infrequent to see symptomatic critical MS below the age of 20 years; 5 and
3. MS can be severe enough to lead to congestive heart failure in the absence of active carditis. Hence, the presence of congestive failure was not sine qua non with active RF and carditis in children and adolescents in India.

These concepts modified the medical and surgical management of ‘young’ patients with RHD in India. Unfortunately, despite knowing this for nearly 50 years, we have still not understood why this happens—it is unlikely that the
organism itself could be the cause. Frequent recurrence of rheumatic carditis may play a role but it is likely that the pathophysiology is more complex.

To the cardiologist of today, the term ‘juvenile mitral stenosis’ gives a clear picture of the patient—a child, often <12 years of age, with severe mitral stenosis associated with a thickened mitral valve and severe subvalvular pathology—the latter is almost universally extensive and is grade 3 or 4 in most of these patients. These patients rarely, if ever, have calcific mitral valves and atrial fibrillation is also uncommon, partly due to the disease not having existed for long enough to lead to changes in the left atrium. However, severe pulmonary artery hypertension (PAH) defined as a mean PA pressure >50 mmHg is seen in over one-third of these patients. Recurrence of RF is more common in these patients, given their age. The results of percutaneous transluminal mitral commissurotomy (PTMC) are similar to those in adults, though the incidence of restenosis may be higher, especially in those who have active disease at the time of the intervention.

In conclusion, this article coined the term ‘Juvenile Rheumatic MS’, which identified how mitral stenosis behaves in young patients in the Indian subcontinent. Cardiologists all over the world took cognizance of this ‘diagnosis’ as a specific disease entity.

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Obituary

Many doctors in India practise medicine in difficult areas under trying circumstances and resist the attraction of better prospects in western countries and in the Middle East. They die without their contributions to our country being acknowledged.

The National Medical Journal of India wishes to recognize the efforts of these doctors. We invite short accounts of the life and work of a recently deceased colleague by a friend, student or relative. The account in about 500 to 1000 words should describe his or her education and training and highlight the achievements as well as disappointments. A photograph should accompany the obituary.

—Editor