Cardiovascular Manifestations and Surgery for Marfan's Syndrome*

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Five patients with Marfan's syndrome and heart failure, their ages ranging from three to 49 years, were operated upon between September, 1966 and October, 1967. In four, aneurysm of the ascending aorta with aortic regurgitation, and in one severe mitral regurgitation were present. In three patients the aneurysmal part of the ascending aorta was excised and replaced by a Dacron graft and the aortic valve replaced by prosthesis. In another, a six-year-old boy, aortic aneurysmorrhaphy and annuloplasty was performed. In the fifth, a three-year-old child, the mitral valve was replaced. One patient (with aortic lesion) expired because of gastrointestinal tract bleeding following surgery. Pathologic examination of the excised parts in each patient showed typical features occurring in Marfan. The follow-up extending from nine to 22 months after surgery has shown marked improvement in functional capacity with significant decrease of heart size in the four surviving patients, among them two children ages three and six years.

The association of cardiovascular lesions with Marfan's syndrome is well known and occurs in about 60 percent of the cases.1-4 Sometimes the cardiovascular lesion is the single manifestation known otherwise as "forme fruste" Marfan.4 A variety of lesions have been described, among which the more common are: aortic regurgitation, fusiform aneurysmatic dilatation of the aorta, dissecting aneurysm of the aorta, aneurysmatic dilatation of the pulmonary artery, aneurysm of the sinus of Valsalva, bicuspid aortic valve and rupture of the aortic valve. Rarely other lesions may be found, notably, ventricular septal defect, coarctation of aorta, patent ductus arteriosus, mitral valve deformities with various degrees of regurgitation and combined mitral and tricuspid regurgitation.5-17

The aortic pathologic process which was originally described by Erdheim18 is cystic medial necrosis. Whenever this process is associated within the ascending aorta and the aortic annulus, the term "annulo-aortic-ectasia" is given to specify this entity.19,20

During the last decade, more attention has been paid to this syndrome because of successful surgical management. The purpose of this report is to describe the clinical and pathologic features of five patients with Marfan's syndrome with various cardiovascular lesions. The youngest was three years and the oldest 49 years of age. In four patients, severe aortic regurgitation with aneurysmatic dilatation of the ascending aorta and in the fifth, severe mitral regurgitation, were present. Each patient was operated upon and the follow-up period extending up to two years is discussed.

Case Reports

Case 1

A 49-year-old farmer was admitted on August, 1966 because of heart failure. Complete hemodynamic and angiographic evaluation revealed the presence of aortic regurgitation and aneurysmatic dilatation of the ascending aorta. The patient was asymptomatic until 1964 when he began experiencing exertional dyspnea and palpitations, orthopnea, paroxysmal nocturnal dyspnea, hemoptysis and fainting spells.

History revealed that he had had rheumatic fever at the ages of 15 and 47 years, leptospirosis at the age of 32, and twice repair of inguinal hernias at the ages 16 and 40. No history of trauma was obtained. Family history disclosed features of the Marfan syndrome in one of his sons and a heart condition with sudden death of his brother.

Physical examination revealed mild scoliosis, a wide span of the upper extremities (height 1.36 m and span of arms 1.60 m) and prognathism. Jugular venous pulse showed prominent "a" waves. Peripheral arterial pulses were typical for aortic regurgitation, namely, bisferious carotid pulse,
FIGURE 1 (Case 1). Picture taken at surgery showing aortic aneurysm (left) arising from the base of the heart and extending to the aortic arch. Following excision of the aneurysm the ascending aorta has been reconstructed by a Dacron graft (right).

DIS. CHEST, VOL. 56, NO. 1, JULY 1969
Table 2—Clinical data in five patients with Marfan Syndrome

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (Yrs)</th>
<th>Sex</th>
<th>External Stigmata</th>
<th>Family History</th>
<th>Duration of Symptoms (Mo.)</th>
<th>Cardiovascular Lesion</th>
<th>Pathology</th>
<th>Operation Procedure</th>
<th>By Pass Duration (Min.)</th>
<th>Follow-Up (Mo.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>49</td>
<td>M</td>
<td>+</td>
<td>+</td>
<td>24</td>
<td>Aneurysmatic fusiform dilatation of ascending aorta; aortic regurgitation</td>
<td>Cystic necrosis with mucoid degeneration of aorta</td>
<td>Excision of ascending aorta; Dacron graft (35 mm) aortic valve replacement (Magovern No 7)</td>
<td>67</td>
<td>Well 22</td>
</tr>
<tr>
<td>2</td>
<td>44</td>
<td>M</td>
<td>+</td>
<td>+</td>
<td>24</td>
<td>Aneurysmatic fusiform dilatation of ascending aorta; aortic regurgitation</td>
<td>Cystic necrosis with mucoid degeneration; dissecting aneurysm of aorta</td>
<td>Excision of ascending aorta; Dacron graft (35 mm) aortic valve replacement (Magovern No 6)</td>
<td>105</td>
<td>Well 19</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>M</td>
<td>+</td>
<td>-</td>
<td>6</td>
<td>Aneurysmatic dilatation of ascending aorta; aortic regurgitation</td>
<td>Cystic necrosis with mucoid degeneration of aorta</td>
<td>Excision of ascending aorta; Dacron graft (30 mm) aortic valve replacement (Magovern No 7)</td>
<td>80</td>
<td>Died 2nd postoperative day, gastrointestinal tract bleeding</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>M</td>
<td>-</td>
<td>-</td>
<td>36</td>
<td>Saccular aneurysm of ascending aorta; aortic regurgitation</td>
<td>Cystic necrosis with mucoid degeneration; dissecting aneurysm of aorta</td>
<td>Endaneurysmorrhaphy and aortic annuloplasty</td>
<td>30</td>
<td>Well 13</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>M</td>
<td>-</td>
<td>+</td>
<td>12</td>
<td>Mitral regurgitation</td>
<td>Mucoid degeneration of mitral valve</td>
<td>Mitral valve replacement (Starr No 0)</td>
<td>48</td>
<td>Well 9</td>
</tr>
</tbody>
</table>

X-ray examination of palms and feet was normal.

Catheterization data are presented in Table 1. Selective angiocardiography showed aortic regurgitation grade 4 and aneurysmatic dilatation of the ascending aorta.

In September, 1966 the patient was operated upon utilizing extracorporeal circulation. The operative procedure is summarized in Table 2 (Fig 1). The microspecimen of the aorta revealed cystic medial necrosis.

Case 2

A 44-year-old man was admitted on November, 1966. The patient started having exertional dyspnea and palpitations one year prior to this admission associated with stabbing pain in the neck. History was negative for rheumatic fever or lues. Family history revealed the presence of arched palate, recurrent inguinal hernias and floppy ears in three other members of his family.

Physical examination revealed a 1.84 m tall thin man with wide span of upper extremities, arachnodactyly, long thin feet, funnel chest, flaring ribs and floppy ears. Peripheral arterial pulses were characteristic of severe aortic regurgitation. Myopia and subluxation of both lenses were found on examining his eyes. Physical findings were typical for aortic regurgitation. Blood pressure was 140/120 mm Hg. Electrocardiogram showed sinus rhythm, left axis deviation, left ventricular hypertrophy and strain. Chest x-ray film showed enlarged hili of both lungs, left ventricular enlargement and dilatation of the ascending aorta. Forward angiocardiography revealed aneurysmatic dilatation of the ascending aorta extending from the annulus up to the origin of the innominate artery and aortic regurgitation grade 4 (Fig 2). Catheterization data are presented in Table 1.

The surgical procedure is described in Table 2. In the immediate postoperative period, intermittent A-V block appeared which was treated by an external pacemaker via endocardial electrode. By the 30th postoperative day, the A-V block persisted and an epicardial implantable pacemaker was installed. The gross and microspecimen examination of the ascending aorta revealed incomplete dissecting aneurysm and cystic medial necrosis.

Case 3

A 21-year-old man was admitted in December, 1966 following heart catheterization and angiocardiography which...

FIGURE 2 (Case 2). Forward angiography showing aneurysmatic dilatation of the ascending aorta combined with left ventricular enlargement.
revealed aortic regurgitation and fusiform dilatation of the ascending aorta.

History revealed he had had rheumatic fever in early childhood; no acute or trauma were noted. Six months prior to his admission, the patient started having exertional dyspnea and fatigue, and a single episode of fainting. Physical examination revealed typical external features of Marfan's syndrome associated with severe aortic insufficiency. Angiocardiography showed aortic regurgitation and fusiform dilatation of the ascending aorta and the aortic annulus. The surgical procedure is presented in Table 1.

Immediately following operation, the patient began bleeding through the chest drains. After 12 hours, re-exploration of the chest wound was carried out which revealed diffuse oozing. The next day epistaxis was noted. A few hours later the patient went into shock, although the bleeding from the chest ceased. Necropsy examination revealed massive intestinal bleeding. The graft between the heart and the aortic arch, as well as the aortic prosthesis, were found intact. The pathologic findings were identical to those in case 1.

Case 4

A six-year-old boy was admitted after a hemodynamic evaluation which revealed the presence of aneurysm of the ascending aorta and aortic regurgitation. History revealed only a febrile episode at the age of three years, when his heart disease was first discovered. During the last year easy fatigue was noted.

Examination revealed a physically underdeveloped child. No cyanosis or clubbing was present. Jugular venous pulse was not pronounced. The apex of the heart was palpated at the left 5th intercostal space 1 cm lateral to the mid-clavicular line. A systolic thrill was palpated over the base. First heart sound was normal, followed by an aortic click and an aortic ejection murmur grade 3/6 maximally audible at the second right intercostal space, radiating to the neck. An early diastolic blow was also heard. Atrial pulses were typical for aortic regurgitation with blood pressure of 110/60/30 mm Hg. Laboratory and eye examination were normal. The electrocardiogram showed sinus rhythm left axis deviation, combined with left ventricular hypertrophy. X-ray examination revealed normal vascularity of the lung, left ventricular enlargement and widening of the upper mediastinum. Catheterization results are presented in Table 1.

Angiography performed twice showed the presence of an aneurysm of the ascending aorta (Fig 3). Aorto-left ventricular tunnel was also suspected, but excluded at surgery. Operative findings and surgical procedures are described in Table 2.

The examination of the specimen revealed aortic aneurysm with incomplete dissection of the ascending aorta due to cystic medial necrosis (Fig 4).

Case 5

A three-year-old boy was admitted on September, 1967 after having diagnostic studies which revealed the presence of severe mitral regurgitation. The valvular lesion was first discovered at the age of two and one-half years and endocardial fibroelastosis was clinically suspected. Family history
ventricle and vigorous contraction and emptying of the left ventricle combined with grade 4 mitral regurgitation (Fig 5). The contractility of the left ventricle excluded endocardial fibroelastosis and surgery was undertaken (Table 2).

The microexamination of the mitral valve revealed advanced mucoid degeneration of the valve stroma (Fig 6).

**Surgical Considerations**

**Technic:** All operations were performed utilizing total cardiopulmonary bypass. In every case a simple method, previously described, utilizing a plastic disposable oxygenator priming the extracorporeal system with dextrose/Ringer solution and without donor blood was used. In four of the cases the lesion was approached through the mid sternum and in the fifth, the child with the mitral lesion, by right thoracotomy. The extracorporeal circulation method was identical in each, namely venous blood derived by cannulating both venae cavae and arterial return via femoral artery. The level of hypothermia was 30°C in each case.

The aortic aneurysm was treated in three of the four patients by excision and replacement of the ascending aorta by a Dacron graft (Fig 7). The proximal anastomosis was done first followed by insertion of the valve prosthesis and completed by the distal anastomosis. The fourth patient, age six years, with an incomplete dissection of the aorta, was treated by excision of the aneurysm and endoaneurysmorrhaphy, restoring the aortic wall with his own tissue. Additional support was given to the ascending aorta in this patient only by wrapping it with a Dacron cuff (Fig 8).

The aortic valve incompetence was treated by replacing the valve in three patients (cases 1, 2, 3)

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FIGURE 5 (Case 5). Selective left ventriculogram with tip of the catheter in the left ventricle. Dye has opacified the left ventricular and the left atrial cavities indicating severe mitral regurgitation.

revealed his father and uncle had cataracts. His aunt was known to have heart disease and was operated upon. Another uncle was known to suffer from inguinal hernias.

History revealed pneumonia and mumps. On admission, mild cyanosis of the lips and nails was present. There were no skeletal deformities or ocular lesions. Peripheral pulses were normal. The first heart sound was normal, followed by a holosystolic murmur (grade 3/6) maximally heard over the apex and radiating to the axilla. The second sound was normal and a prominent third heart sound was present. The ECG showed sinus rhythm and left ventricular hypertrophy. The chest x-ray film illustrated increased central vascular markings and enlarged heart due to the left atrium and ventricle. Selective retrograde (Table 1) angiocardiogram of the left ventricle showed hypertrophy of the

FIGURE 6 (Case 5). Gross (left) and microspecimen (right) of the anterior leaflet of the mitral valve typical of Marfan cystic mucoid degeneration of the valve stroma (x 400).

FIGURE 7. Schematic illustration of the surgical technic employed in three of the cases showing graft replacement of the ascending aorta and a Magovern valve prosthesis for replacement of the aortic valve.
and aortic anuloplastic in one (case 4)—the six-year-old boy. A Magovern-type prosthesis has been used in each. In all patients the coronary arteries were individually perfused with blood at 30°C temperature while restoring the ascending aorta and/or replacing the aortic valve. The total pump time varied between 30 to 105 minutes (Table 3). The fifth patient (with mitral insufficiency) was treated by mitral valve replacement utilizing Starr-Edwards prosthesis.

**COMMENT**

From this group of five patients, only three presented the classic features of Marfan's syndrome. Three had, in addition, a family history of the Marfan syndrome. In the two children, (cases 4 and 5) only the histologic findings of the specimens removed at surgery established the correct diagnosis. Therefore, they may fall into the category of *forme fruste* Marfan.

Accuracy of diagnosis during life in the Marfan syndrome may be as low as 50–60 percent. A careful family history may be quite helpful, particularly when the case under discussion lacks the external features of the syndrome. In 85 percent of the cases with the Marfan syndrome will the family history be positive, if seriously sought. Of particular difficulty in establishing the correct diagnosis are the cases which have no family history for the syndrome and clinically present with aortic insufficiency or aortic aneurysm alone. In this regard, it is of interest to note the observation made by Hirst who reported that of 212 necrospy cases of dissecting aneurysm of the aorta, 62 percent were due to cystic medial necrosis.

In McCloy's report of 40 patients with dissecting aneurysm, 83 percent were dead within one year, and of these, over 50 percent died within one week. In this regard it might be worthwhile to mention the following: A 42-year-old woman was admitted to our hospital recently with signs of shock and severe chest and back pains of sudden onset. Within 12 hours, without responding to medical treatment, the patient expired. At necrospy, dissection of the ascending aorta, about one inch above the aortic valve, was present, without aneurysm. This patient was known to be asymptomatic and to have mild aortic regurgitation for several years. The microspecimen revealed cystic medial necrosis with extensive mucoid degeneration. No other outward symptoms or family history suggestive of the Marfan syndrome were present.

The most frequent cardiovascular manifestation in the Marfan syndrome is aortic insufficiency with aneurysm. On angiography, the aneurysm usually is pear-shaped. There is also marked dilatation of the annulus with resulting valve insufficiency. The aortic leaflets, however, appear normal in configuration and in micro examination.

Contrary to that, when the mitral or tricuspid

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**Table 3—Cardiopulmonary bypass data in five patients**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Total Time (Min.)</th>
<th>Cor. Left</th>
<th>Perfus. Right</th>
<th>Flow ml/min.</th>
<th>Lowest Body Temp. °C</th>
<th>Priming* ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (56 kg)</td>
<td>67</td>
<td>39</td>
<td>29</td>
<td>2600</td>
<td>30</td>
<td>2200 (No Blood)</td>
</tr>
<tr>
<td>2 (70 kg)</td>
<td>105</td>
<td>25</td>
<td>26</td>
<td>2100</td>
<td>30</td>
<td>2200 (No Blood)</td>
</tr>
<tr>
<td>3 (65 kg)</td>
<td>80</td>
<td>45</td>
<td>29</td>
<td>2100</td>
<td>30</td>
<td>2200 (No Blood)</td>
</tr>
<tr>
<td>4 (17 kg)</td>
<td>30</td>
<td>17</td>
<td>—</td>
<td>700</td>
<td>30</td>
<td>1500 (500 Blood)</td>
</tr>
<tr>
<td>5 (14 kg)</td>
<td>48</td>
<td>—</td>
<td>—</td>
<td>950</td>
<td>30</td>
<td>1300 (500 Blood)</td>
</tr>
</tbody>
</table>

*Ringer and D,W (1:1)*

**DIS. CHEST, VOL. 56, NO. 1, JULY 1969**
valves are involved in the Marfan syndrome, one finds significant mucoid cystic degeneration of the valves, with resulting valve regurgitation.\textsuperscript{5,13} This occurs rarely and was present in our group of patients in case 5 only. It is assumed that the myxomatous degeneration of the valves is also part of the intrinsic defect in the development of connective tissue. Thus, when the atrioventricular valve is involved, it leads to a loss of valve substance and secondary valve prolapse which clinically is represented by valve regurgitation. Frequently, the atrioventricular annuli as well are involved by the same process leading to an annular enlargement.

Surgical correction for the Marfan syndrome appears to be the treatment of choice. Naturally, this is reserved only for the more advanced cases with progressive dilatation of the aorta, progressive valve regurgitation or any sign of rupture.\textsuperscript{28} In this respect all our patients presented the clinical picture of severe valve regurgitation; in four of them huge aortic aneurysm was present and two of these had incomplete aortic dissection.

Of particular interest is the boy (case 4) with the aortic aneurysm and insufficiency. The surgical procedure in this case was not the conventionally accepted one, because of the patient’s size. We were unable to find in the literature a younger patient developing dissection from aortic aneurysm secondary to cystic medial necrosis who was treated surgically.

The follow-up period in our group of patients and also those reported in the literature is too short to indicate to what extent life will be prolonged in those patients. However, in none of our cases or in the cases reported in the literature has recurrence of the aneurysm been observed. As far as the aortic regurgitation is concerned in the Marfan syndrome, experience has shown that valve replacement is preferable to valve reconstruction, whenever indicated.

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REFERENCES

Reprint requests: Dr. Morris Levy, Bellinson Hospital, Petach Tiqva, Israel.

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