Cardiovascular Lesions in Arachnodactyly


The cardiovascular lesions in 34 cases of Marfan's syndrome which were studied post mortem are reviewed. Recent reports show that the most common and most important lesion is cystic necrosis of the media which results in aneurysmal formations of the ascending aorta. The aneurysm may be fusiform and the aortic ring dilated, producing a marked aortic insufficiency, or there may be a dissecting aneurysm, either recent or chronic. Valvular lesions are common but probably not important. Septal defects are occasionally encountered but are not functionally significant.

ARACHNODACTYLY (Marfan's syndrome) is a relatively rare disorder characterized by widespread disturbances in the development of tissues of mesoblastic origin. Disability may be caused by the skeletal and ocular deformities which result, but death, which is usually premature, is due to involvement of the cardiovascular system. The disease is well known to ophthalmologists and pediatricians and is frequently described in the ophthalmologic and pediatric literature. We wish to report another case and to briefly summarize the usual features and to emphasize the cardiovascular lesions associated with it, particularly those involving the aorta and the valvular endocardium.

CASE REPORT

A 23 year old corporal was admitted to Fitzsimons Army Hospital on Oct. 28, 1951, complaining of intense dyspnea and orthopnea. The patient's family history was negative. He had always been extremely tall and slender and had a pigeon chest deformity. He had been in good health until the age of 16 when he noted that he tired more easily and became somewhat short of breath on strenuous exertion. In 1946 he was told that he had a heart murmur. He was inducted into the Army on Nov. 15, 1950 and his cardiovascular system was considered normal. Three weeks later he was admitted to a hospital complaining of shortness of breath which had come on suddenly. There was no chest pain. Physical examination at that time showed no abnormality of the cardiovascular system. He was discharged five days later. He got along well until Sept. 16, 1951. On that date, while playing cards, he suddenly complained of pain in his chest and back, dyspnea, and began to perspire profusely. He was hospitalized and for the first time, abnormalities of the cardiovascular system were noted. The cardiac impulse was diffuse and there were loud systolic and diastolic murmurs at the base of the heart. His blood pressure was 130/80, respirations 22, and pulse rate 80. There was no evidence of congestive heart failure. A few days later it was noted that he had marked pulsations of the carotid arteries; the peripheral pulsations were of the Corrigan type; and the apical impulse was visible and palpable in the sixth intercostal space at the anterior axillary line. The aortic second sound was loud and tambour-like. There was a grade III, early, blowing, diminuendo, diastolic murmur, maximal in the third left intercostal space. There was a short, soft, grade I systolic murmur at the aortic area. A diastolic gallop rhythm was present. His blood pressure was 144/42.

Laboratory studies revealed a slightly elevated white cell count and an elevated sedimentation rate. Electrocardiogram revealed a sinus tachycardia with a right bundle branch block. Chest x-ray films showed pulmonary congestion and slight generalized cardiac enlargement. While in the hospital the patient continued to have a tachycardia, his dyspnea progressed, and he developed orthopnea, signs of pulmonary congestion and an enlarged, tender liver. It was thought that he had rheumatic heart disease with aortic insufficiency and, because of a persistently elevated sedimentation rate and slight fever, that he had active rheumatic carditis. He was transferred to Fitzsimons Army Hospital.

Physical examination on admission showed a very tall, slender, white man, who was 76 inches tall and weighed 151 pounds. The fingers were long and narrow. The lower jaw was prominent. The ears were long and pointed. The forehead was high and the patient had an old, sad appearance. Eyegrounds were normal. The palate was high and arched. There was a pigeon breast deformity. The cardiac findings were essentially as previously described.

The initial impression was rheumatic heart disease, active, with aortic insufficiency and mitral stenosis, with left ventricular hypertrophy and left auricular enlargement. Chest x-ray films on admission are shown in figures 1 and 2. It was thought that the patient was in congestive heart failure and he was treated accordingly. He failed to respond and died rather suddenly on his tenth hospital day.

Autopsy Findings. Except for congestive splenomegaly and hepatomegaly the significant findings

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were limited to the cardiovascular system. The heart weighed 698 Gm and appeared dilated in all chambers. The left ventricular wall averaged 2.1 cm. in thickness and the right ventricular wall 0.5 cm. The valve cusps were thin and delicate. The aortic valve was incompetent and measured 12 cm. in circumference. The foramen ovale was patent measuring 1.6 cm. in diameter. The coronary arteries were normal except the right artery arose 5.0 cm. above the coronary ring. The aorta above the aortic valve showed an aneurysmal dilatation with a circumference of 13 cm. There was a sharp break in the intima of the aorta 6.5 cm. above the aortic ring, and at this point the aorta became a tube within a tube (fig. 3). At the beginning of this dissecting aneurysm the outer tube was 9.6 cm. in circumference while the inner was 6.0 cm. The inner tube was incompletely separated from the outer. The dissecting aneurysm extended through the entire length of the aorta and into the innominate artery for a distance of 3.0 cm., into the left common carotid for 0.3 cm., into the left subclavian for 5.0 cm., and into each common iliac artery for 3.5 cm. The end of the dissection in these vessels was clearly defined and sharp. The lumina of all branches of the aorta communicated with the lumina of both tubes of the dissecting aneurysm except the left renal artery which had no communication with the outer tube. The outer tube was corrugated and "geographic" in appearance but was lined by a smooth membrane, only slightly rougher than the normal intima.

Microscopic examination of the heart showed hypertrophy of the myocardial fibers. The sections of the aorta showed the dissection occurring between the outer and middle thirds of the media. Sections taken from the aneurysmal portion of the aorta proximal to the dissecting aneurysm showed cystic spaces in the media filled with lightly basophilic fibrillar and finely granular material. There was a numerical reduction and disorganization of smooth muscle cells. Elastic tissue stains showed marked disruption, fragmentation, and condensation of elastic fibers with indistinct internal and external laminae (fig. 4). The final diagnoses were: (1) Marfan's syndrome. (2) Dissecting aneurysm of the aorta.

**DISCUSSION**

Arachnodactyly was first described in 1896 by Marfan, who called it dolichostenomelie.
Achard in 1902 called it arachnodactyly (spider fingers). Salle in 1912 reported the first case associated with heart disease, confirmed by autopsy. The first report in the American literature was by Piper and Irvine-Jones in 1926. This report stressed the frequency with which arachnodactyly was associated with congenital malformations of the heart. About 350 cases have been described but in spite of this rather extensive literature, there have been only 33 previously reported cases with necropsy findings. Twenty-three of these have been published in the last 10 years and it is only during this period that the reports have been detailed concerning the cardiovascular system.

Detailed descriptions of the various clinical features have been given by numerous authors and are well known, so only a summary of these will be given here. The disease is frequently familial and congenital. Several cases in one family are not uncommon. The affected person is slender and often abnormally tall. The limbs are disproportionately long and the more distal segments of the limbs show a relatively greater increase in length. The fingers are long and thin, having been described as spider-like and are the outstanding characteristic of the disease. The head is usually dolichocephalic. The face is long and thin and appears prematurely old. The ears are long and pointed and the lower jaw juts forward. The teeth are usually long and narrow. The palate is high and arched. These features, coupled with the wearing of glasses, which is seen in the majority of patients, tend to give them a serious, prematurely aged, wise appearance. Their apparent slenderness is aggravated by a scanty amount of subcutaneous fat and a poorly developed, hypotonic musculature. The ligaments are lax and poorly developed, permitting increased mobility of the joints which may be marked enough to allow dislocations. There are frequent spinal and thoracic deformities which are often thought to be the result of the inadequate muscular development. However, these deformities have been noted before the child is able to sit or walk. The most common spinal deformities are kyphosis and scoliosis but funnel chests and pigeon breasts are frequently seen.

Ocular abnormalities are present in about 50 to 75 per cent and are often characteristic. These include congenital bilateral dislocation of the lenses and because the lens is unsupported, the iris often appears tremulous (iridosclerosis). Myopia is the rule. The pupils are usually small and respond poorly to mydriatics. The vision is seriously impaired and may progressively deteriorate.

The incidence of lesions of the cardiovascular system is uncertain but has been reported as being present in 30 to 60 per cent. The exact incidence is difficult to determine because many of the patients are seen by ophthalmologists only and have been recorded only for their ophthalmic interest and external appearance. Another difficulty is that cardiac lesions may not become apparent until shortly before death. Murmurs are frequently described, but in view of the severe spinal and thoracic deformities

Fig. 4. Aorta. Verhoeff's elastic tissue stain ×140.
often present, such findings may not be indicative of organic heart disease unless supported by other evidence.

All of the above deformities may be present in a single case of arachnodactyly and there is no difficulty in recognizing a typical case in which the triad of skeletal, ocular and cardiac abnormalities are all present. As a rule, one or more features will be missing and the presence of the commonest characteristic is sufficient for the diagnosis. The less complete cases may go undiagnosed unless the condition is borne in mind. In some cases the diagnosis may be impossible unless the disease is also present in relatives in a more typical form.

The syndrome affects both sexes equally, probably occurs in all races but most frequently in the white. The etiology is unknown but thought to be a congenital defect.

**Cardiovascular Lesions**

The cardiovascular lesions of the 34 patients whose postmortem findings are known are summarized in table 1. The initial reports of congenital septal defects were the most common anomalies to be found. More recent studies show that this is not true as there have been only eight such defects found. These were all of questionable clinical significance and four were associated with aneurysms of the aorta and one with valvular lesions.

The most common lesion encountered has been involvement of the aorta which was found in 22 patients. In addition, there are reports of patients with aortic insufficiency or with definite evidence of aortic aneurysm on fluoroscopy but without post-mortem confirmation. Several other cases of sudden death without autopsy examination have been reported in young patients with arachnodactyly.

The gross descriptions have differed in detail. A few patients have shown only a dilated ring, others have shown a fusiform or saccular aneurysm and others have had a dissecting aneurysm. The aneurysms usually begin just distal to the aortic valve, are usually fusiform in shape and may be very large. They usually are rather short, ending just beyond the innominate artery but they may extend as far as the left subclavian or into the abdominal portion of the aorta. They frequently end abruptly and not uncommonly are associated with narrowing or stenosis of the aorta and two have been associated with coarctation. Some of the dissecting aneurysms have ruptured, producing death, while other dissections have been chronic and become healed. Another common finding has been a high origin of the coronary arteries, particularly the right.

Although the gross appearance varies widely, the microscopic description is usually identical. In both the fusiform and dissecting types the essential lesion is always in the media, the elastic and muscle fibers are deficient and replaced by loose, collagenous, fibrous tissue. It is generally felt that the lesion is indistinguishable from "medionecrosis aortae idiopathica cystica" as first described by Erdheim as the cause of dissecting aneurysm in middle aged and elderly people with hypertension.

The most consistent clinical features of aortic involvement are the complaint of chest pain and the signs of aortic insufficiency. The chest pain is usually substernal in location but not infrequently is also present in the back. The pain is very similar to angina pectoris except that it is frequently of longer duration. Only one patient had the complaints typical of dissecting aneurysm. She was suddenly seized
with severe, oppressive, tearing pain. The next most common complaint is that of dyspnea on exertion. Sometimes this has been present without any signs of cardiac failure. It is usually the initial symptom in those patients who die of congestive heart failure. Signs of marked aortic insufficiency are frequently described prior to death.

A common description is that of a young person with arachnodactyly whose heart is usually considered normal until the patient reaches the early teens. Then a routine examination often reveals a systolic murmur which is usually along the left sternal border or at the apex and the heart may appear slightly enlarged. Both findings are apt to be explained on the basis of the chest deformity which is usually present. A few years later the classical signs of aortic insufficiency are found.

Chest x-ray films and fluoroscopic examination with barium have been very disappointing and often misleading because a definite aneurysm is not usually demonstrated. The most common finding on chest x-ray study is generalized cardiac enlargement, particularly involving the left ventricle. The pulmonary artery is often described as being prominent and definite enlargement of the left auricle is frequently demonstrated.

Only a few reports mention the electrocardiographic findings. A bundle branch block was described in four patients, in three of whom it involved the left bundle branch system. The pattern of left ventricular hypertrophy or left heart strain was reported five times and partial auriculoventricular block has been described in three patients. Auricular fibrillation was noted three times.

The most common cause of death is congestive heart failure, usually the result of the marked aortic insufficiency. Sudden death is common and is usually due to a dissecting aneurysm.

The next most common lesion is involvement of the valvular and mural endocardium, noted in 21 patients, and which is frequently considered as evidence of rheumatic heart disease. Some authors described typical cases of arachnodactyly which had recurrent illnesses that seemed to be rheumatic fever. The usual finding in the valve is that the leaflets are rolled and thickened, frequently described as bolster or cushion shaped, the cusps may be thickened and shortened, the edges are often hard and nodular, and fenestrations of the cusps have been described. Occasionally the chordae tendineae are shortened. Aortic insufficiency, if present, was always due to the aneurysm, not to aortic endocarditis. Several patients were thought to have mitral stenosis on clinical grounds but autopsy showed normal mitral valves or minimal involvement without stenosis but with a marked dilatation of the aortic ring which produced an Austin Flint murmur at the apex. Microscopic examination of the involved valves rarely ever confirmed the presence of rheumatic fever. The usual finding is that of collagenous thickening or a myxomatous fibrosis similar to that seen in normal infants and on valves of hearts with congenital heart lesions. Examination of the myocardium also fails to reveal the evidence of previous rheumatic infection. The similarity to rheumatic fever is frequently increased by the x-ray findings because of an enlarged left auricle and a prominent pulmonary artery. Also, it is not unusual for these cases to run a low grade fever which was present in one third of the reported patients. The diagnosis is further complicated by the frequent presence of well marked aortic insufficiency without the demonstrable evidence of aortic aneurysm. The electrocardiogram has tended to add to the confusion because both patients who showed partial auriculoventricular block and all three patients who showed auricular fibrillation had aneurysms of the aorta. Generally speaking, the valvular lesions have not been important factors in the autopsied cases.

In view of the frequency of aortic aneurysm in arachnodactyly, it is interesting to speculate on how many cases of aortic aneurysm in normotensive adolescents and young adults may have skeletal changes without the significance of these being recognized. The lesion of the aortic wall seems to be identical with that found in most aneurysms, other than syphilitic, and the etiology may be the same. Although aneurysms have been considered rare in young
persons, Schnitker and Bayer found 141 of 580 dissecting aneurysms to be in persons under the age of 40. These authors concluded that medionecrosis was the usual cause and this conclusion has been confirmed by others. Cystic medionecrosis is the basis of nearly all dissecting aneurysms regardless of age.

Fusiform aneurysms are much rarer at this age; Bronson and Sutherland collected descriptions of 12, the eldest patient being 26 years. Fusiform aneurysms have been described in young adults in which histologic examination has shown cystic medionecrosis. There have been occasional patients with dissection of the aorta with a fusiform aneurysm. Thus, the pathologic process in the aortic wall seems to be identical whether the aneurysm is dissecting or fusiform. It seems almost incredible that an identical pathologic process can be found in different types of aortic aneurysms unless there is some causal relationship. On the other hand, the good development and athletic ability in young people dying suddenly of a ruptured aneurysm is often stressed. This fact would tend to exclude arachnodactyly except in a “forme fruste.”

It is conceivable that cardiac lesions, particularly dissecting aneurysms or aortic dilatation, can occur as an isolated lesion in some families with arachnodactyly. Other components of the triad have been reported as isolated lesions. It is of interest that the family history is most often positive when the disease is mild. A recent report described two patients with chronic dissecting aneurysm which simulated rheumatic heart disease. One case had arachnodactyly in addition to the typical findings in the aorta so this doubtless represents another case of Marfan's syndrome which was missed clinically. A diagnosis of dissecting aneurysm or aortic dilatation in a young person should therefore lead to a search for arachnodactyly in the patient and amongst his family. The possibility of aortic aneurysm should also be remembered in known cases of arachnodactyly or where there is a positive family history.

**Summary**

Another case of Marfan's syndrome that died of cardiovascular disease is reported. The cardiovascular lesions in arachnodactyly have been reviewed and discussed. They are common and are an important cause of death. They include aortic medial necrosis and endocardial lesions. The former is more dangerous as it leads to dilatation of the aortic ring producing aortic insufficiency which results in marked left ventricular hypertrophy and dilatation with death from congestive heart failure, or the disease of the aortic wall may result in aneurysmal formation which may rupture or dissect. A fusiform or dissecting aneurysm in normotensive adolescents or young adults may represent a "forme fruste" of arachnodactyly.

**SUMARIO ESPAÑOL**

Las lesiones cardiovasculares en 34 casos del síndrome de Marfan que fueron estudiados con autopsia se revisan. Reportes recientes demuestran que la lesión más común y más importante es necrosis cística de la lámina media que resultan en formaciones aneurismicas de la aorta ascendente. La aneurisma puede surgir de manera disectante o con insuficiencia aórtica, o un aneurisma disectante, reciente o crónico. Lesiones valvulares son comunes pero probablemente no importantes. Defectos del tabique son ocasionalmente encontrados pero funcionalmente sin importancia.

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