Association of Aortic Valvular Disease and Cystic Medial Necrosis of the Ascending Aorta

Report of Four Instances

By Victor A. McKusick, M.D., R. Bruce Logue, M.D., and Henry T. Bahnson, M.D.

In 4 patients with aortic stenosis and regurgitation, progressive dilatation of the ascending aorta and dissecting aneurysm developed. Cystic medial necrosis was discovered histologically. It is suggested that the change in the aorta is secondary to hemodynamic stresses imposed by the disease at the aortic valve.

In 4 patients we have observed the association of aortic stenosis with large fusiform and dissecting aneurysm in the ascending aorta. In each case Erdheim’s cystic medial necrosis was present. It is our purpose, in describing these cases, to suggest that the association is more than coincidence.

Case Reports

Patient 1. A. H. (J. H. H. 714094), a 31-year-old male school teacher, was first told he had a heart murmur when he was 15 years old. There was no history suggestive of rheumatic fever. The patient was completely asymptomatic and engaged actively in athletics. He remained well until the spring of 1953, when he had an attack of severe substernal pain lasting 10 to 12 hours. A roentgenogram of the chest was interpreted as normal. (On later review dilatation of the ascending aorta was suspected.) Thereafter he noted that his physical stamina was somewhat reduced. He could, however, walk a mile or more and climb stairs without dyspnea. Beginning May 15, 1955, he again developed substernal pain in mild attacks lasting 30 to 40 minutes, not clearly related to exertion and occurring mainly on first arising in the morning. Furthermore, increasing dyspnea and fatigue with exertion were noted.

The patient’s habitus was in no way unusual. He was heavy-set, athletically built, and well muscled. The pulse was small in volume and the pulse pressure somewhat narrow (blood pressure, 114/84 mm. Hg). There was an active systolic pulsation in the second right intercostal space. On auscultation the predominant finding was the loud systolic murmur in the right second interspace, transmitted up the right side of the neck. It was also audible to some extent at the apex. The second aortic sound was quite distinct and there was a faint, early, decrescendo diastolic murmur. At the base of the neck in the region of the lower end of the sternocleidomastoid muscle, there was a peculiar, high-pitched systolic “coo.”

Fluoroscopy revealed marked enlargement of the ascending aorta to the right. An electrocardiogram showed left axis deviation and a pronounced pattern of left ventricular strain.

Thoracotomy was performed on August 31, 1955, through a right anterolateral incision. The ascending aorta was found to be dilated to about 30 cm. in circumference. It diminished in size at the end of the ascending portion to measure 15 cm. just proximal to the innominate ostium, beyond which point the aorta seemed to be of normal caliber. There was a mass of fibrin and fibrous tissue suggesting previous inflammation on the anterior surface of the ascending aorta. The ascending aorta was mobilized and almost half its circumference was excised. In this process it became apparent that there was a dissection in the wall of the ascending aorta. A finger was introduced into the aorta through a diverticulum sutured to the aorta, and the aortic valve was palpated. The right anterior commissure was fused and the 2 cusps adjacent to it constituted almost a single large cusp. Calcified, rigid areas were felt. The other 2 commissures were free; the tip of the finger could be fitted through the orifice and, in general, the stenosis was not thought to be of high grade. Finger-fracture of the aortic valve was not attempted for fear of aggravating the hemodynamic disturbance at that site. The ascending portion of the aorta was wrapped in a Nylon suctactus binder.* At the close of the procedure the ascending portion of the aorta was uniformly 12 to 13 cm. in circumference.

Histologic study of the removed aortic tissue showed cystic medial necrosis.

* Surgical features of this and the following case have been described elsewhere and illustrated by means of chest x-rays and artist’s sketches of the findings at operation.
Postoperatively the patient has done well. That he has no longer had chest pain suggests that the preoperative pain may have been caused by the aneurysm and did not represent myocardial ischemia. Exercise tolerance is probably increased and certainly no less than before operation. The “coo” at the base of the neck on the right persists in apparently unaltered form.

Patient 2. T. G. M. (726673), a 50-year-old attorney, had numerous episodes of acute tonsillitis during his youth in a southern state but recalled no frank rheumatic fever.

At the age of 24 years he was first told that he had mitral stenosis. At the age of 35 years he was twice rejected for service in the Merchant Marines and in the Army because of murmurs. He was still asymptomatic. Exertional dyspnea had its onset at the age of 43 years and soon thereafter attacks of paroxysmal nocturnal dyspnea developed. Aortic aneurysm was discovered when he was 48 years old. Chest pain was never a conspicuous feature.

Physical examination revealed a blood pressure of 198/94 mm. Hg in both arms, 235/108 in both legs. There was an active, expansile, systolic pulsation in a large area below the right clavicle and the same area was dull to percussion. In this same area, furthermore, there was a grade IV systolic murmur accompanied by a thrill and followed by a decreasing diastolic murmur typical of aortic regurgitation. What seemed to be the same diastolic murmur was heard out toward the right axilla, where it acquired a delicate high-pitched quality, down the left sternal border, and in the apical area, where its quality was more low pitched and rumbling. The heart was strikingly enlarged to the left. Atrial fibrillation was present.

In general nothing about the patient's habitus or family history suggested the Marfan syndrome. The ophthalmologist could find no evidence of ectopia lentis.

Roentgenograms showed a large aneurysm of the ascending aorta and considerable enlargement of the left ventricle.

An operation similar to that used in the first patient was planned and at thoracotomy an enormous aortic aneurysm was discovered as anticipated. After application of clamps and excision of the occluded portion of the aorta, it was found that dissection had in fact occurred with a characteristic sheathlike double channel in the ascending aorta. The false channel was traversed by typical fibrous cords. The surgical procedure was performed according to plan without evidence of cardiac embarrassment. Soon after the clamp was removed from the aorta, pulsations of the heart became weak and ventricular fibrillation began. Cardiac massage and other efforts at resuscitation were of no avail.

At autopsy the heart weighed 900 Gm., the excess weight being mainly the result of left ventricular hypertrophy. There was calcific aortic stenosis with fusion of 1 commissure, and the valve also appeared regurgitant (figs. 1 and 2). An aortic dissection extended from 4 cm. above the aortic valve through the end of the aortic arch and into the innominate and subclavian arteries. The thoracic aorta was of normal size. Microscopic study showed cystic medial necrosis in the ascending aorta and to much less extent in the subclavian, mesenteric, and pulmonary arteries and abdominal aorta.

Patient 3.* W. M., a 40-year-old man, had known for many years that he had valvular heart disease, presumably rheumatic. Previously a diagnosis of aortic stenosis and regurgitation had been made. He had never experienced symptoms referable to the cardiovascular system and his exercise tolerance

\* Case 8 in a series of dissecting aneurysm previously reported by one of us.2
had always been normal. On the day of admission to the hospital he developed a slight pain at the base of the neck that was followed shortly by a severe precordial pain.

Examination showed a man of normal habitus with no evidence of the Marfan syndrome. The blood pressure was 110/90 mm Hg in the right arm and 120/100 in the left arm. The blood pressure was not recorded in the legs. The heart was enlarged to the left. There was a pronounced systolic propulsion at the second and third right intercostal spaces. A harsh systolic murmur, with accompanying thrill, was heard over the precordium with maximal intensity at the first and second right intercostal spaces adjacent to the sternum. The murmur was transmitted to the carotid arteries. The aortic second sound was diminished. The lungs were clear. The remainder of the examination revealed no significant abnormalities.

Following the administration of an opiate the pain gradually subsided. Six days after admission the patient suddenly died.

Autopsy revealed the weight of the heart to be 650 Gm. There was advanced calcific aortic stenosis with thickening of the mitral chordae tendineae. Death was caused by hemopericardium due to rupture of a dissecting aneurysm. There was an intimal tear 2.5 cm. above the aorta and the dissection extended through the length of the aorta and in a retrograde fashion to rupture into the pericardial sac. Cystic medial necrosis was noted in the microscopic sections of the aorta; there was no evidence of rheumatic lesions in the aorta.

**Patient 4.** M. I., a white male student of theology, age 27, had been known to have a heart murmur since the age of 3. There was no history of rheumatic fever, and he had never had symptoms referable to the cardiovascular system. In 1948, an x-ray of his chest showed dilatation of the ascending aorta with a heart of normal size (fig. 3A). On the day of admission he suddenly developed severe constant dull aching substernal pain extending from the epigastrium to the neck. The pain increased in severity, and he was admitted to the student infirmary.

Physical examination showed no evidence of the Marfan syndrome. The blood pressure was 106/84 mm Hg in both arms; it was not recorded in the legs. The heart was normal in size. The cardiac rhythm was regular. There was a harsh, grade III systolic murmur accompanied by a systolic thrill at the first and second right intercostal spaces.
The aortic second sound was replaced by a faint, early, high-pitched, blowing diastolic murmur. The systolic murmur was transmitted over the precordium toward the apex. The first sound at the apex was normal. The systolic murmur was not transmitted to the axilla. No diastolic murmurs could be heard at the apex. The lungs were clear and resonant. Liver and spleen were not tender or palpable. The remainder of the examination was normal. An electrocardiogram taken the day after admission showed left ventricular hypertrophy. On the following day the electrocardiogram showed changes consistent with acute pericarditis. During his hospital stay the patient continued to complain of chest pain requiring opiates for relief. During the following 3 days the pain became less severe; 4 days after admission, however, there was an increase in severity of chest pain associated with sudden gasping respiration that continued for 10 minutes, when he died.

Autopsy showed aortic stenosis (fig. 3B) with some calcification of the valve and with left ventricular hypertrophy. There was no evidence of rheumatic involvement of the mitral valve and the aortic stenosis was thought to be of congenital origin. There was a dissecting aneurysm, which began within the first few centimeters of the aortic valve in the area of dilated aorta. There was retrograde extension of the dissection with rupture into the pericardial sac. Death occurred as a result of tamponade (fig. 4). Microscopic examination showed cystic medial necrosis of the aorta.

Discussion

As is so often the case, whether the aortic valve disease was of rheumatic, congenital, or other origin in these instances cannot be stated with certainty. In the fourth patient, the history of murmur from the age of 3 years and the
absence of rheumatic stigmata by history or necropsy satisfy the usual criteria for congenital aortic stenosis. In the second patient the minor changes in the mitral chordae tendineae at necropsy and the history of frequent tonsillitis in youth are consistent with a rheumatic etiology. Changes in the mitral chordae tendineae were present also in the third patient.

In all 4 patients the stenosis of the aortic valve was only moderately severe and aortic regurgitation was also present in some degree. These may be important considerations in connection with development of changes in the ascending aorta.

If instances of cystic medial necrosis in association with coarctation of the aorta are excluded, of 4 patients seen at the Johns Hopkins Hospital in the last 2 years with large aneurysm of the ascending aorta associated with cystic medial necrosis, 2 had aortic valvular disease and are reported above as patients 1 and 2. The etiology in the other 2 patients is completely obscure. Mattison and Cluff have put on record 1 of these other cases.

In the second patient, there was no history one could relate to acute dissection of the ascending aorta although such a history was present in the first patient and was the presenting and predominating feature of patients 3 and 4.

The finding in the second patient of widespread cystic medial changes in the mesenteric, pulmonary, and subclavian arteries as well as throughout the aorta is disturbing to the theory that the changes in the ascending area are the result solely of hemodynamic stresses related to the disease of the aortic valve.

The presence of an unusual musical systolic “coo” over the innominate-carotid-subclavian axis in case 1 is of note. This was seemingly completely distinct from the murmur of aortic stenosis, which was of conventional quality. In other cases of dissection in the ascending aorta, musical murmurs, in either systole or diastole, have been heard over the course of the aorta. Anatomically at least 2 types of anomalous structures are present and might be playing a role: (1) fiddle-string bands usually traverse the false channel in the ascending aorta; (2) lips are created at the site of the initiating intimal tear or distally at the site of re-entry.

Partial occlusion of a vessel at the arch of the aorta may be the mechanism in the patient described here; although the murmurs resulting from occlusive arterial disease are generally noisy, occasionally they may be musical. A musical murmur well localized to the base of the neck or just below the clavicle on the right, especially if it develops abruptly or is changeable, is a sign suggesting dissecting aneurysm.

Other Cases. Reviewing cases of dissecting aneurysm in persons 40 years of age and less, Schnitker and Bayer in 1944 found that of 141 such cases reported in the literature, rheumatic valvular disease had been present in 9. Aortic stenosis was present in 1, and in a second there were combined lesions of the aortic and mitral valves. The remaining 7 cases were reported to have had mitral lesions.

Under the title of “Congenital Aortic Aneurysm with Valvular Stenosis and Dissecting Aneurysm,” Petch, in 1952, described a 35-year-old man in whom a cardiac murmur had been heard from the age of 5 years and noted again during a period of service in the army. There was no history of rheumatic fever. Fatal dissection with rupture into the pericardial sac occurred. Autopsy revealed fusion of the 2 posterior aortic cusps and calcification of the valve.

Lewes found 1 instance of dissecting aneurysm among 25 cases of aortic stenosis. The patient (case 7), a 65-year-old man, had a small pulse but a blood pressure of 105/75 mm. Hg. There was no evidence of associated aortic regurgitation. Anatomically the grade of stenosis was considered to be moderately severe. Cystic medial necrosis was present in the aorta.

No other cases precisely like those presented here have been found, although a comparable situation does occur in coarctation of the aorta in which dissection beyond the stenosis may occur.

Since it was first noted by Chevers of Guy’s Hospital in 1842, poststenotic dilatation of the
ascending aorta (fig. 3A) has been frequently observed with aortic stenosis of either rheumatic or congenital origin.\(^3\)\(^{-}\)\(^{15}\) At times the dilatation has attained relatively mammoth proportions, especially in cases of aortic stenosis of only moderate severity.\(^8\)\(^{-}\)\(^{18}\)

**Cystic Medial Necrosis.** The 2 clearest clinical associations with cystic medial necrosis of the aorta are hypertension and genetic inferiority of the aortic media, of which the Marfan syndrome\(^9\) is the most familiar example. In patients in whom congenital aortic stenosis is suspected, a congenital weakness of the aorta cannot be excluded but is unlikely in our opinion. In general, cystic medial necrosis may be a nonspecific morphologic expression of structural fatigue in a normal aorta subjected to unusual hemodynamic stresses or in a genetically inferior aorta exposed only to the usual stress. Aging, in the sense of accumulated physiologic stresses, seems to be another factor. Whatever the precise mechanics, disease of the aortic valve appears to result in a poststenotic hemodynamic set-up that is unusually stressful of nearly the whole of their curtains into rigid masses of calcareous substance—conditions which are productive of impediment to the passage of the blood from the ventricle. In cases of this description, I have observed that the aorta, at a short distance above its valves, becomes considerably dilated, its walls at the same time appearing remarkably thin. It might, at the first glance, be expected that, in this disease, as the blood really has great difficulty in entering the artery, a contrary state of the vessel would occur, and that the whole of its canal would become diminished in calibre; but the dilatation probably results from the long continuance of a degree of stagnation in the contents of the tube, the thickened and narrowed state of the passage preventing the systolic impulse of the ventricle from being conveyed into the vessel with sufficient force to propel the blood freely through the arteries. It may also be in great measure due to the fixed and hardened state of the valves, which instead of yielding with a moderate degree of elasticity under the pressure of the blood during the ventricular diastole, remain perfectly rigid, and, in this way, cause the whole of the blood contained in the artery to fall upon the sides of that vessel, which are thus compelled to yield. The thinning of the vessel's tunics evidently arises from the loss of their elastic power, in consequence of the long-continued over distension.

to the aorta. The occurrence of cystic medial necrosis in association with aortic stenosis seems to be more than coincidence.

**Summary**

A clinical syndrome—the association of disease of the aortic valve (stenosis and regurgitation) with diffuse aneurysm of the ascending aorta with or without dissection—is described on the basis of 4 patients in whom dissection occurred. Histologically, cystic medial necrosis of the aorta was present. It is suggested that this association represents further evidence that cystic medial necrosis of the aorta is a nonspecific result of hemodynamic stress on the aorta.

**SUMMARIO IN INTERLINGUA**

Un syndrome clinic—le association de morbo del valvula aortica (stenose e regurgitation) con aneurysma diffuse del aorta ascendente con o sin dissection—es describite super le base del casos de 4 patientes in qui dissection occurreva. Ab le puncto de vista histologic, cystic necrose medial del aorta esseva presente. Es formulate le opinion que iste association representa un prova additional que cystic necrose medial del aorta es un resultat non-specific de stress hemodynamic in le aorta.

**REFERENCES**

A CARDIOLOGIST'S HIPPOCRATIC OATH

Perhaps the physician should have a personal creed in respect to the handling of patients, and particularly apprehensive ones. Such a creed might consist of something like the following.

First, I shall avoid any thoughtless expression, deed or statement that might initiate, in a healthy or relatively healthy patient, the idea that the heart is abnormal; briefly, I shall not be a party to iatrogenic heart disease.

Second, I shall not bring precise instrumental and laboratory methods, such as electrocardiography, into disrepute by consciously gainful or ignorant misinterpretation.

Third, I shall discourage excessive dependence of any patient on a physician, but I shall give freely of time and try to think of satisfaction of the patient, which should include not only his state when he leaves the office but also after six months or a year's time.—HOWARD B. BURCHELL. Cardiac Manifestations of Anxiety. Proceedings of the Staff Meetings of the Mayo Clinic. Vol. 22, No. 20, October 1947.
Association of Aortic Valvular Disease and Cystic Medial Necrosis of the Ascending Aorta: Report of Four Instances
VICTOR A. MCKUSICK, R. BRUCE LOGUE and HENRY T. BAHNSON

Circulation. 1957;16:188-194
doi: 10.1161/01.CIR.16.2.188
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1957 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/16/2/188