STRUCTURE—FUNCTION CORRELATIONS IN CARDIOVASCULAR AND PULMONARY DISEASES (CPC)

Cardiac Sarcoidosis*

A Major Cause of Sudden Death in Young Individuals

Renu Virmani, M.D.; J. Conrad Bures, M.D.; and William C. Roberts, M.D., F.C.C.P.

Dr. William C. Roberts: Herein we will discuss certain findings in a patient with cardiac sarcoidosis. Dr. Virmani will describe the patient.

Dr. Renu Virmani: A 35-year-old white man, a college philosophy professor who died Jan 9, 1979, was observed to have occasional ventricular premature beats during a medical check-up in March 1978 (ten months before death). No other abnormalities were found on examination. Specifically, he had no precordial murmur. He weighed 73.6 kg and was 175 cm tall. The ECG (Fig 1) showed low voltage, and chest roentgenogram (Fig 2) showed a normal sized heart and normal hilar and pulmonary shadows. In May 1978, he had an "upper respiratory infection," and in June 1978, he noted exertional dyspnea, two-pillow orthopnea, pedal edema, and severe fatigue.

*From the Pathology Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, and the Department of Pathology, Montefiore Hospital, University of Pittsburgh Health Center, Pittsburgh.
Reprint requests: Dr. Roberts, NIH, Bldg 10A, Room 3E30, Bethesda 20205

He was hospitalized in July 1978, his first and only hospitalization. The blood pressure was 110/70 mm Hg. The jugular veins were distended; rales were heard over both lungs; the heart was enlarged; a grade 2/6 holosystolic murmur now was heard at the lower left sternal border and it increased with inspiration; a third heart sound was present; and the feet were edematous. The blood hematocrit value was 45 percent; white blood cell count, 10,200/cc mm; blood urea nitrogen value, 38 mg/100 ml; serum creatinine level, 1.4 mg/100 ml; and serum total cholesterol value, 126 mg/100 ml. The IgG immunoglobulins were "low." The ECG was similar to the preceding one. The echocardiogram disclosed the maximal dimensions of the left ventricle to be 70 mm (normal, 40 to 52; left atrium, 45 mm (normal, 15 to 35); and the aorta, 30 mm (normal, 20 to 35). The walls of both the left ventricle and ventricular septum were 10 mm thick. Catheterization on July 25, 1979, disclosed the following pressures (mm Hg): pulmonary arterial wedge mean, 28; a-wave, 30, o-wave, 44; pulmonary trunk, 55/30 (mean 40);

![Electrocardiograms](image)

**Figure 1.** Electrocardiograms taken 3/6/78 (upper) and 9/6/78 (lower). Both show low voltage and nonspecific T-wave changes. One extrasystole is present in the lower electrocardiogram.

CHEST, 77: 3, MARCH, 1980
right ventricle, 55/12; and right atrial mean, 10, a-wave 16. A diagnosis of idiopathic dilated cardiomyopathy was made and he was treated with digitalis, quinidine, chlorothiazide, and warfarin sodium. The dyspnea lessened considerably, the edema vanished, and he returned to his teaching duties. In September 1978, his weight was down to 146 pounds, his neck veins were flat, there was no edema, but a grade 3/6 murmur of tricuspid regurgitation persisted and a right ventricular lift was present. On Oct 13, 1978, he was started on a regimen of prednisone (10 mg daily), but during the next ten days, no subjective improvement was noted, and therefore, this medication was gradually discontinued over several more days. He remained asymptomatic until about Dec 20, 1978, when mild exertional dyspnea and orthopnea returned. His neck veins were distended, and the liver was both palpable and pulsatile. The weight had increased to 156 pounds, but he was not overtly edematous. He collapsed suddenly 19 days later while teaching and died.

Dr. Roberts: Dr. Bures, would you describe the findings at autopsy.

Dr. J. Conrad Bures: At necropsy (Montefiore Hospital, Pittsburgh), the heart weighed 460 g. All four cavities were dilated. The walls of both ventricles and both atria contained firm white deposits which histologically were typical sarcoid granulomas (Fig 3 to 6). The four cardiac valves and the coronary arteries were normal. Calcific deposits were present in a few myocardial fibers in the walls of all four cardiac chambers. The lungs together weighed 1.040 g; A 0.4-cm sized subpleural sarcoid granuloma was present in the right upper lobe. The tracheobronchial nodes measured up to 2 cm in diameter and they were nearly totally replaced by sarcoid granulomas (Fig 7). The liver (weight, 1,800 g) and spleen (weight, 300 g) were congested but free of granulomas. The rest of the organs were normal.

Dr. Roberts: Dr. Bures, would you describe the findings at autopsy.

Dr. J. Conrad Bures: At necropsy (Montefiore Hospital, Pittsburgh), the heart weighed 460 g. All four cavities were dilated. The walls of both ventricles and both atria contained firm white deposits which histologically were typical sarcoid granulomas (Fig 3 to 6). The four cardiac valves and the coronary arteries were normal. Calcific deposits were present in a few myocardial fibers in the walls of all four cardiac chambers. The lungs together weighed 1.040 g; A 0.4-cm sized subpleural sarcoid granuloma was present in the right upper lobe. The tracheobronchial nodes measured up to 2 cm in diameter and they were nearly totally replaced by sarcoid granulomas (Fig 7). The liver (weight, 1,800 g) and spleen (weight, 300 g) were congested but free of granulomas. The rest of the organs were normal.
Figure 4. Sites of maximal involvement of walls of right ventricle (RV) ventricular septum (VS), left ventricle (LV), and left atrium (LA). There is extensive replacement by sarcoid granulomas (Movat stains, original magnification × 27), (RV, LV and LA) and × 21 (VS).

Dr. Roberts: The patient described exemplifies some of the diagnostic and therapeutic problems of patients with cardiac sarcoidosis. First, sarcoidosis was never diagnosed in life in our patient. Indeed, his clinical diagnosis was idiopathic dilated cardiomyopathy and this diagnosis seems, in retrospect, quite appropriate in view of the clinical findings. The patient was young (35 years old). His initial

Figure 5. Extensive, sarcoid granulomatous involvement of left atrium. b (right). Close-up of giant cell, epitheloid cells and lymphocytes, a (left), Movat stain, original magnification × 130, and b (right), hematoxylin-eosin, original magnification × 880.
manifestation was ventricular premature beats which were noted on routine physical examination ten months before death, and he remained asymptomatic until six months before death when evidence of congestive heart failure appeared. He had cardiomegaly, a murmur of tricuspid regurgitation, and overt congestive heart failure which initially was quite responsive to medical therapy, but in his last month, reappeared. Because he was young and never had chest pain, coronary heart disease as a possibility never arose. The absence of a precordial murmur at the onset of his illness ruled out organic valvular heart disease as a reasonable diagnosis. During life, there were no signs suggesting the possibility of sarcoidosis. Chest roentgenogram showed normal lungs and no hilar adenopathy. Furthermore, lymph nodes were never palpated on physical examination. Moreover, there were no signs or symptoms of pulmonary disease. The mild hepatomegaly and splenomegaly were consistent with congestive heart failure and certainly did not suggest an infiltrative process, and at necropsy, no granulomas were present in either the liver or the spleen, and indeed, only one granuloma was observed in the lungs. There were no demonstrated ventricular arrhythmias other than an occasional ventricular premature beat during his illness. There were no cardiac conduction disturbances, heart block, syncope, or dizzy spells. Thus, clinically either retrospectively or prospectively, a diagnosis of sarcoidosis in the present patient would have been extremely difficult.

Approximately three months before death, the pa-
CHEST, 77: 3, MARCH, 1980

CARDIAC SARCOIDOSIS 427

tient was given prednisone for about 15 days. Because no subjective improvement was noted, this medication was stopped. This patient brings up the possibility of a trial period of corticosteroid medication for all young patients who have congestive heart failure which is not secondary to valvular or coronary heart diseases or to hypertrophic cardiomyopathy. Possibly, if the corticosteroid treatment had been continued for a longer period and with higher doses, improvement may have occurred.

Sudden death is one of the well recognized modes of death in patients with cardiac sarcoidosis. Indeed, it is the most common mode of death in patients with cardiac sarcoidosis extensive enough to cause cardiac dysfunction, and it is the first manifestation of sarcoidosis in about 20 percent of patients with cardiac sarcoidosis. It is relatively unusual, however, for a patient with cardiac sarcoidosis and evi-

dence of chronic congestive heart failure to die suddenly. Most patients with sudden death from cardiac sarcoidosis have preceding evidence of ventricular arrhythmias (most commonly ventricular tachycardia) or evidence of high degrees of heart block (most commonly complete heart block). Our patient never had evidence of multifocal or runs of ventricular premature beats or ventricular tachycardia or complete heart block.

One of the unique features of cardiac sarcoidosis is that patients with infiltration of the heart by sarcoid granulomas extensive enough to cause cardiac dysfunction infrequently have evidence of dysfunction of another body organ. Our patient only had evidence of cardiac dysfunction and no dysfunction of another body organ. At necropsy, only sites where sarcoid granulomas were observed were in the heart, mediastinal lymph nodes, and lung.

FIGURE 7. Tracheobronchial lymph node showing extensive replacement by sarcoid granulomas (hematoxylin-eosin, original magnifications a [left], × 8 and b [right], × 196).

FIGURE 8. Good and bad effects of corticosteroid therapy in patients with cardiac sarcoidosis (reprinted with permission from Roberts WC, and the Yorke Medical Group).

Downloaded From: http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21125/ on 05/29/2017
(one minute focus). A corollary to this is that the occurrence of symptomatic involvement of a noncardiac organ by sarcoid generally indicates that symptom-producing cardiac involvement by sarcoid is unlikely to occur. Flemming,2 in search of patients with cardiac sarcoid, surveyed the chest, eye, and skin clinics in his hospital for patients with sarcoidosis and found this search unprofitable in revealing patients with cardiac sarcoid. Thus, cardiac sarcoidosis severe enough to cause cardiac dysfunction tends to be an all-or-none process: if it causes cardiac dysfunction, it tends not to cause dysfunction of another organ system; conversely, if it causes dysfunction of a noncardiac organ, it infrequently causes cardiac dysfunction. Although patients with fatal cardiac sarcoidosis may have sarcoid granulomas in other body organs, the extent of the sarcoid granulomas in the heart, in general, appears to be out of proportion to the extent in other body organs. Our patient had extensive granulomatous infiltrates in his myocardium, particularly the ventricles, but only one sarcoid granuloma was found in the lung and the only other body organ containing granuloma was lymph node.

One of the unusual histologic findings in sections of myocardium in our patient were granulomas around intramural coronary arteries. Dr. Virmani, can you summarize observations of others regarding cardiac sarcoid granulomas and their relationship to the coronary arteries?

Dr. Virmani: No one has reported sarcoid granulomas in extramural coronary arteries, but Morales and associates,3 and more recently, James4 pointed out that granulomas frequently surround the intramural coronary arteries of either cardiac atria or ventricles or both, and that the lumens of these arteries may be narrowed. The narrowing, in general, appears to result from intimal proliferation rather than from actual granulomatous invasion of the lumens. The medial and adventitial walls, however, have been observed to contain sarcoid granulomas. In our patient granulomas surrounded many intramural coronary arteries, particularly in the ventricles, and epithelioid cells were found to invade the wall of several intramural coronary arteries. Thus, sarcoidosis must be added to the list of causes of intramural coronary arterial disease. The functional significance of the involvement of the intramural coronary arteries, however, is uncertain. We suspect that it has little to no functional significance. Involvement of the small arteries in the lung by sarcoid granuloma has been noted in the past by others.5 There is no surprise, therefore, that the small cardiac arteries may be involved by sarcoid granulomas.

Dr. Roberts: Dr. Virmani, the diagnosis of cardiac sarcoidosis clinically generally appears to be either simple or extremely difficult. Is this diagnosis easy at necropsy, and what morphologic criteria should be used to establish the diagnosis of cardiac sarcoidosis?

Dr. Virmani: To make the diagnosis of cardiac sarcoidosis at necropsy, we have required the presence of noncaseating granulomas in heart muscle and in lymph nodes.1 The absence of noncaseating granulomas in lymph nodes, but their presence in the heart does not allow one to say, in our view, that sarcoidosis is the proper diagnosis. There have been a number of patients described with so-called "giant cell myocarditis." We believe that most of these patients in actuality had cardiac sarcoidosis. A problem here is that sarcoid may extensively involve the heart, and yet, although granulomas may be present in lymph nodes, the lymph nodes may not be enlarged. Because they are not enlarged at autopsy, histologic sections may not be prepared from them. If histologic sections are not prepared, certainly one cannot confirm or deny the presence of granulomas in these structures.

Dr. Roberts: One final comment regarding treatment. It seems reasonable to treat with corticosteroids any patient with documented cardiac sarcoidosis, be he (she) symptomatic or asymptomatic. As shown in the accompanying diagram (Fig 8), it appears that corticosteroid therapy causes shrinkage and conversion of the sarcoid granulomas into relatively dense scar tissue. In our patient, the cardiac sarcoid granulomas appeared quite active in that numerous lymphocytes surrounded the epithelioid and giant cell granulomas. In patients treated for long periods with corticosteroids, the cardiac sarcoid granulomas tend to be converted to scar tissue and the granulomas may disappear entirely. In our patient, relatively little myocardial scarring was observed.

REFERENCES

1 Roberts WC, McAllister HA Jr, Ferrans VJ: Sarcoidosis of the heart: a clinicopathologic study of 35 necropsy patients (Group I) and review of 78 previously described necropsy patients (Group II). Am J Med 1977; 63:86


