Myocardial Sarcoidosis

By Robert A. Peacock, M.D., Eugene J. Lippshutz, M.D., and Agnes Lukas, M.D.

Systemic sarcoidosis frequently involves the heart and is usually diagnosed at autopsy, often as a single granuloma. An extensive review of the literature was prompted by a very interesting clinical problem of etiology in the frequent syncope and Stokes-Adams attacks in an otherwise apparently healthy young girl. The pathologic findings and therapeutic dilemmas are reviewed in detail.

Sarcoidosis is generally regarded as a systemic disease of unknown etiology that may involve any organ in a usually benign granulomatous process. In recent years it has become apparent that the myocardium is frequently involved and may result in bizarre arrhythmias or sudden death. This paper presents a review of 28 cases proved by autopsy and adds an additional case manifested by Stokes-Adams attacks.

In table 1 we have listed the cases of myocardial sarcoidosis with autopsy evidence.

The following case presentation (case 29) was puzzling clinically; during the hospital stay virtually every diagnostic and therapeutic test was attempted without success. In retrospect the case was typical of myocardial sarcoid, that is, sudden death in a young individual with a relatively short history of Stokes-Adams attacks.

Case Presentation

A 27-year-old white woman was admitted June 23, 1955, with a 6-week history of frequent episodes of syncope. An electrocardiogram had revealed the presence of complete heart block. She had been treated unsuccessfully with both sympathomimetic and ganglionic-blocking drugs. The heart rate was reported to vary between 20 and 150. The past history was noncontributory with the exception of albuminuria at the age of 6. She had successfully completed 3 normal pregnancies. A physical examination 15 months previous to admission was normal.

The blood pressure was 110/54 with irregular bradycardia of 28. Temperature was 100 F. rectally and varied between 98 and 100, rising to 101 F. on 3 occasions. Physical examination was entirely normal except for bradycardia and a soft grade II systolic murmur at the apex. Seven complete blood counts and urinalyses were all normal. The sedimentation rate was 8 mm. per hour or less. The fasting blood sugar was 126 mg. per cent, blood urea nitrogen 16 mg., calcium 10.1 mg., phosphorus 4.6 mg., and sodium, potassium, chloride, and CO2 combining power were all normal. The cephalin flocculation, Wassermann, and Kahn tests were negative. The bromsulfalein retention was 3 per cent. Five blood cultures were sterile. The anti-streptolysin titer was 50 units and the C-reactive protein was negative. Agglutinations for Salmonella typhosa H and O, Brucella abortus, and cold agglutinins were all negative. Complement fixation for Q fever, psittacosis, and lymphogranuloma venerum were all normal. The lupus erythematosus preparation was negative. Skin and muscle biopsies on 2 occasions were reported as showing parimesial reaction only. The electroencephalogram was interpreted as normal. The basal metabolic rate was —25 per cent. Fluoroscopic and radiographic examination of the heart and chest were originally reported within normal limits but on review after autopsy lesions were demonstrable. The esophagram revealed no abnormalities. The electrocardiograms on numerous occasions showed 2:1, 3:1, and complete A-V block.

The patient was given 2.4 mg. of atropine intravenously without effect. She received phenobarbital and also ammonium chloride with no appreciable change. Sodium lactate orally was used in an attempt to raise the pH. A trial of prednimove and large doses of salicylates to the point of toxicity were without effect. Intravenous and repository ACTH for 2 days and 7 days each proved unsuccessful. A trial of thyroid because of the low basal metabolic rate was ineffective.

Numerous syncopal attacks with asystole occurred during the hospital stay. Following a second course of ACTH and 4 weeks without seizures, she was discharged on September 2, 1955.

The patient did well at home until September 24, 1955, at which time she had 2 seizures and was readmitted the next day, in coma. Once again physical examination was not remarkable except for the heart block. An electroencephalogram was again repeated because anoxic changes were feared. The patient did well for 1 day, but on September 27 she suddenly developed complete asystole. Despite intravenous molar lactate and active attempts at...
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<tr>
<td>28. 54, W, F</td>
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<td>Sudden death</td>
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<tr>
<td>29. 27, W, F</td>
<td>Myocardium</td>
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resuscitation, including the use of the cardiac pacemaker, the patient died.

**Autopsy Findings**

The findings in the heart at autopsy revealed the immediate cause of death. The heart was distinctly enlarged, especially the right ventricle, and to a lesser degree the right atrium, presenting the picture of cor pulmonale with slight hypertrophy of the right ventricular wall and distinct dilatation of the right ventricle. The thickness of the right ventricular wall was 0.6 cm.

The endocardium lining both ventricles was smooth except for an area in the left ventricle just below the right posterior semilunar valve, above the interventricular septum, where the endocardium showed distinctly granular protrusions of slightly yellowish brown color. The clearly noticeable area measured about 1.5 cm. along the heart axis and 1.0 cm. in transverse diameter.

On cut section through this raised area, the underlying myocardium appeared finely nodular. On several cross sections the myocardium was firmer than normal, gray-brown in color, with scattered minute, somewhat yellow nodules. Apart from this finding of the heart, the endocardium, and myocardium appeared entirely normal in both ventricles and atria.

Three sections of the lower part of the membranous septum and through the bundle of His revealed that the endocardium and the underlying muscle bundles were completely replaced by nodular tubercle-like lesions (fig. 1). Serial sections of the area of the atrioventricular node laterally and medially did not show gross or microscopic lesions of sarcoid.

Five sections of the interventricular septum and left ventricle showed sarcoid lesions also in the endocardium and subendocardial myocardial muscle fibers. Sections of the ventricular septum and right ventricle were normal. The other 25 sections of the heart taken from the papillary muscles, apex, left ventricle, anterior and posterior wall, and right ventricle were free of sarcoid lesions.

Sections through the above-mentioned granular protrusions showed nodular masses, discrete and confluent tubercle-like lesions, composed of epithelioid cells with Langhans-type giant cells. There was no caseation necrosis and no inflammatory reaction, although there were scattered lymphocytes around the nodules and considerable hyalinization of the endocardium, as well as of the subendocardial tissue.

Special stains for fungi, acid-fast bacilli, and Gram stain were negative.

These histologic findings were typical of sarcoidosis.

The other positive findings were limited to the lungs, lymph nodes, and spleen. The lower lobes of the lungs grossly showed minute, tan-colored granulomatous lesions, largely around the pulmonary arteries. The intrapulmonary lymph nodes were distinctly enlarged and granular. A few granulomatous lesions were found in the upper lobes.

The bronchomediastinal and peritracheal lymph nodes were markedly enlarged and on section, finely granular and gray-white.
The spleen was of normal size, with an irregular surface. On section the spleen was spotted with irregularly outlined granulomatous lesions, yellow-gray and bulging somewhat from the congested parenchyma.

Histologically, all these granulomatous lesions from the lungs, spleen, and lymph nodes were characteristically sarcoid with epithelioid cells and Langhans giant cells. In the lower lobes the intrapulmonary lymph nodes were completely replaced by these nodules. Around the arteries large confluent areas of sarcoidosis showed marked hyalinization in the center.

**DISCUSSION**

The incidence of sarcoid in the general population is unknown. It is a disease often confused with tuberculosis. Frequently suspected cases fail to be proved by biopsy or autopsy. Freiman estimated 1000 cases reported by 1948. Longcope and Freiman estimated a total of 523 cases of sarcoid reported in this country by 1952. They reviewed 92 cases that had been autopsied and found the heart involved in 20 per cent. However, in a disease that is often without symptoms and in which all evidence of involvement may disappear, it is difficult, if not impossible, to estimate incidence in any postmortem organ clinically. As early as 1938, Pinner, in reporting 18 autopsies, pointed out that 10 of these were unsuspected during life. Ricker and Clark reported 22 cases of which 14 were unsuspected before autopsy. Gilg reported a follow-up study of 191 cases of sarcoid in which there had been 44 deaths; only 10 cases were proved by autopsy and in only 6 was the cause of death directly attributed to sarcoid. The heart was directly involved in only 1 of his cases. It is safe to assume from the statistics presented that sarcoid is a fairly common disease and that in those cases where death has been due to sarcoid, the heart is frequently involved.

The diagnosis of myocardial sarcoidosis has rarely been made during life. Salvesen described a case with tachycardia and heart block in a patient with the skin lesions of sarcoidosis. He attributed the cardiac changes in this patient and in 3 others to sarcoidosis of the myocardium. Bates and Walsh in 1948 attributed ST and T-wave changes to sarcoid of the heart and in 1951 Adickes considered sarcoid as the cause of carditis in 1 patient.

In reviewing the proved cases in the literature, it becomes apparent that when the heart is involved directly by the sarcoid granuloma, the patient often has heart block that may result in sudden death. Of the 29 cases reviewed, 10 terminated in sudden death. Fourteen were described as either Stokes-Adams disease or had clinical features of heart block.

The frequency of tachycardia or other arrhythmias has been pointed out by other authors. In several articles the electrocardiographic changes in cases of suspected myocardial sarcoid have been described. Reference has been made to the frequency of uveoparotid fever in myocardial sarcoidosis. The duration of clinical sarcoid before death with myocardial involvement has varied from 3 months to 15 years. The majority of the fatal cases are in the third decade (13 out of 29 in table 1).

The diagnosis of myocardial sarcoidosis is most frequently made at autopsy. There was no appreciable sex or racial difference. The transient nature of the cardiac involvement has been pointed out previously and recovery may occur.

**Summary**

Twenty-nine proved cases of sarcoidosis of the myocardium are reviewed and an additional case is reported. Many additional cases in the literature may be sarcoid of the myocardium. The heart is involved in one fifth of the cases of sarcoid. When death is due to direct involvement of the myocardium, it is likely to be associated with heart block or some other arrhythmia resulting in sudden death.

**Summario in Interlingua**

Es presentate un revista de 29 provate casos de sarcoidosis del myocardio. Un caso additional es reportate. Multe altere casos trovate in le litteratura es possibilemente etiam sarcoide del myocardio. Le corde es afficate in un quinto del casos de sarcoide. Quando le morte resulta directemente del affection del myocardio, illo occurre con alte grados de probabilitate subitemente e in association con bloco cardiac o un altere arrhythmia.
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The subtility of nature is greater many times over than the subtility of the senses and understanding; so that all those pretty meditations, speculations, and controversies in which men indulge are really quite mad, only there is no one detached enough to observe it.—BACON, 1561–1626.
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