Sarcoidosis of the Heart
A Cause of Sudden and Unexpected Death

By William E. Kulka, M.D.

Sarcoidosis (Benier–Boeck's disease) is not limited to skin or eye as once thought. Now it is known to be a chronic granuloma of the reticulo-endothelial system, dispersing tubercle-like nodes over all organs. Assumption of benignity had to be abandoned. Supporting proof that it can be the cause of death is this report of an autopsy of a young woman following sudden death due to extensive sarcoidosis of the heart, with miliary nodes scattered in most of the organs. No signs of tuberculosis could be found.

SARCOIDOSIS, or Besnier-Boeck-Schau- mann's disease, has attracted the interests of the research worker as well as the clinician in an ever increasing degree during the last decade. From its status as a medical curiosity it has emerged as a more widely recognized and fairly well-defined entity. Its occurrence seems universal. 2

What was first described as an interesting, although rare, disease of the skin by Besnier, in 1889, and independently by Boeck, 3 also in 1899, was later found in the eye and salivary glands and is now considered a systemic disease presenting the features of a chronic infectious granuloma. Like its counterpart, tuberculosis, it can invade every organ of the body as well as bone marrow, dura and the eye. The skin manifestations, although frequent, probably are not present in more than 20 per cent of all cases. 3

The experiences of the last twenty years have stressed the fact that sarcoidosis is a general spreading disease with a predilection for the lymph-reticulo-endothelial and hematopoietic systems. 4 The assumption of the absolute benignity had to be abandoned when there were occasional reports of autopsies performed on patients who had died as a direct consequence of the disease. Even though one would wish to exclude caseating tuberculosis as a natural development of sarcoidosis 4 and limit the number of direct casualties to those who succumbed to direct effects of specific conditions, the refutation of the benignity

stands. This observation was made by M. Pinner, 5, 6 in 1939, in a collective report of thirty-nine autopsies. Rubin and Pinner, 7 in 1944, described twenty-five autopsies with the same deduction. Reiser, 7, 8 Rosenthal, 9 and Freimann 9 also arrived at the same conclusion. The latter author, up to 1948, had collected altogether seventy autopsied cases. He included nineteen from their own institution in Boston; the remainder were compiled from the literature. He stated that many of them were incompletely described or complicated by other diseases, chiefly tuberculosis and syphilis. In several the diagnosis was open to doubt.

Recognition of the damage caused by sarcoidosis in one specific focus, or its dissemination, was instigated by Longscope, 10, 11 with his discussion of involvement of the heart. He added three autopsies of his own, one of which was complicated by syphilis. Apparently Cotter 1 was the first to present the extensive changes in the myocardium caused by these nodes found at autopsy which resembled tubercles but differed from tuberculosis. He reported the case of an 18 year old Negro who was observed clinically prior to his death. There was considerable anergy against tuberculin during life. The histologic findings post mortem of tubercle-like noncaseating nodes in the skin, spleen, lymph nodes and alimentary tract, as well as the extensive specific infiltration of the cardiac wall corroborated the diagnosis of sarcoidosis. The only complicating factor was a strongly positive Wassermann reaction. Another death due to widespread involvement of the heart by tubercle-like noncaseating nodes was re-
ported by Johnson and Jason in 1946 (see addendum).

The paucity of reported autopsies on such cases influenced the writer to publish the following case in which extensive damage to the myocardium due to sarcoidosis was found.

Case Report

History: A 26 year old Negro woman collapsed and expired suddenly on the street. Her sudden and unexplained death became a subject for the Coroner’s investigation. A scant history was pieced together from information obtained from her husband and a physician who had seen her several times in the three months prior to death because of a complaint of chronic inflammatory condition within the pelvis. At the beginning of the treatment period this physician had noticed several nodes which resembled sarcoids on her arms, legs and chest. These disappeared without medication. No biopsy was taken. There was no history of fever or chills. There was a history of some intermittent attacks of slight cardiac palpitation during the last few months prior to her death. She was never hospitalized. No electrocardiogram was taken. Urine examination and serology were negative. There were no microscopic or chemical examinations of the blood. Latex x-ray films of the chest showed some blurred increase in the mediastinal lymph nodes. The deceased was not engaged in factory work or otherwise gainfully employed.

Abstract of Autopsy Findings: The body is that of a colored female 66 inches tall and weighing 132 pounds. The skull and brain show no abnormalities.

Lymph Nodes: The cervical and axillary lymph nodes are not enlarged. There are clusters of enlarged grayish red and moderately soft lymph nodes along both sides of the trachea, at its bifurcation and along the main bronchi. Some of them are matted together. On cross section, these lymph nodes are grayish red. Where matted together the outlines of the individual lymph nodes are distinctly visible. The mesenteric lymph nodes show no gross abnormalities. There is, however, a number of retroperitoneal lymph nodes along the abdominal aorta from the hiatus of the diaphragm to the bifurcation of the aorta, which are moderately enlarged and yellowish or grayish pink on cross section.

Spleen: The spleen weighs 250 grams and is dark red and congested. On cross section the follicles appear irregularly enlarged.

Pericardial Sac and Heart: There is about 30 cc. of clear fluid in the pericardial sac. The heart is moderately enlarged, weighing 300 grams. The right ventricle is markedly dilated and its walls thinned. There are large areas of white discoloration at the anterior and posterior wall of the left ventricle. On cross section, more than half of the lower portion of the left ventricle, including septum and apex as well as both papillary muscles, appears yellowish white and glistening (fig. 1). The rest of the cardiac musculature is light grayish red. All the valves are free and tender. The epicardium outside of the dull whitish area is smooth. The coronary arteries are patent and elastic but the left lateral limbs of the anterior descending branch of the left coronary artery leading into the whitish area described above seem to be somewhat compressed and narrowed. Aorta and pulmonary artery show no marked abnormality.

The gastrointestinal tract, liver, pancreas and kidneys are of normal appearance. There are bilateral parametrial adhesions and a moderate degree of hydrosalpinx. The menstruating uterus is of medium size.

There are no gross abnormalities of the endocrine glands including the persistent thymus.

Histologic Findings:

Mediastinal, paratracheal and some of the retroperitoneal lymph nodes in the bifurcation of the diaphragm: Many of the lymphoid follicles are replaced by nodes consisting of a fibrous capsule rich in collagen which surrounds groups of epitheloid (reticulo-endothelial) cells and one or several multinucleated giant cells. The darkly staining nuclei in these giant cells, twenty or more, are arranged in clusters or in the periphery of the slightly acidophilic cytoplasm. Some of these nodes are surrounded by lymphoid cells, but there is a striking absence of eosinophile or polynuclear neutrophile leukocytes.
Fig. 2.—Sarcoidosis of spleen

Fig. 3.—Sarcoidosis in left cardiac wall infiltrating the cardiac musculature
Some increased fibrosis with a scarlike density may appear in some of the larger lymph nodes. However, nowhere is the fibrous capsule penetrated.

Spleen: Among the normal looking lymphoid follicles are many tubercle-like nodes of the character described above (fig. 2).

Heart: Sections taken from the whitish areas of the left ventricle show that most of the cardiac musculature is replaced by a network of fibroblasts, which enclose multiple tubercle-like nodes with many polynuclear giant cells. A number of nodes are fused together. In some places where the fibrosis of stroma is increased, the number of typical nodes is decreased.

In the periphery of the granuloma, where bundles of muscle fibers remain, clusters and columns of mononuclear white cells can be seen infiltrating the interstitial tissue. The corresponding epicardium presents multiple perivascularly arranged tubercle-like nodes in the subepicardial layers (figs. 3 and 4). Right Ventricle: Only a few scattered nodes are seen in the epicardium and between the cardiac muscle fibers.

Lungs: A number of small tubercle-like nodes are present in the perivascular connective tissue but there is no fibrosis or necrosis.

A few characteristic nodes are seen in the gastric mucosa, liver, kidneys, thyroid, adrenals and pituitary gland.

There are no specific changes in blood or bone marrow.

Silver stains of tubercles in lymph nodes and in the affected area of the heart revealed a delicate network of fibrils.

Specific stains failed to reveal the presence of any characteristic organisms.

**Diagnosis:** The cause of death was acute cardiac failure in a case of generalized sarcoidosis with extensive specific infiltration of the wall of the left ventricle of the heart.

**FIG. 4.—Typical polynuclear giant cell in reticular stroma (left cardiac ventricle)**

**Discussion**

A classic picture of sarcoidosis is delineated by (1) the simultaneous spread of tubercle-like nodes of granulomatous tissue formed by epitheloid and reticulo-endothelial cells encasing the typical multinucleated giant cells, (2) the absence of eosinophiles, in contradistinction to Hodgkin's disease, (3) the absence of polynuclear neutrophiles, i.e., lack of evidence of acute inflammation, (4) the absence of caseating necrosis and (5) the minimal amount of fibrosis.

Remarkable in this case is the simultaneous dissemination through the organs and the
lympho-endothelial system with a semblance of the spread of miliary tuberculosis. However, there is no reckless destruction of the organ parenchyma. Where reticulo-endothelial tissue was involved, in some instances, an increased degree of fibrosis resulted.

Attention is called to the fact that in many sites the presence of the nodes was discovered only by means of microscopic examination. Many such nodes may heal and disappear with no remaining evidence or sometimes leaving only a non-specific scar. In this particular case an exception is seen in the extensive destruction in the heart muscle described above. Often this was a result not only of the confluence of the tubercle-like nodes but also of a fibrosis or a widespread infiltration by reticulo-endothelial and lymphoid-like cells causing atrophy of the cardiac musculature. It seems worthy of mention that where normal heart muscle and sarcoi
d tissue meet in the left ventricle one can see the invasion of the former by finger-like processes.

Progressive decrease in the efficiency of the left ventricle was followed by acute dilatation and subsequent failure of the right ventricle due to the overload. The marked involvement of the epicardium and the specific perivascular localization of the granulomatous process hastened the failure. There was no increased resistance to the pulmonary circulation due to massive infiltration or interstitial fibrosis of the lungs, which has been mentioned as one cause of death in sarcoiosis of the heart.\(^2\).\(^3\) The destruction in this case was so widespread as to cause the myocardial failure in contradistinction to the assumption of a specific interference with the cardiac conductive system described by Longscope.\(^5\),\(^6\),\(^9\)

This case is distinguished by the fact that it was not influenced by additive effect of such complications as manifest tuberculosis or syphilis. This absence of tuberculosis seems remarkable, since the study of the literature leads one to parody Ewing's expression for the association of Hodgkin's disease and tuberculosis, i.e., we might say: "Tuberculosis follows sarcoiosis like a shadow."

It would exceed the scope of this paper to discuss the etiology of this protean malady. Let us simply agree with Freimann's conclusion: "The etiologic issue is still far from solution and has made little progress in the last twenty years."

**Summary**

An autopsy performed on a 26 year old Negro woman who died suddenly and unexpectedly is reported.

The gross anatomic impression was of a widespread fibrosis of the left cardiac ventricle. The microscopic examination revealed that a granuloma-like tissue, characteristic of sarcoiosis, had replaced the greater part of the musculature of the left ventricle and its papillary muscles. The process also affected the overlying epicardium. The right ventricle, less affected, was acutely dilated.

Sarcoi
d nodes were found disseminated in the lungs, mediastinal and retroperitoneal lymph nodes, spleen, gastric mucosa, liver, kidney, thyroid and pituitary glands.

The case was free of evidence of tuberculosis or syphilis.

**Addendum**

An additional case of sarcoiosis of the myocardium was reported recently in a clinicopathologic review of 300 cases of sarcoiosis compiled by Ricker and Clark.\(^9\)

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