CASE REPORT

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Cardiac Sarcoidosis—An Occult Cause of Sudden Death: a Case Report and Literature Review

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ABSTRACT: Sarcoidosis is a multi-systemic granulomatous disease of unknown cause. It commonly involves lymph nodes, lungs, eyes, and skin. Cardiac sarcoid may be isolated, or associated with systemic involvement. Cardiac involvement is found in 20–50% of autopsied patients with sarcoidosis. However, it only gives rise to clinical manifestations in about 5% of patients. Cardiac involvement by sarcoid has been reported to manifest as complete heart block, papillary muscle dysfunction, congestive heart failure, pericarditis and/or effusion, conduction abnormality or arrhythmia, chest pain, and sudden death.

The most common site of involvement is the interventricular septum base, which when involved may lead to heart block or arrhythmia. We report a case of sudden death in a 33-year-old male with a history of surgically repaired congenital heart disease. Although his congenital heart disease was originally postulated to be important in his death, autopsy examination revealed cardiac sarcoid with prominent involvement of the conduction system.

KEYWORDS: forensic science, heart, myocardium, sarcoid, sarcoidosis, sudden death, conduction system

This 33-year-old male patient had previously surgically corrected congenital heart disease, that he was told would not limit his life span. From sleep one night, he awoke with dyspnea, palpatations and nausea and suddenly collapsed. Resuscitation was unsuccessful and included intubation and electrical defibrillation for ventricular tachycardia and fibrillation. He had no known medical problems aside from his heart disease, and was thought to be in excellent health prior to his sudden and unexpected demise.

Pathological Findings at Autopsy

When the chest was opened for observation, the most prominent finding was pulmonary edema and marked lymphadenopathy of the mediastinal and hilar lymph nodes (Fig. 1). Grossly this was thought to be a neoplastic process, likely lymphoma, and the provisional cause of death was reported to be respiratory insufficiency related to extrinsic bronchial compression by the mediastinal tumor, type to be determined by microscopic examination. Due to the history of the previously repaired congenital heart disease, the heart was referred to a cardiac pathologist for complete cardiac examination. Toxicology was negative.

The heart weighed 620 g after fixation. Two findings of congenital heart disease were noted. There was a left sided superior vena cava which drained into the coronary sinus causing dilatation of it. There was no evidence of an unroofed coronary sinus or cor triatriatum.

In addition, the tricuspid valve septal leaflet was firmly adherent to the area of the membranous septum. The aortic valve had had a Trusler plication whereby the right and non-coronary cusps were re-suspended by a suture. There changes were indicative of a membranous ventricular septal defect (VSD) closure with a Trusler plication due to aortic valve incompetence from prolapse of the cusps into the VSD.

By microscopic examination there were scattered foci of granulomatous inflammation with epitheloid giant cells and foci of myocyte necrosis. The granulomata were most marked at the base of the inferior wall of the left ventricle. Special stains, including silver stain for fungi and stain for acid fast bacilli, were negative.

An abbreviated conduction system examination was undertaken with sections of the sinoatrial (SA) and atrioventricular (AV) nodes sampled. Granulomatous inflammation in the region of the SA and AV nodes was noted (Figs. 2–3). The inflammation was also noted in the myocardium just superior to the AV node in the lower interatrial septum, and in the myocardium in the upper portion of the interventricular septum just after the bifurcation into the Bundle branches.

Microscopy confirmed that the mediastinal lymphadenopathy was due to sarcoidosis with considerable fibrosis. Sarcoid also involved the lung parenchyma, liver, and spleen, although these areas of involvement were not as marked as the involvement of the heart myocardium and the lymph nodes.

Comment

Sarcoidosis is a multisystem granulomatous disease of unknown etiology. It commonly involves the mediastinal lymph nodes, lungs, liver, eyes, and skin. Patients classically present with lung disease and hilar lymphadenopathy. Cardiac sarcoid may occur in isolation, or more commonly, be part of wider disease involvement in other organ systems. Some studies have found an inverse relationship between cardiac and extracardiac involvement (1,2).

In autopsy studies, up to 20% to 50% of autopsied patients with

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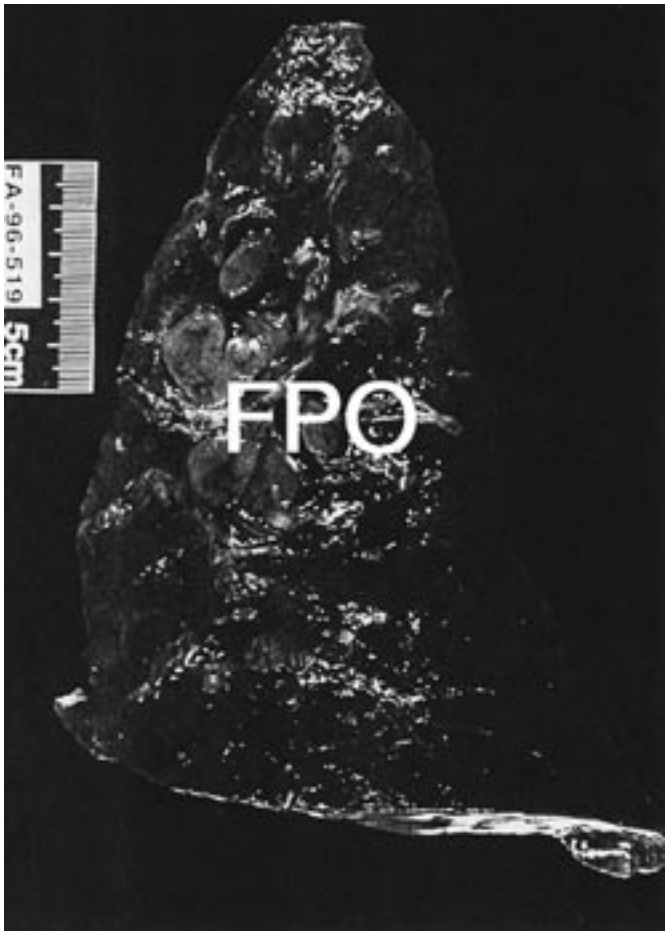

FIG. 1—*Cut surface of the lung demonstrates marked lymphadenopathy. The nodes were fleshy to palpation and were thought to be involved by lymphoma.*

sarcoid have cardiac involvement (3–7). The bias of the population is obvious, as sudden death is a common manifestation of cardiac involvement, thus favoring autopsy of those patients with cardiac involvement. Clinical manifestations of sarcoidosis are much less common; occurring in about 5% of cases (6,7). The clinical presentation depends upon the degree of involvement, and equally upon the location of the lesions.

The most common manifestations include complete heart block, papillary muscle dysfunction, congestive heart failure, pericarditis, pericardial effusion, conduction abnormalities, chest pain, and various arrhythmias (2,5,6,8–11). When the hemodynamics are studied, restrictive cardiac dysfunction may be present. This vast array of symptoms parallels the most common sites of involvement—the interventricular septum base (conduction abnormalities, heart

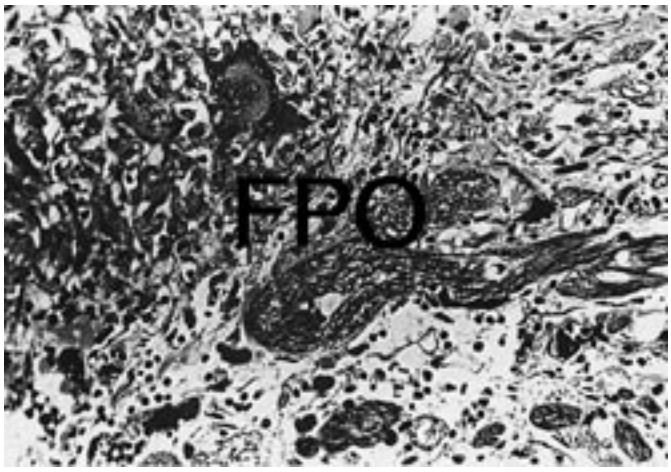

FIG. 3—*Photomicrograph of the left ventricular myocardium near the approach to the atrioventricular node (AV node). Granulomatous inflammation is evident. A small artery is also present.*

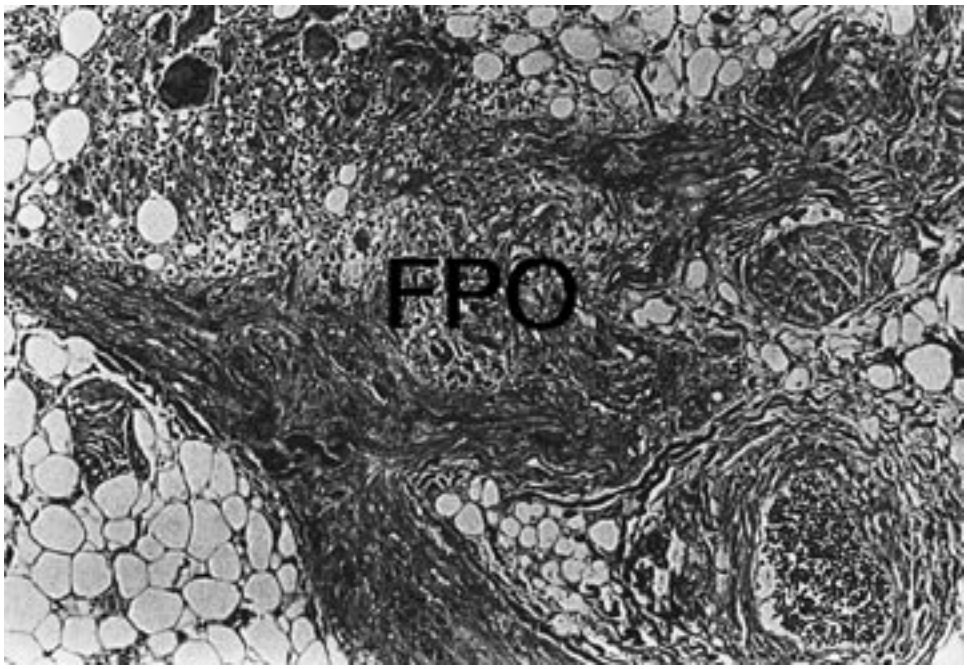

FIG. 2—*Photomicrograph of the sinoatrial node (SA node). The node consists of a conglomerate of small specialized myocytes (central), the SA node artery (lower right corner) and nerve bundles (mid right). Mononuclear and giant cell infiltration is evident, as seen in the upper left corner of the photomicrograph.*

block), the left ventricular free wall (aneurysms, heart failure, arrhythmias) and the papillary muscles (heart failure) (10).

The major causes of death in patients with cardiac sarcoid are arrhythmias or conduction block, and congestive heart failure (8,12). Death may also occur due to respiratory failure from progressive severe pulmonary fibrosis or from right heart failure (cor pulmonale).

Unfortunately sudden death is not uncommon (8,13), and this predilection has been recognized for some time (14–17). Sudden death was the initial presentation of the disease in 17–25% of patients in some series (1,2). In another series of 38 autopsy patients with sarcoid (4), there was a high incidence of cardiac involvement (76%), accounting for half of all deaths. In only 29% of cases was an antemortem diagnosis accurate (4).

The diagnosis of sarcoidosis, including those with cardiac involvement, is usually difficult to make pre-mortem. In cases of known extracardiac disease, often cardiac dysfunction is assumed to be a result of cardiac involvement (4). Since the right ventricle apex is not commonly involved, the utility of endomyocardial biopsy has been debated. If a biopsy is positive for sarcoid granulomas, these findings would strongly support the diagnosis of cardiac involvement. However, a negative biopsy does not rule it out (1,3,6). Angiotensin converting enzyme (ACE) levels are often elevated, but these are not specific for sarcoid. Echocardiography may also demonstrate enhancement of the lesions allowing diagnosis. Changes on electrocardiogram may mimic myocardial infarction (9).

On gross examination of the heart at the time of autopsy, grossly visible lesions are the exception. In a large autopsy series of sarcoid patients, gross myocardial lesions were found in only 17% of cases involved (5). When seen, the areas are pale, white, infiltrative and may be centered near the base of the left ventricle.

By microscopic examination, sarcoidosis overlaps morphologically with giant cell myocarditis, although some differentiating criteria have been proposed (18). Commonly there are collections of non-caseating granulomas with histiocytes surrounded by lymphocytes and occasional plasma cells. The giant cells may contain asteroid bodies, Schaumann bodies or other microcalcifications. With therapy, or by regression, fibrosis may be prominent, which may lead to ventricular aneurysm formation.

As with any granulomatous disease, special stains to rule out mycobacterial or fungal infections are needed. Other diseases with a myocardial granulomatous component must also be considered, including rheumatoid arthritis, rheumatic fever, hypersensitivity myocarditis, Takayasu's aortitis, Wegener's granulomatosis, and infectious endocarditis (2). The granulomas may be focal and many sections may need to be examined.

In routine sections of the myocardium, sarcoid may be missed due to the distribution of the disease. Sections further up the base of the left ventricle, especially of the inferior wall (the anatomic posterior wall) must be examined (11).

Conduction system examination in those cases with or without other myocardial involvement may prove useful. Conduction system examination is likely to have a high yield in those patients with known pre-mortem arrhythmias. Sarcoid involvement of the conduction system has been reported, and some feel that the disease has an affinity for this area of involvement (8,11,16). Determination of calcium levels in postmortem blood or vitreous humor may also prove informative as hypercalcemia may also contribute to fatal arrhythmias. Involvement of the conduction system or ventricular aneurysm formation may lead to ventricular arrhythmias and sudden death. Automatic implantable defibrillator devices have been used in patients with ventricular arrhythmias, with some success (12).

In the present case, the patient's congenital heart disease and the sequelae of repair were initially thought to be important contributing factors in the patient's death. Instead the congenital heart disease was likely incidental, whereas involvement of the conduction system and myocardium by sarcoid was probably the etiology of his lethal arrhythmia. Cardiac sarcoidosis certainly deserves mention as an infrequent, but important cause of sudden unexpected death.

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