Cardiac Sarcoidosis
Detected by Delayed-Hyperenhancement Magnetic Resonance Imaging

We report the case of a patient with sarcoidosis and ventricular tachycardia in whom cardiac magnetic resonance imaging provided supportive evidence of cardiac involvement by delineating regions of myocardial inflammation and fibrosis inconsistent with ischemic injury. The identification of cardiac involvement in patients with sarcoidosis is problematic, and the true incidence is unknown. Cardiac magnetic resonance imaging may help establish the actual incidence of cardiac involvement and allow further advances in monitoring and treatment options. (Tex Heart Inst J 2004;31:99-102)

Sarcoidosis is a multisystem disease of unknown etiology that can affect virtually any organ: most typically the lungs, liver, skin, and eyes. Infiltrating, noncaseating granulomas, which constitute a defining characteristic of sarcoidosis, may occur in the heart in as many as 50% of patients with systemic sarcoidosis, although clinical manifestations are thought to occur in only 5%. Cardiac involvement in sarcoidosis is not invariably associated with fulminant or widespread disease; but when present, it is associated with a poor prognosis. The clinical sequelae of sarcoïd granulomas within the myocardium range from asymptomatic conduction abnormalities to fatal ventricular arrhythmias. We report the case of a patient who had sarcoidosis and ventricular tachycardia. Cardiac magnetic resonance imaging (MRI) provided supporting evidence of cardiac involvement by delineating regions of myocardial inflammation and fibrosis inconsistent with ischemic injury.

Case Report

In October 2002, a 45-year-old black woman presented at the emergency department of our institution with new-onset chest tightness and palpitations following a 3-week period of worsening cough and dyspnea that had not responded to an outpatient treatment regimen of albuterol, ipratropium bromide, fluticasone, salmeterol, and theophylline. The patient had a history of reactive airway disease and presumed pulmonary sarcoidosis, and had taken long-term steroids for her lung disease; however, she had discontinued the steroids 2 months before this presentation. Physical exam revealed a blood pressure of 121/87 mmHg, a respiratory rate of 26 breaths/min, and an oxygen saturation of 96% on 3-L oxygen by nasal cannula. In addition, she had resting tachycardia, diffusely diminished breath sounds, and distant polyphonic wheezes. Chest radiography showed no abnormalities. An electrocardiogram (ECG) revealed a wide-complex tachycardia consistent with ventricular tachycardia (VT) (Fig. 1). Prednisone and hand-held nebulizers were administered for the dyspnea and wheezing, and a lidocaine infusion was started for the dysrhythmia. The patient had a history of reactive airway disease and presumed pulmonary sarcoidosis, and had taken long-term steroids for her lung disease; however, she had discontinued the steroids 2 months before this presentation. Physical exam revealed a blood pressure of 121/87 mmHg, a respiratory rate of 26 breaths/min, and an oxygen saturation of 96% on 3-L oxygen by nasal cannula. In addition, she had resting tachycardia, diffusely diminished breath sounds, and distant polyphonic wheezes. Chest radiography showed no abnormalities. An electrocardiogram (ECG) revealed a wide-complex tachycardia consistent with ventricular tachycardia (VT) (Fig. 1). Prednisone and hand-held nebulizers were administered for the dyspnea and wheezing, and a lidocaine infusion was started for the dysrhythmia. An echocardiogram revealed normal left ventricular size and function, with no evidence of focal wall motion abnormality or valvular heart disease. The systolic pulmonary artery pressure was estimated as 40 to 45 mmHg. Laboratory tests of serial creatine phosphokinase and troponin I yielded normal results. The VT resolved with lidocaine administration, and verapamil was subsequently administered for presumed verapamil-sensitive VT in the setting of a structurally normal heart. Given the possibility of occult sarcoïd involvement of the myocardium, MRI of the heart was performed to further define myocardial tissue characteristics and to provide evidence of antecedent or ongoing injury.

Magnetic Resonance Image Acquisition Technique. All imaging was performed on a 1.5-T commercial imager (Philips NT-Intera with software Release 8, Philips Medical Systems; Cleveland, Ohio), with a 5-element cardiac coil for signal reception.
and ECG gating. Fifteen minutes after the administration of an MRI contrast agent (gadolinium-DTPA, 0.2 mmol/kg), an inversion-recovery prepared, T₁-weighted, gradient-echo sequence (delayed-hyperenhancement MRI or DE-MRI) was used to collect tissue characterization data. After a 180° inversion pulse, 16 to 24 gradient echoes (TR/TE/flip: 7.0/2.0/15°) were collected per heartbeat during diastole, with an inversion delay that was iteratively adjusted to optimally null signal from normal myocardium. The total acquisition time was 16 heartbeats/slice. Ten-mm-thick, selected, long-axis slices were acquired, along with a series of contiguous short-axis slices, to cover the entire left ventricle. Global and segmental wall motion were determined with a steady-state free-precession cine sequence having a 2-mm in-plane spatial resolution and a 40-msec temporal resolution.

MRI Findings. Moderate adenopathy was present in the subcarinal and hilar regions. Increased signal intensity on T₁-weighted imaging was identified in the perihilar pulmonary parenchyma, consistent with pulmonary sarcoidosis. The cardiac chamber sizes were normal, and there were no abnormal cardiac or paracardiac masses. The DE-MRI revealed hyperenhancement intramyocardially in the basilar anterior, anterolateral, and lateral walls (Figs. 2 and 3). The pattern of hyperenhancement was not typical of acute or chronic myocardial infarction, in that the increased signal intensity was present in the mid-portion of the myocardium and epicardium, and not in the endocardium. In addition, T₂-weighted imaging (sensitive to edema) revealed subtle myocardial abnormalities in the same anatomic locations, suggesting an infiltrative or inflammatory process.

Cine imaging revealed no segmental wall motion abnormalities associated with the areas of hyperenhancement on DE-MRI. The left ventricle was normal in size and shape, with mildly globally depressed

Fig. 1 An electrocardiogram illustrates ventricular tachycardia that originates from the basal lateral wall of the left ventricle.

Fig. 2 DE-MRI images of the left ventricular outflow tract (A) and the 4-chamber projections (B) show patchy infiltration of the left ventricular lateral wall (arrows).
function (left ventricular end-diastolic volume, 85 cc; left ventricular ejection fraction, 0.49).

Hospital Course. The patient continued to have recurrent episodes of nonsustained VT, and treatment was changed to amiodarone, which improved the dysrhythmia but made the wheezing slightly worse. On hospital day 7, the patient underwent an electrophysiologic study, which showed inducible nonsustained VT with morphology similar to that of her clinical VT, for which an implantable cardioverter-defibrillator was placed without complication. The inducible focus corresponded to the location of the cardiac lesions seen on MRI. Biopsy of a paratracheal lymph node revealed noncaseating granulomas consistent with sarcoidosis. The episodes of nonsustained VT abated, and she was discharged from the hospital on continued high-dose steroids.

Discussion

Bernstein, in 1929, was the first to describe cardiac involvement in a patient with systemic sarcoidosis. However, not until 1977, when Roberts studied 113 patients with autopsy-proven cardiac sarcoidosis unassociated with coronary artery disease, was the spectrum and importance of cardiac involvement more fully realized. Subsequent autopsy studies confirmed and extended this knowledge base. These studies reported that noncaseating granulomas may occur in the myocardium in up to 50% of cases of fatal sarcoidosis, and cardiac dysfunction with sudden death may occur in up to 67% of patients with evidence of cardiac sarcoidosis found at autopsy. Moreover, 11% to 15% of these patients had sudden death as their initial presentation, presumably the result of ventricular arrhythmia. Only 23% of patients with cardiac involvement had progressive congestive heart failure cited as the cause of death.

The actual incidence of cardiac sarcoidosis is not known, yet early and accurate diagnosis is clearly crucial when considering the oftentimes unheralded and potentially lethal outcomes. Autopsy studies of fatal sarcoidosis understandably present an ascertainment bias on the incidence of disease, although even unselected autopsy series report cardiac involvement in 20% to 27%. It has been reported that only 5% of patients manifest clinical signs and symptoms of myocardial involvement, raising concern for those patients with subclinical cardiac disease for whom the incidence and prognosis have yet to be determined. Antemortem recognition of sarcoidosis affecting the heart remains challenging, in part due to the non-specific nature of electrical or functional sequelae of the patchy inflammatory injury, and in part to the difficulty in confirming the diagnosis, whether by invasive or noninvasive means. However, with the availability of effective treatment alternatives for patients at high risk for arrhythmogenic death, and medical therapies that may alter the course of disease, early and accurate diagnosis of myocardial sarcoidosis may substantially alter the outcome of this small, but potentially high-risk population.

Accurate, practical methods of screening for sarcoidosis and confirming myocardial damage associated with sarcoidosis have not been described. Echocardiography is hampered by a lack of sensitivity when myocardial destruction or dysfunction is insufficient to produce ventricular wall motion abnormalities. Rarely, large granulomas are recognized as echo-dense regions in the interventricular septum and free wall of the left ventricle. The capability of nuclear scintigraphy is also limited, but by poor spatial resolution and imaging artifacts that can limit both sensitivity and specificity. Right ventricular endomyocardial biopsy (EMB) provides irrefutable evidence of disease when typical granulomas are present in sampled tissue; however, sampling error renders the results inconclusive when negative, due to the patchy nature of the disease. Insensitivity and procedural risk make EMB an impractical diagnostic tool.

Magnetic resonance imaging is a powerful tool for general tissue characterization via the standard array of T1-, T2-, and proton-density-weighted imaging, as well as contrast-enhanced techniques. The
most recent advance in cardiac MRI is the DE-MRI technique, performed after the administration of gadolinium contrast agent, which provides an accurate and noninvasive means for delineation of regions of myocardial cell death. Both animal and human studies using DE-MRI have provided strong evidence that regions of hyperenhancement correspond to regions of irreversible injury or fibrosis. In addition, the spatial resolution of 1.5-mm in-plane or better allows a more precise inspection of tissue characteristics (for example, infiltration) than do other techniques currently used.

In our patient, abnormal myocardial hyperenhancement was seen corresponding to the arrhythmogenic focus localized on ECG. Further, the primarily mid-myocardial and epicardial pattern of hyperenhancement was inconsistent with ischemic myocardial injury and likely indicated sarcoid infiltration. Along these lines, cardiac sarcoidosis has been described as producing zones of thinning and segmental myocardial wall motion abnormalities similar to those in chronic infarctions, but in a noncoronary distribution (for example, thinning and fibrosis of the basilar left ventricular myocardium absent distal disease). Previous studies using older MRI techniques in patients with acute disease and symptoms have described patchy areas of heterogeneous tissue in normal or increased-thickness myocardium, presumably indicating acute infiltration.

The DE-MRI technique has the advantage of providing high contrast between normal and abnormal tissue, which increases lesion conspicuity. This factor, in combination with the superior spatial resolution of DE-MRI, portends multiple advantages for the detection of cardiac sarcoid infiltration. With such a dire prognosis, as suggested by evidence in the medical literature, a method of screening for and establishing the true risk attendant to cardiac sarcoidosis is crucial. Cardiac MRI using the DE-MRI technique offers a rapid, high-resolution, noninvasive method of screening for myocardial fibrosis and infiltration that warrants additional study in this setting. This imaging technique may help establish the actual incidence of cardiac involvement and allow further advances in patient monitoring and treatment options.

References
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