Cardiac involvement in sarcoidosis is being increasingly noted since it has been recognized in the early 20th century and is associated with poor prognosis. Cardiac sarcoidosis is rare but is potentially fatal with a wide spectrum of clinical manifestations ranging from an incidentally discovered, benign condition to fatal cardiomyopathy, arrhythmias, and even sudden cardiac death. Cardiac involvement may occur at any point during the course of sarcoidosis, may occur in the absence of pulmonary or systemic involvement, and may be a presenting feature. Arrhythmias or conduction defects are the most common cardiac manifestations reflecting granulomatous infiltration within the conduction system or ventricular walls and are the most common causes of death due to cardiac sarcoidosis; however, progressive heart failure due to massive granulomatous infiltration of the myocardium accounts for at least 25% of deaths. Sarcoidosis can involve any part of the heart, including myocardium, endocardium, and pericardium. The areas of involvement in descending order of frequency are the left ventricular free wall, ventricular septum, papillary muscles, right ventricle, and atria. Obliteration of the sinoatrial node, atrioventricular node, or the bundle of his may occur. Valvular dysfunction may result from localized involvement of the papillary muscles causing significant valvular insufficiency in rare cases.

Diagnostic Challenge of Cardiac Sarcoidosis

Cardiac involvement in sarcoidosis has been extremely difficult to diagnose clinically because the clinical manifestations are non-specific, and the sensitivity and specificity of diagnostic modalities are limited. A resting electrocardiogram (ECG) is an appropriate screening test to order in all patients with confirmed or suspected sarcoidosis. Abnormalities on ECG including conduction disturbances, arrhythmias, or nonspecific ST and T-wave changes can be demonstrated in up to one-third of sarcoid patients. However, ECG remains a poorly sensitive test since the significance of these alterations and their relation to cardiac lesions and the patients’ symptoms are often unclear. Twenty-four-hour Holter monitoring and exercise ECGs can detect abnormalities even when resting ECGs are normal. Technetium-99m scintigraphy is more sensitive than thallium-201 scintigraphy. Both modalities exhibit the “reverse distribution” phenomenon (i.e., the focal defects detected in the resting phase of thallium scanning disappear or decrease in size during thallium stress imaging or after dipyridamole infusion). These results are quite different from those observed in patients with coronary artery disease, in which defects are unchanged or enhanced after exercise or intravenous dipyridamole. Gallium-67 heart uptake predicts a better response to corticosteroid treatment. Contrast-enhanced magnetic resonance imaging and 18F-fluorodeoxyglucose positron emission tomography are most sensitive, and the findings seem to correlate with disease activity (Table 1). An endomyocardial biopsy is preferable, but the procedure has a sensitivity as low as 20%.

Thus the search for a reliable, reproducible, and easily available diagnostic tool for cardiac sarcoidosis continues. A recent updated guideline was established in 2006 by the Japanese Ministry of Health and Welfare since it was first published in 1993 (Table 2).
Echocardiography may be a useful imaging tool for myocardial sarcoidosis. Echocardiographic abnormalities have been reported in patients with cardiac sarcoidosis, but the prevalence, spectrum, and clinical significance of echocardiographic findings are still unknown. Abnormalities seen on transthoracic echocardiography, which include septal thinning, left ventricular regional systolic dysfunction, pericardial effusion, ventricular aneurysms, left ventricular diastolic dysfunction, and valvular abnormalities, are usually seen in advanced disease and can be detected in only 14% of patients with systemic sarcoidosis and cardiac involvement. Cardiac lesions may also produce an increase in the thickness of the interventricular septum, mimicking hypertrophic cardiomyopathy. This suggests that two dimensional echocardiography may not be sensitive enough to detect mild or small localized abnormalities, which may occur in the early stages of cardiac involvement.

In this issue of the Korean Circulation Journal, Sun et al. reported that the prevalence of two characteristic echocardiographic findings suggesting cardiac sarcoidosis (basal septal thinning or localized aneurysmal dilatation without coronary artery disease) in patients with pacemaker or implantable cardiac defibrillator (ICD) was very low (1.2% in the pacemaker group and 4.0% in the ICD group, 1.5% in the study subjects). And the prognosis was poor in patients with cardiac sarcoidosis. Considering low yield of endomyocardial biopsy and rare systemic involvement in patients with cardiac sarcoidosis, the authors suggest that echocardiographic findings can be useful in the selected group of patients, as characteristic basal septal thinning or aneurysmal dilatation can be regarded as a supporting evidence of cardiac involvement in sarcoidosis. The most important issue in cardiac sarcoidosis is the diagnostic difficulty and poor prognosis. As the authors have noted, clinical impact of diagnosis of cardiac sarcoido-
sis based on combination of both the clinical features of significant arrhythmias warranting device therapy and the characteristic echocardiographic findings needs to be tested in future investigations.

In conclusion, clinicians should consider the possibility of cardiac sarcoidosis in the evaluation of an otherwise healthy young patient who develops unexplained cardiomyopathy or arrhythmias. Given the grave prognosis of cardiac sarcoidosis, cardiac signs or symptoms in a patient with known sarcoidosis should alert the physician to perform an aggressive workup including ECG screening and multimodality imaging for confirming the diagnosis of cardiac sarcoidosis.

REFERENCES

1) Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med 2007;357:2153-65.
2) Kim JS, Judson MA, Donnino R, et al. Cardiac sarcoidosis. Am Heart J 2009;157:9-21.
3) 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;63:86-108.
4) Silverman KJ, Hutchins GM, Bulkley BH. Cardiac sarcoidosis: a clinicopathologic study of 84 unselected patients with systemic sarcoidosis. Circulation 1978;58:1204-11.
5) Yazaki Y, Isebe M, Hiramitsu S, et al. Comparison of clinical features and prognosis of cardiac sarcoidosis and idiopathic dilated cardiomyopathy. Am J Cardiol 1998;82:537-40.
6) Tahara N, Tahara A, Nitta Y, et al. Heterogeneous myocardial FDG uptake and the disease activity in cardiac sarcoidosis. JACC Cardiovasc Imaging 2010;3:1219-28.
7) Diagnostic standard and guidelines for sarcoidosis. Jpn J Sarcoidosis Granulomatous Disord [in Japanese] 2007;27:89-102.
8) Burstow DJ, Tajik AJ, Bailey KR, DeRemee RA, Taliercio CP. Two-dimensional echocardiographic findings in systemic sarcoidosis. Am J Cardiol 1989;63:478-82.
9) Sun BJ, Lee PH, Choi HO, et al. Prevalence of echocardiographic features suggesting cardiac sarcoidosis in patients with pacemaker or implantable cardiac defibrillator. Korean Circ J 2011;41:313-20.