Clinical Characteristics of Definite or Suspected Isolated Cardiac Sarcoidosis: Application of Cardiac Magnetic Resonance Imaging and ^{18}F-Fluoro-2-deoxyglucose Positron-Emission Tomography/Computerized Tomography

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ABSTRACT

Background: Isolated cardiac sarcoidosis (iCS) is difficult to diagnose in patients without histologic evidence of sarcoidosis. We aimed to clarify the clinical characteristics of iCS, including imaging features on cardiac magnetic resonance imaging (MRI) and ^{18}F-fluoro-2-deoxyglucose positron-emission tomography/computerized tomography (FDG-PET/CT) scans. We also reviewed the therapeutic effect of corticosteroids and determined the long-term prognosis.

Methods and Results: We retrospectively reviewed 83 consecutive patients with suspicious CS from 1997 to 2013. Systemic sarcoidosis with CS (sCS, n = 30) and iCS (n = 11) were diagnosed according to clinical criteria. In iCS cases, sarcoidosis was not detected in any other organs. The clinical features did not significantly differ between sCS and iCS cases, except for ejection fraction, which was lower in iCS ($P = .025$). Nine sCS and 4 iCS cases showed late gadolinium enhancement, and the lesions tended to be on the epicardial side (76.9% $P = .011$) and septal wall (52.9% $P < .001$). The coefficient of variance for the myocardial standardized uptake value of FDG-PET/CT was higher in sCS (0.32 ± 0.13; n = 19) and iCS (0.32 ± 0.09; n = 7) than in control cases (n = 31; $P < .001$). B-Type natriuretic peptide level was improved after prednisolone treatment in both groups. Kaplan-Meier curve indicated that prognosis was not different between sCS and iCS cases.

Conclusions: The clinical cardiac characteristics of iCS cases were similar to those of sCS. Cardiac MRI and FDG-PET, noninvasive imaging modalities, could be useful modalities to detect myocardial involvement in the cases with definite or suspected iCS. (*J Cardiac Fail 2015;21:313−322*)

Key Words: Isolated cardiac sarcoidosis, left ventricular dysfunction.

Sarcoidosis is a systemic inflammatory disease characterized by the formation of noncaseating granulomas in multiple organs.[1] Granulomatous infiltration of the myocardium in cardiac sarcoidosis (CS) can lead to sudden death[2−4]; however, another report indicated that only 40%−50% of patients who were found to have CS at autopsy had clinical evidence of the condition during their lifetime.[5] The prompt diagnosis of CS is an important clinical topic and enables the initiation of therapy before the occurrence of fatal complications.[6] We reported a case of isolated CS (iCS) in 2000,[7] but there have been few studies on iCS.[8-10]

There are 2 main problems in the diagnosis of iCS. First, the diagnostic sensitivity of endomyocardial biopsy is 20%−30% because of sampling errors.[11] Moreover, a greater proportion of patients present with nonspecific findings on

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See page 321 for disclosure information.

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endomyocardial biopsy, such as interstitial fibrosis. If a sarcoid granuloma is present in patients in the early phase, sarcoidosis is gradually replaced by fibrosis.[12] Furthermore, only a few biomarkers exhibit specificity for CS, because sarcoidosis presents with a weak systemic immunologic response despite the associated extensive local inflammation.[1] Serum angiotensin-converting enzyme and lysozyme levels have been accepted as diagnostic aids in sarcoidosis, but they do not increase in all cases. The utility of troponin T in the diagnosis of CS has been reported[13]; however, no studies since then have reported on the phenomenon. Therefore, managing cases clinically suspected as iCS without histologic manifestation is a critical issue for therapy, particularly when prescribing prednisolone.

Recent studies have focused on the usefulness of cardiac magnetic resonance imaging (MRI)[14] and ^{18}F-fluoro-2-deoxyglucose positron-emission tomography (FDG-PET) for CS diagnosis.[15] On cardiac MRI, late gadolinium enhancement (LGE) can be used to identify myocardial fibrosis, and in cases of CS this modality shows mid-to-epicardial wall enhancement in the thinning septal or posterior wall.[16,17] FDG-PET has been generally used in inflammatory cardiovascular diseases.[18] FDG is an analogue of glucose and is taken up by leukocytes that are activated by cytokines during systemic immunologic responses to inflammatory diseases.

Here, we aimed to identify common features in patients with clinically suspected iCS according to conventional guidelines. Furthermore, CS-specific features were investigated based on cardiac MRI findings and compared with those of iCS. A secondary aim was to quantitatively assess FDG uptake during FDG-PET/computerized tomography (CT) to identify iCS cases. We further assessed the therapeutic effect of prednisolone and compared the long-term outcomes in sCS and iCS cases.

Materials and Methods

Study Patients, Clinical Classification, and Clinical Assessment

We performed a retrospective review of our database of 11,033 patients who were referred to the Department of Cardiovascular Medicine of Tokyo Medical and Dental University from 1997 to 2013; 83 consecutive patients who were referred for CS or sarcoidosis as an initial diagnosis were identified. The patients had undergone electrocardiography and echocardiography and were diagnosed according to the 2006 version of the Diagnostic Standard and Guideline for Sarcoidosis by the Japan Society of Sarcoidosis and Other Granulomatous Disorders[4] (Table 1). Patients who had undergone endomyocardial biopsy were assessed for the presence of not only noncaseating granulomas but also myocarditis and other cardiomyopathies. All cases of iCS were evaluated the presence or absence of systemic involvement with ophthalmologic examination and close inspection of skin. They were examined with the use of chest X-ray, chest CT, gallium scintigraphy, and/or FDG-PET/CT. The cases were divided into 3 groups: (i) systemic sarcoidosis with CS (sCS), (ii) definite or suspected iCS, and (iii) systemic sarcoidosis without CS (Fig. 1).

If sarcoidosis was not present in the other organs, iCS was determined based on the presence of granulomas in the myocardium (histologic iCS). If a patient fulfilled the clinical criteria for CS (Table 1; Fig. 1) but did not have any histologic manifestations, he or she was assessed to ascertain whether ischemic heart disease had been ruled out by means of coronary angiography or coronary CT angiography. Additionally, suspected iCS patients who had been examined by means of cardiac MRI or FDG-PET were included if they met each criterion for CS.

Suspected iCS cases were further investigated for systemic reactions of sarcoidosis. The conventional guidelines refer to 6 systemic reactions of sarcoidosis.[4] Moreover, the lysozyme level and sustained increase of troponin levels were reviewed. After the classification, we compared differences in therapeutic backgrounds, including the use of intracardiac devices and cardiac involvement, between the sCS and iCS groups. The study protocol was approved by the Institutional Ethics Review Committee of Tokyo Medical and Dental University, and informed consent was obtained from each patient for this study and initiation of corticosteroids.

Cardiac MRI Studies

Cardiac MRI was performed at the Cardiovascular Imaging Clinic and Tokyo Medical and Dental University. At Tokyo Medical and Dental University, the images were acquired during repeated breath-holds with the use of a 1.5-T scanner (Excelart Vantage powered by Atlas; Toshiba Medical Systems) with a phased-array coil. The cardiac MRI procedure involved the use

Table 1. Clinical Diagnosis of Guidelines for Diagnosis of Cardiac Sarcoidosis (2006)—Japan Society of Sarcoidosis and Other Granulomatous Disorders

(1) Major criteria
  (a) Advanced atrioventricular block.
  (b) Basal thinning of the interventricular septum.
  (c) Positive ^{67}gallium uptake in the heart.
  (d) Depressed ejection fraction of the left ventricle (ejection fraction < 50%).
(2) Minor criteria
  (a) Abnormal electrocardiography findings: ventricular arrhythmias, complete right bundle branch block, axis deviation, abnormal Q-wave.
  (b) Abnormal echocardiography: regional abnormal wall motion or morphological abnormality (ventricular aneurysm, wall thickening).
  (c) Nuclear medicine: perfusion defect detected by ^{201}thallium or ^{99m}technetium myocardial scintigraphy.
  (d) Gadolinium-enhanced cardiac MR imaging: delayed enhancement of myocardium.
  (e) Endomyocardial biopsy: interstitial fibrosis or monocyte infiltration over moderate grade.
1. 2 or more of the 4 major criteria are satisfied.
2. 1 in 4 of the major criteria and 2 or more of the 5 minor criteria satisfied.