Sarcoidosis with Cardiac Involvement

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Patients with significant cardiac sarcoidosis are at increased risk of sudden death from ventricular dysrhythmias or conduction disturbances. We report a patient in whom there. was radiographic and histologic evidence of systemic sarcoidosis; though histologic confirmation of involvement of heart by sarcoidosis is lacking, the clinical manifestations, radionuclide image findings, rhythm disturbances, and the response to steroid therapy are strong evidence in favor of myocardial involvement by the granulomatous process.

Key Words: Cardiac sarcoidosis, ventricular dysrhythmias, steroid therapy

Sarcoidosis is a systemic granulomatous disorder of unknown etiology. It is characterized by noncaseating epithelioid cell granulomas involving almost any organ with associated immunologic abnormalities (Daniele *et al.* 1980). Clinically recognizable sarcoid involvement of the heart is rare, and cardiac involvement has been demonstrated in 13 to 27% of autopsy series (Ratner *et al.* 1986). Rhythm disturbances are common in patients with sarcoid heart disease and are presumed to be the cause of sudden death in most patients. Radionuclide imaging studies, cardiac magnetic resonance imaging, and transvenous endomyocardial biopsy facilitated earlier diagnosis and treatment (Riedy *et al.* 1988). We report a successful management with corticosteroids in a patient with proved sarcoidosis, presumed to involve the heart.

CASE REPORT

A 54-year-old woman was referred to Severance hospital, Seoul, Korea due to sustained chest discomfort and bilateral hilar lymph node enlargement. She was treated conservatively for 6 months at another hospital prior to admission where she took a computerized tomography (CT) scan of the chest which revealed bilateral hilar and multiple mediastinal lymph nodes enlargement.

She had no significant family and past histories.

On physical examination the blood pressure was 110/70 mmHg, pulse rate 72 per minute and regular, respiratory rate 18 per minute, and body temperature was 36.5℃. There were no visible abnormal skin lesions. The neck veins were not distended and cervical lymph nodes were not palpable. Breath sounds were clear without any adventitious sounds. There was a grade 2/4 late systolic murmur at the apex and no gallop sound was heard. There

was mild direct tenderness on epigastrium and left upper quadrant without any palpable organomegaly in abdominal examination. There was no pretibial pitting edema.

Laboratory studies including serum angiotensin converting enzyme (ACE) and serum beta-2 microglobulin were unremarkable. Skin tests with second strength PPD, PW, and CS were negative. Chest X-ray film showed bilateral hilar lymph node enlargement without any pulmonary parenchymal infiltrates (Fig. 1).

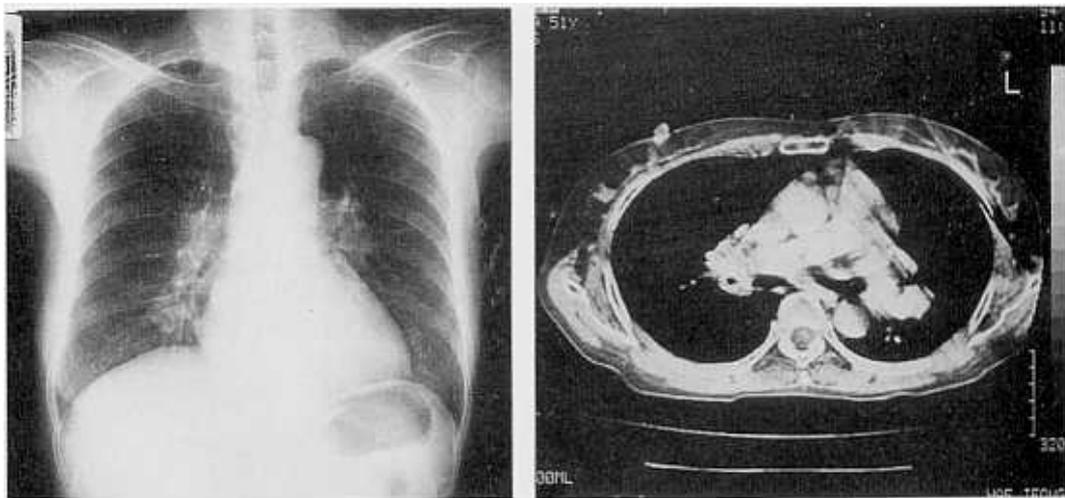Her initial electrocardiogram showed sinus tachycardia with frequent premature ventricu-

Fig. 1. Chest x-ray showing bilateral hilar lymph node enlargement without any pulmonary parenchymal infiltrates.
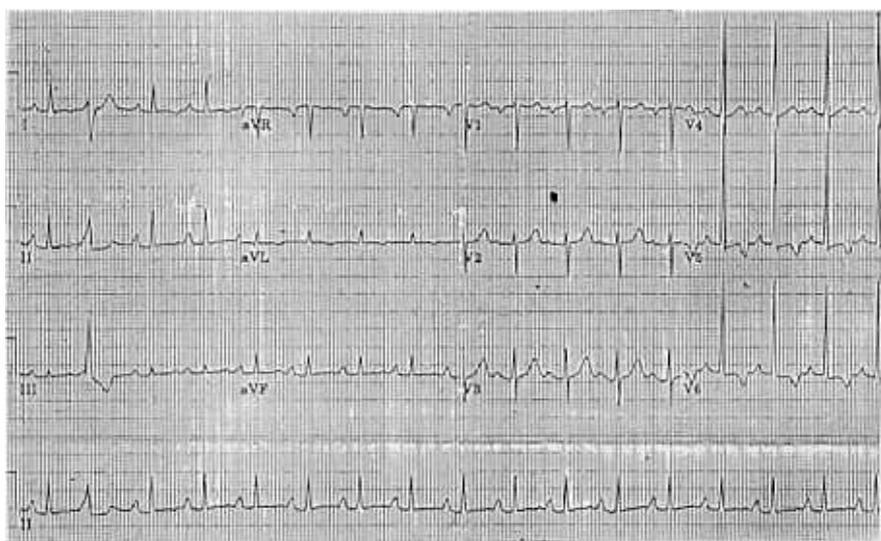

Fig. 2. Initial electrocardiogram shows sinus tachycardia with occasional premature ventricular contractions.
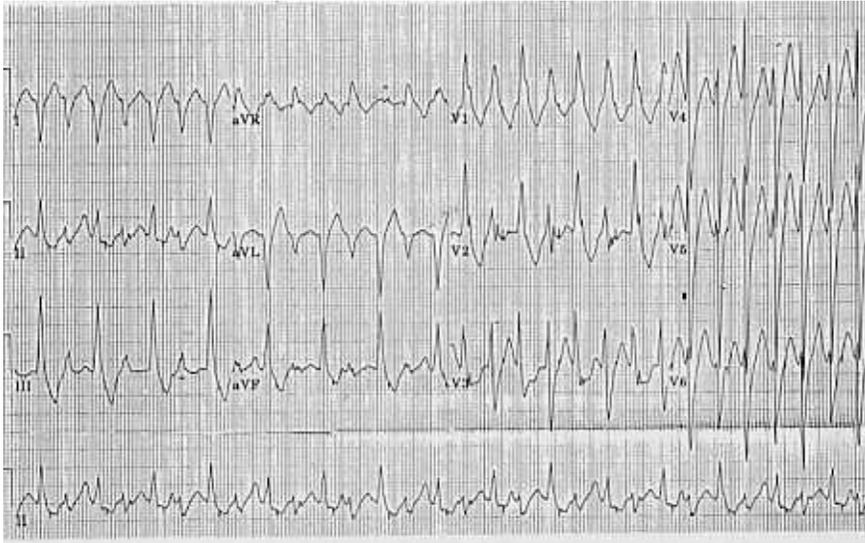
Fig. 3. Follow up electrocardiogram shows non-sustained ventricular tachycardia.
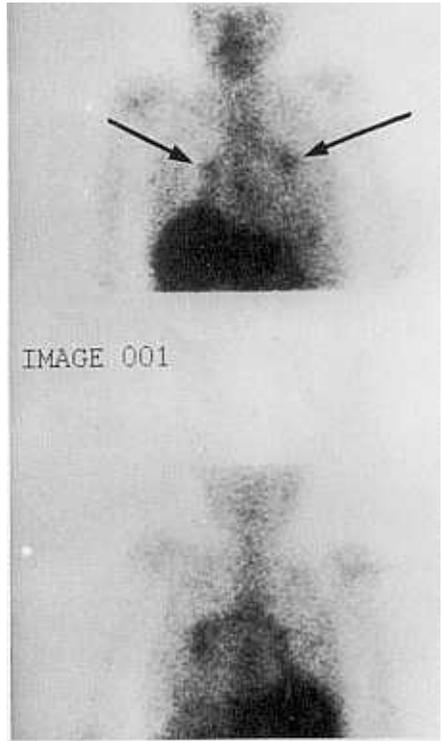

Fig. 4. Gallium scan image. Note the gallium uptake in the myocardium and bilateral hilar lymph nodes.
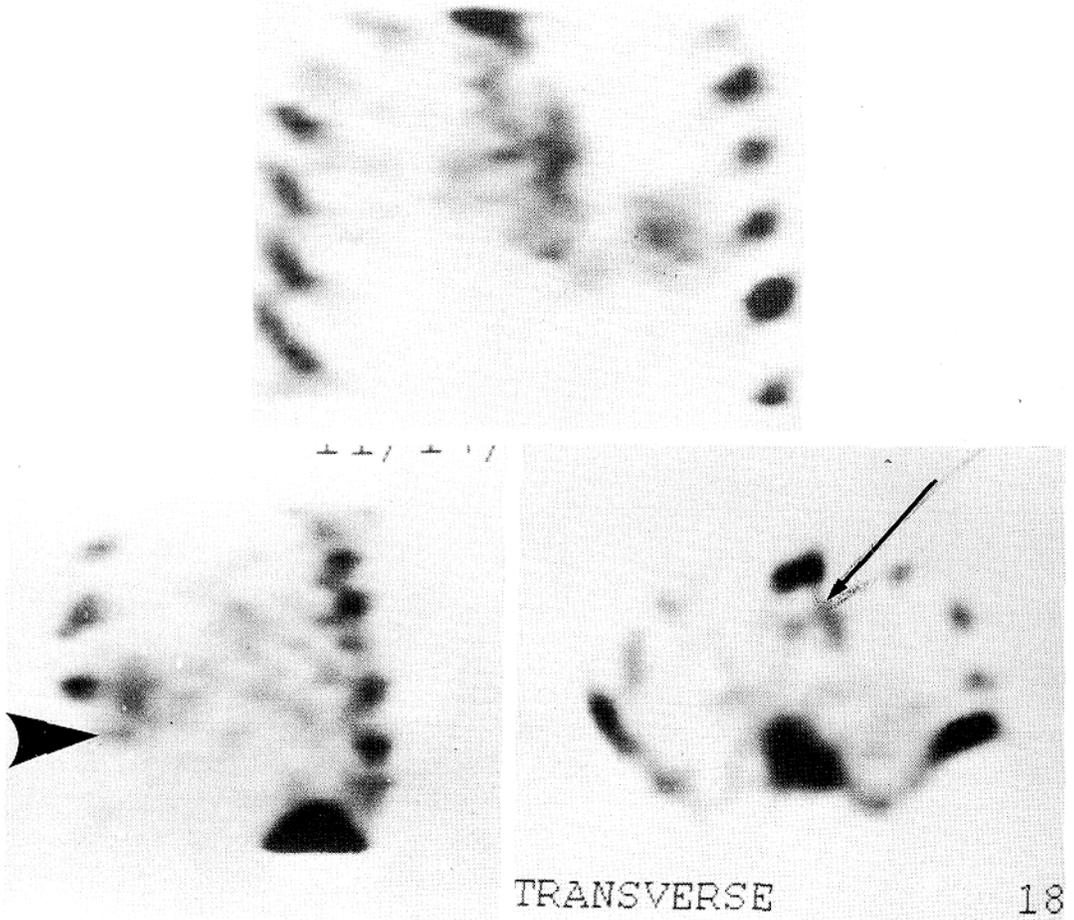
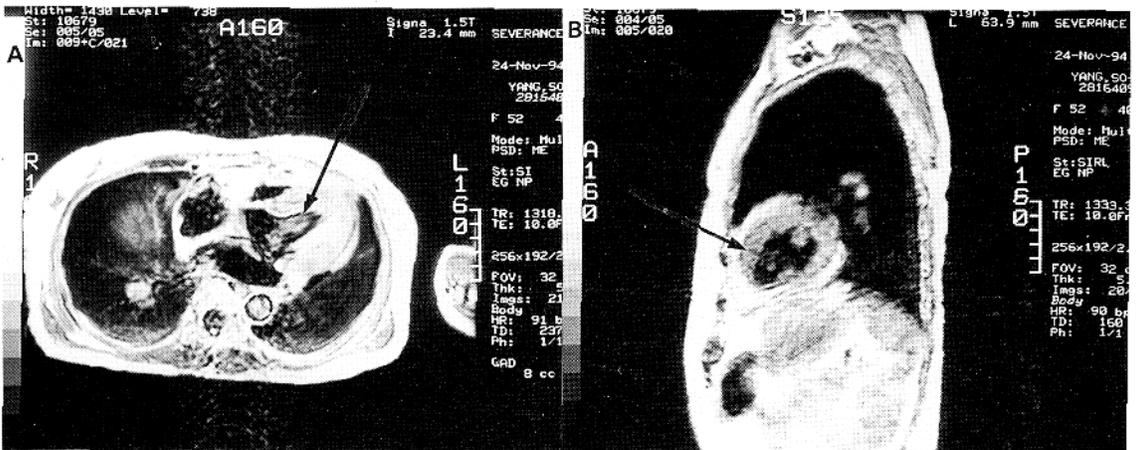**Fig. 5.** ⁹⁹ᵐTc-pyrophosphate scan. Note the increased focal uptake in left ventricle.

Fig. 6. Gated cardiac magnetic resonance image shows increased signal intensity in papillary muscles of left ventricle(arrow) A: Axial view, B: Sagittal view

lar contractions (Fig. 2). After admission, her previous chest discomfort disappeared and she began to complain of diffuse migrating abdominal pain. Abdominal ultrasonography and pelvis CT scan showed normal findings without enlargement of lymph nodes. On the 6th hospital day, the patient complained of severe migrating diffuse abdominal pain and the electrocardiogram taken at that time revealed non-sustained ventricular tachycardia (Fig. 3). She was given 50 mg bolus intravenously followed by a continuous infusion (1 mg/min) of lidocaine and oral prednisolone 30 mg was given. Sinus rhythm was quickly restored. However, on the 7th hospital day, non-sustained ventricular tachycardia reappeared and lidocaine infusion rate was increased to 3 mg/min. Sinus rhythm was restored but sinus
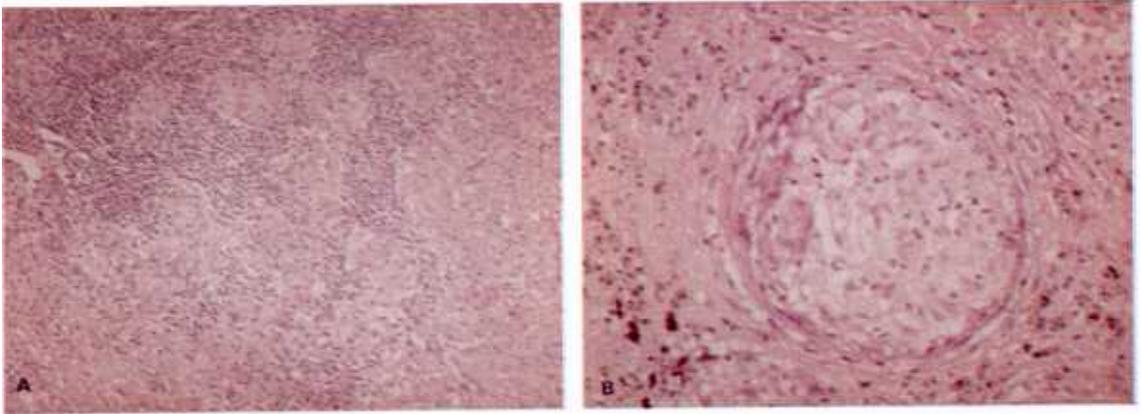

Fig. 7. *Mediastinoscopic lymph node biopsy revealed noncaseating granulomatous inflammation consistent with sarcoidosis(Hematoxylin-Eosin stain, A: ×100, B: ×400).*
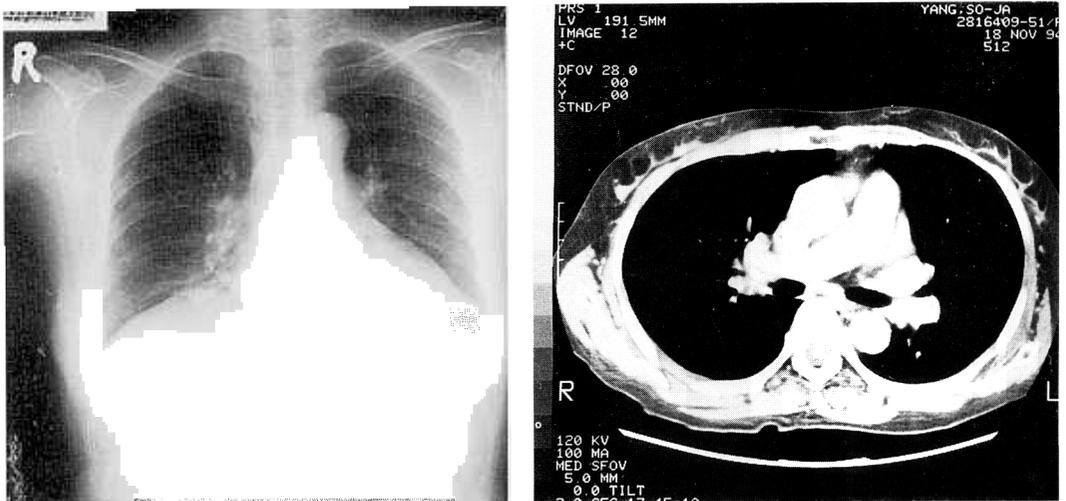

Fig. 8. *Follow up chest x-ray after 2 weeks of steroid therapy shows reduction in size of mediastinal and hilar lymph nodes.*
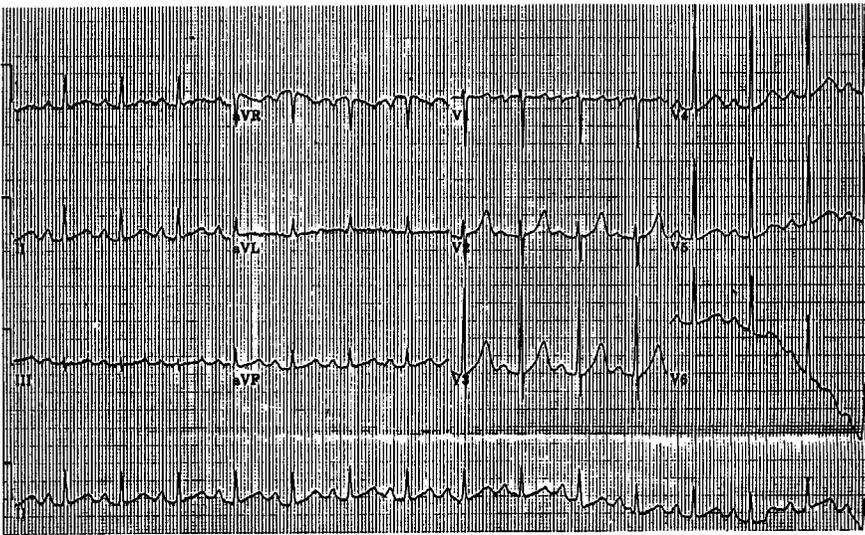
Fig. 9. *Electrocardiogram taken 2 weeks after start of steroid therapy shows normal sinus rhythm with first degree AV block.*

tachycardia with frequent premature ventricular contractions persisted. Lidocaine infusion was stopped after 2 days when her condition improved and oral prednisolone 30 mg per day was maintained without further non-sustained ventricular tachycardia attacks. 2-D echocardiography showed normal morphology except for exaggerated bowing motion of the anterior mitral leaflet without prolapse. Gallium scan (Fig. 4) and ^{99m}Tc-pyrophosphate scan (Fig. 5) showed abnormal uptake within myocardium, especially at the anterior aspect of the left ventricle and cardiac magnetic resonance image (Fig. 6) showed high signal intensity lesions at the papillary muscles of the left ventricle. Mediastinoscopic lymph node biopsy disclosed noncaseating granulomatous inflammations consistent with sarcoidosis (Fig. 7). However, endomyocardial biopsy of the right ventricular septum failed to show any granulomatous lesions.

After 2 weeks of steroid therapy, chest PA and computerized tomographic scan showed a reduction in size of the mediastinal and hilar lymph nodes (Fig. 8). Electrocardiogram showed no evidence of ventricular arrhythmia except for intermittent premature ventricular beats (Fig. 9). Her flank and abdominal discomforts gradually subsided. She was discharged with maintenance therapy of oral predinisolone 30 mg per day.

DISCUSSION

Sarcoidosis, a noncaseating granulomatous disorder of undetermined etiology, is a multisystem disease with various manifestations. The clinical spectrum of sarcoidosis is related to the variability of the site and extent of organ involvement by this disease of protean manifestations. Bernstein *et al.* (1929) were the first to describe the pathologic pattern of cardiac involvement by sarcoidosis. Cardiac involvement in the form of cor pulmonale is usually indirect and secondary to progressive destructive pulmonary fibrosis (Siltzbach *et al.* 1974; Mitchell and Scadding, 1974). Based upon postmortem studies, the estimated incidence of direct myocardial involvement in patients with sarcoidosis is 25 to 27% (Silverman *et al.* 1978). Clinically, the involvement of the heart is less frequently recognized with a reported

incidence of about 5% (Fields *et al.* 1990).

Granulomatous infiltrations of the heart in sarcoidosis can affect the heart in a number of ways. The major clinical manifestations of cardiac involvement are conduction disturbances, disorders of impulse formation, and progressive heart failure (Gozo *et al.* 1971). Infrequent manifestations include mitral regurgitation from fibrous replacement of papillary muscles, left ventricular aneurysm, pericardial effusion, mural thrombi, hemorrhagic pericarditis, and electrocardiographic patterns of transmural infarction (Walsh, 1978). Excluding nonspecific T wave abnormalities, conduction disturbances are the most common clinical manifestations of primary cardiac involvement (Gozo *et al.* 1971). Any portion of conduction pathways may be affected by granulomatous infiltrations. However, the atrioventricular bundle in the cephalad portion of the muscular intraventricular septum appears to be a common and particularly vulnerable site (Roberts *et al.* 1977). Recurrent Stokes-Adams attacks are frequent once complete A-V block develops, and sudden death is common. Disorders of impulse formation constitute the second most common clinical manifestation of cardiac involvement. Ventricular arrhythmias account for more than half of recorded arrhythmias and ventricular tachycardia as in this case, is the most common rhythm abnormality (Gozo *et al.* 1971). Heart failure is less common and may be a manifestation of a rhythm disturbance, widespread fibrosis resulting from granulomatous infiltration of myocardium, or rarely cor pulmonale secondary to pulmonary fibrosis and pulmonary hypertension, or a combination of any of these processes (Walsh, 1978).

Our patient developed recurrent non-sustained ventricular tachycardia responding to oral corticosteroids. Administration of antiarrhythmic agent (lidocaine) did not seem to have a marked effect on converting the non-sustained ventricular tachycardia to sinus rhythm since the patient was able to maintain sinus rhythm long after lidocaine was discontinued.

The diagnosis of myocardial sarcoidosis is difficult without involvement of other organs and a high index of suspicion is needed to make premortem diagnosis. Various radionuclide imaging studies such as Gallium 67 scan, ^{99m}Tc-pyrophosphate scan, Thallium-201 scintigraphy, and cardiac MRI as well as angiotensin I converting enzyme are useful in evaluating cardiac sarcoidosis (Forman *et al.* 1983). However, endomyocardial biopsy is the only means by which a specific diagnosis of heart involvement can be made. This method is a safe and informative mean of establishing a specific diagnosis in a patient with diffuse disease. However, patchy distribution of the typical granulomas presents a significant potential for sampling errors (Ratner *et al.* 1986). This present case in which radionuclide imaging studies suggested involvement of the left ventricle failed to show any granulomatous infiltrations on endomyocardial biopsy of the interventricular septum.

In general, sarcoidosis has a mortality rate of only 0.2 per 100,000 cases, but the prognosis in case of cardiac involvement is much worse, being about 40% by five years (Kinney and Caldwell, 1990).

Corticosteroids are the most widely used agent in the treatment of patients with sarcoidosis. Despite their long and frequent use, steroids remain controversial in regard to the appropriate dosages and clinical efficacy. Corticosteroid therapy is generally effective in the early stage of myocardial involvement (Ishikawa *et al.* 1984). In contrast, the effect of steroid administration is questionable in the late stage. However, there is no question that corticosteroids effectively suppress the activated T-helper cell processes occurring at the site of the disease. Thus, the major problem in making decisions concerning steroid therapy in sarcoidosis is to determine not the time of the disease but the activity of the inflammatory process in the organ (Shiotani *et al.* 1991). In our patient, administration of steroids led to successful improvement of the patient's condition and arrhythmia.

Immunosuppressive agents have been used only in patients with critical organ involvement and who failed a course of treatment with steroids. However, there is no substantive evidence that these agents are more ef-

fective than corticosteroids or that the additional improvement above effects obtained with corticosteroids might be achieved (Demeter, 1988).

REFERENCES

Bernstein M, Konzleman FW, Sidlick DM: Boeck's sarcoid. Report of a case with visceral involvement. *Arch Intern Med 44: 721-734, 1929*

Daniele RP, Dauber JH, Rossman MD: Immunologic abnormalities in sarcoidosis. *Ann Intern Med 92: 406-416, 1980*

Demeter SL: Myocardial sarcoidosis unresponsive to steroids. Treatment with cyclophosphamide. *Chest 94: 202-203, 1988*

Fields CL, Ossorio MA, Roy TM, Denny DM, Varga DW: Thallium-201 scintigraphy in the diagnosis and management of myocardial sarcoidosis. *South Med J 83: 339-342, 1990*

Forman MB, Sandler MP, Sacks GA, Kronenberg MW, Powers TA: Radionuclide imaging in myocardial sarcoidosis. Demonstration of myocardial uptake of technetium pyrophosphate 99m and gallium. *Chest 83: 578-580, 1983*

Gozo EG Jr, Cosnow I, Cohen HC, Okun L: The heart in sarcoidosis. *Chest 60: 379-388, 1971*

Ishikawa T, Kondoh H, Nakagawa S, Koiwaya Y, Tanaka K: Steroid therapy in cardiac sarcoidosis. Increased left ventricular contractility concomitant with electrocardiographic improvement after prednisolone. *Chest 85: 445-447, 1984*

Kinney EL, Caldwell JW: Do thallium myocardial perfusion scan abnormalities predict survival in sarcoid patients without cardiac symptoms. *Angiology 41: 573-576, 1990*

Mitchell DN, Scadding JG: Sarcoidosis. *Am Rev Respir Dis 110: 774-802, 1974*

Ratner SJ, Fenoglio JJ Jr, Ursell PC: Utility of endomyocardial biopsy in the diagnosis of cardiac sarcoidosis. *Chest 90: 528-533, 1986*

Riedy K, Fisher MR, Belic N, Koenigsberg DI: MR imaging of myocardial sarcoidosis. *AJR 151: 915-916, 1988*

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 63: 86-108, 1977*

Shiotani H, Miyazaki T, Matsunaga K, Kado T: Improvement of severe heart failure with corticosteroid therapy in a patient with myocardial sarcoidosis. *Jpn Circ J 55: 393-396, 1991*

Siltzbach LE, James DG, Neville E, Turiaf J, Battesti JP, Sharma OP, Hosoda Y, Mikami R, Odaka M: Course and prognosis of sarcoidosis around the world. *Am J Med 57: 847-852, 1974*

Silverman KJ, Hutchins GM, Bulkley BH: Cardiac sarcoid: a clinicopathologic study of 84 unselected patients with systemic sarcoidosis. *Circulation 58: 1204-1211, 1978*

Walsh MJ: Systemic sarcoidosis with refractory ventricular tachycardia and heart failure. *Br Heart J 40: 931-933, 1978*