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Antemortem diagnosis of cardiac sarcoidosis by abnormal uptake of ^{201}Tl in bilateral hilar lymph nodes

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The antemortem diagnosis of cardiac sarcoidosis is extremely difficult. We present a patient with congestive heart failure and cardiomyopathy of unknown cause who exhibited an abnormal accumulation of ^{201}Tl in both hilar lymph nodes in addition to a perfusion defect of the left ventricular myocardium. The findings ultimately led to a diagnosis of myocardial sarcoidosis, which was treated successfully with prednisolone. Although such uptake in the hilar nodes has rarely been reported previously, and the mechanism is not known, this was a remarkable finding in diagnosing cardiac sarcoidosis in this case. When the abnormal hilar lymph nodes uptake of ^{201}Tl is combined with the defect in the left ventricular myocardium, we should take cardiac sarcoidosis into consideration as the cause of secondary cardiomyopathy.

Key words: cardiac sarcoidosis, ^{201}Tl scintigraphy, ^{67}Ga scintigraphy

INTRODUCTION

ALTHOUGH THE DIAGNOSIS of cardiac involvement in sarcoidosis is difficult, radionuclide methods have been proposed as valuable and noninvasive aids. ^{201}Tl and ^{67}Ga scintigraphy are the two major diagnostic tools. These radionuclides are considered to be more effective in combination. ^{201}Tl myocardial perfusion defects and abnormal accumulations of ^{67}Ga are reported as common findings. The abnormal uptake of ^{201}Tl in both hilar lymph nodes, however, has rarely been reported.

CASE REPORT

This 66-year-old female was transferred to our hospital for evaluation of severe congestive heart failure of unknown cause. She had been treated for diabetes mellitus for seven years, but had been free of subjective symptoms. Six months before admission, she developed a productive cough, general fatigue, and shortness of breath. Cardiopulmonary evaluation showed marked impairment of left ventricular contraction and multichamber cardiac enlargement. The diagnosis was cardiomyopathy of unknown cause.

On physical examination, the patient's blood pressure was 118/68 mmHg, pulse rate 70 beats/min, and respiratory rate 14/min. Her chest was clear to auscultation. The second heart sound was moderately split and a grade 2/6 apical systolic murmur was audible. Chest roentgenogram (Fig. 1) demonstrated cardiac enlargement with mild pulmonary congestion. The cardiothoracic ratio was 59%. The hilar shadow was obscured by the enlarged heart. An electrocardiogram indicated a complete right bundle branch block, left axis deviation of 70° and negative T waves in leads I and aV_L. The echocardiogram revealed severe dilatation (LVDd 6.9 cm) and diffuse hypokinesis (% Fractional Shortening = 8%) of the left ventricle. Severe mitral regurgitation was also detected.

SCINTIGRAPHIC STUDIES

Rest myocardial scintigraphy, performed by injecting ^{201}Tl-Cl, 111 MBq, revealed perfusion defects in the anterolateral and inferoposterior walls without redistribution (Fig. 2, top). Abnormal uptake was also observed in the region of both hilar lymph nodes. Whole body ^{67}Ga imaging indicated an increased activity in the mediastinal area and in the heart. ^{67}Ga cardiac SPECT revealed diffuse accumulation in the ventricular region where the uptake of thallium was decreased (Fig. 2,

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bottom).

Analysis of the patient's serum showed slight increases in the levels of angiotensin-converting enzyme (21.6 mU/m*l*) and lysozyme (11.9 μg/m*l*).

Left ventriculography demonstrated akinesis of the inferior wall and dyskinesis of the anterolateral and posterolateral ventricular walls. The cardiac index was 1.3 liters/min/m^2, and the ejection fraction was 25 percent.

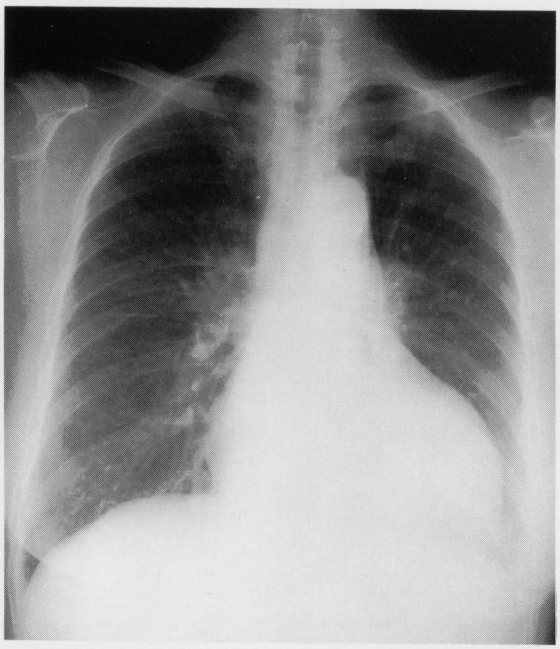

Fig. 1 Chest X-ray. The upright posteroanterior chest roentgenogram obtained before administration of corticosteroid shows mild pulmonary congestion and marked cardiomegaly. Hilar areas were indistinct due to cardiomegaly.

Left ventricular end-diastolic pressure (16 mmHg) was slightly increased. Coronary angiography revealed no significant stenotic lesion. The endocardium of both ventricles was biopsied. Granulomatous inflammation with a multinucleated giant cell and severe interstitial fibrosis were observed in one specimen. The intramyocardial arterioles were stenotic with intimal hyperplasia (Fig. 3). These histopathologic findings were consistent with a diagnosis of myocardial sarcoidosis. We considered that the congestive heart failure was caused by active myocardial sarcoidosis. The administration of prednisolone, 35 mg PO daily, was initiated. Two weeks later, an echocardiogram showed decreased left ventricular dimensions with improvement in wall motion. The cardiothoracic ratio had decreased to 48 percent. Mild hilar lymphadenopathy, which had been indistinct on the initial chest roentgenogram because of cardiomegaly, now became evident due to the subsequent shrinkage of the cardiac silhouette. Serum levels of angiotensin-converting enzyme and of lysozyme returned to normal. On ^{67}Ga imaging, the previously observed areas of high uptake had disappeared. Abnormal accumulation in both hilar lymph nodes had also disappeared on the ^{201}Tl scintigram, but the multiple defects of the myocardium still remained (Fig. 4). The electrocardiogram demonstrated no particular changes.

DISCUSSION

Sarcoidosis is a chronic, multiorgan disorder of unknown etiology. Cardiac sarcoidosis, which is often asymptomatic, can be fatal. The main causes of death are congestive heart failure, heart block, and arrhythmias. However,

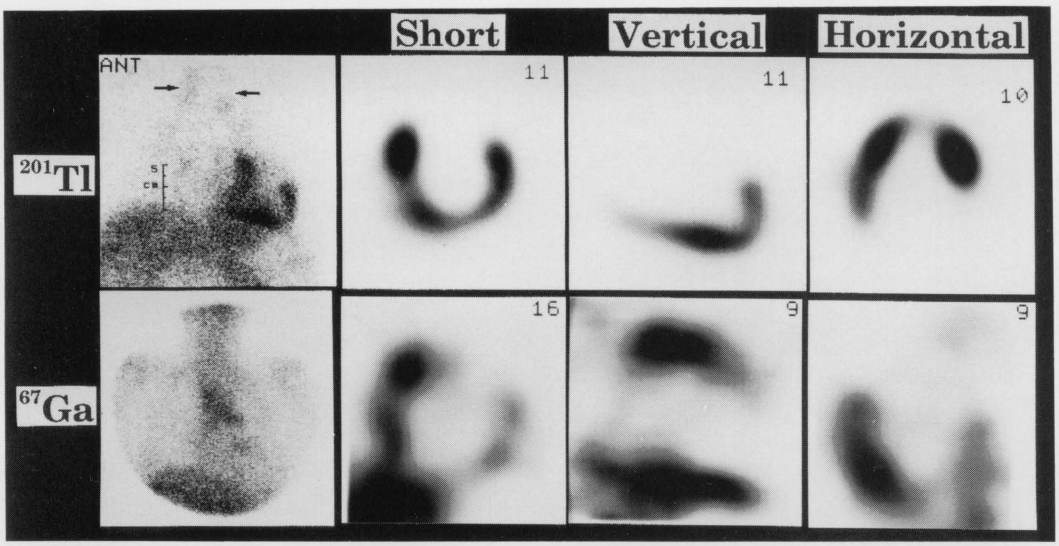

Fig. 2 ^{201}Tl and ^{67}Ga imaging before corticosteroid therapy. Abnormal ^{201}Tl uptake was observed in the regions of the bilateral lymph nodes (arrow), which was ascertained by positive ^{67}Ga accumulation in the same regions. Multiple focal defects of ^{201}Tl scintigram were found in the anterolateral and inferoposterior walls, where ^{67}Ga was accumulated.

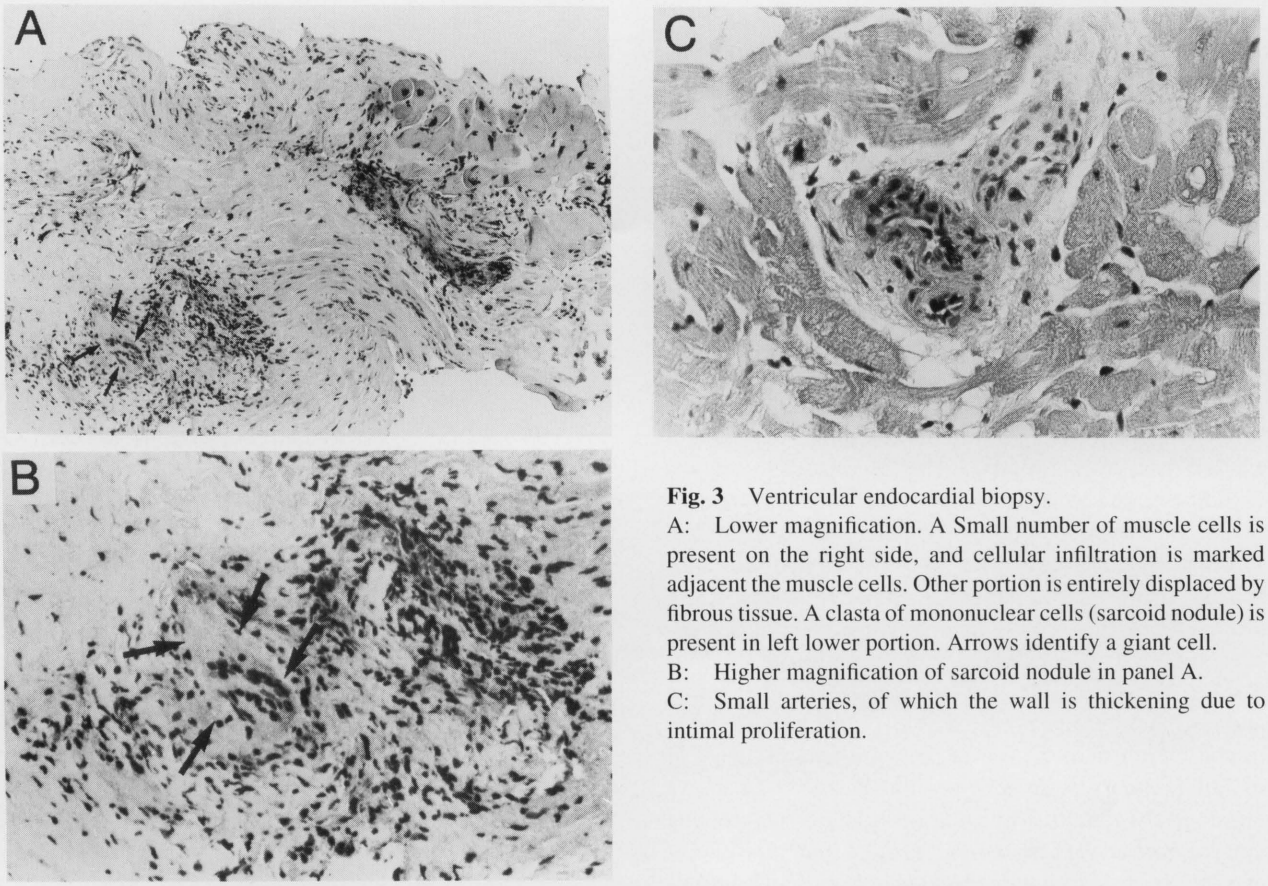

Fig. 3 Ventricular endocardial biopsy.
A: Lower magnification. A Small number of muscle cells is present on the right side, and cellular infiltration is marked adjacent the muscle cells. Other portion is entirely displaced by fibrous tissue. A clasta of mononuclear cells (sarcoid nodule) is present in left lower portion. Arrows identify a giant cell.
B: Higher magnification of sarcoid nodule in panel A.
C: Small arteries, of which the wall is thickening due to intimal proliferation.

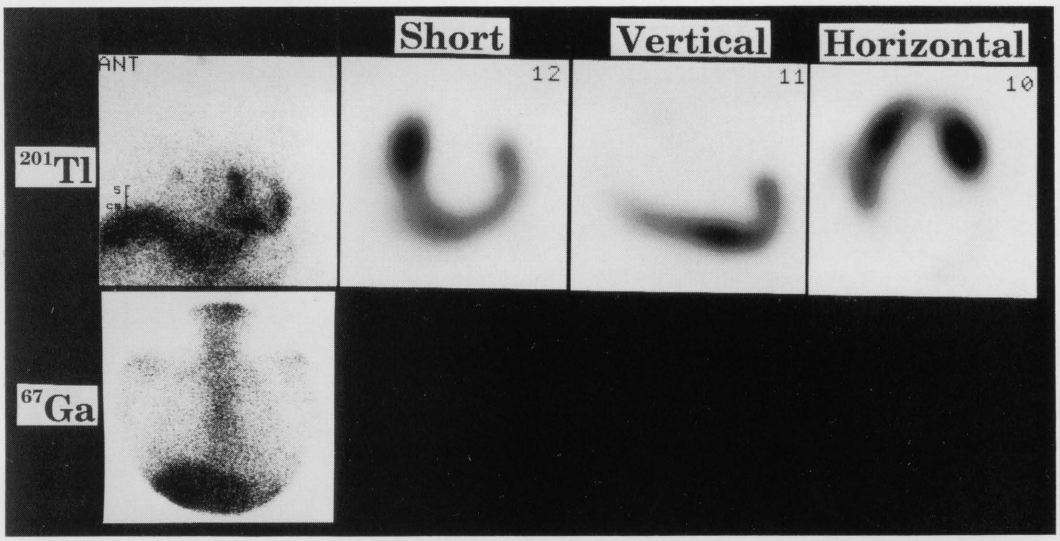

Fig. 4 ^{201}Tl and ^{67}Ga imaging after corticosteroid therapy. Disappearance of the abnormal uptake in hilar lymph nodes was shown in both ^{201}Tl and ^{67}Ga scintigrams.

cardiac involvement is extremely difficult to diagnose clinically. In autopsied cases, the rate of cardiac involvement is reported to range from 13 to 52 percent.[1] Reportedly no more than 5 percent of the patients were correctly diagnosed antemortem.[2] Except for endomyocardial biopsy, no investigative method can detect specific abnormalities that would allow the diagnosis of cardiac sarcoidosis.

Radionuclide methods are proposed as valuable and noninvasive tools for diagnosing cardiac sarcoidosis.[3,4] ^{67}Ga scintigraphy can be used as an index of disease activity[5] and as a screening test for identifying patients

with a high yield of myocarditis seen on endomyocardial biopsy.[6] The method is also useful in evaluating the efficacy of corticosteroid therapy.[7] Myocardial imaging with ^{201}Tl is a proven noninvasive technique for the clinical diagnosis of cardiac sarcoidosis.[3,8] Although a ^{201}Tl defect is a nonspecific finding that can be caused by a variety of pathologic processes, it may indicate a high probability of myocardial involvement due to fibrosis in cases of proven sarcoidosis. Mikami et al. reported that myocardial interstitial fibrosis, which was presumed to be nonspecific, was detected in all cases of cardiac sarcoidosis.[9] They also found that electron microscopic analysis of myocardial capillaries showed frequent basal lamina layering (BLL) in the fibrotic area.[9] Myocardial fibrosis is therefore supposed to be caused by microangiopathy due to BLL, which results in ^{201}Tl myocardial scan defects.

^{201}Tl uptake has been observed in tumors, active inflammatory disorders, and pulmonary tuberculosis,[10] but abnormal accumulation in both hilar lymph nodes has rarely been reported in association with sarcoidosis.[11] Tumor uptake of radionuclides reflects both tumor blood flow and also, more importantly, Na^+/K^+ pump activity in the tumor.[10] Ando et al. examined the biodistribution of ^{201}Tl in inflammatory lesions. They found that ^{201}Tl shows affinity with inflammatory tissue infiltrated by neutrophils and macrophages.[12] Merz et al. reported that ^{67}Ga associates tenaciously with the plasma membranes of lymphocytes and macrophages. In a stimulated state such as inflammation, lymphocytes and macrophages show increased affinity with ^{67}Ga.[13] Although the biodistribution and accumulation mechanism is different for ^{201}Tl and ^{67}Ga, these findings may support the hypothesis that ^{201}Tl uptake in the hilum is due to the increased blood flow caused by inflammation, and affinity with ^{201}Tl to inflammatory tissue infiltrated with activated macrophages around sarcoid lesions. Although the exact mechanism is not well defined, and further studies are required, the abnormal uptake of ^{201}Tl in the hilar lymph nodes, with a perfusion defect in the left ventricle, are notable findings that suggest a diagnosis of sarcoidosis involving the heart.

REFERENCES

1. Mayock RL, Bertrand P, Morrison C. Analysis of 145 patients, with a review of nine series selected from the literature. *Am J Med* 35: 67–89, 1970.
2. Wynne J, Braunwald E. The cardiomyopathies and myocarditis. *In* Heart disease: A textbook of cardiovascular medicine, Brawnwald (ed.), Philadelphia, WB Saunders, pp. 1426–1427, 1984.
3. Kinney EL, Jackson GL, Reeves WC, Zelis R, Beers E. Thallium scan myocardial defects and echocardiographic abnormalities in patients with sarcoidosis without clinical cardiac dysfunction: An analysis of 44 patients. *Am J Med* 68: 497–503, 1980.
4. Valeryre D, Marsac J, Gambini G, Lanfranchi J, Baubion N, Palsky D, et al. Clinical assessment of sarcoid heart disease: A study of 37 patients with thoracic sarcoidosis. *In* Sarcoidosis and other granulomatous disease, Chreiten J, Marsag J, Saltiel JC (eds.), Oxford, Pergamon Press, pp. 296–300, 1983.
5. Alberts C, Van der Schoot JB, Boren AS. Ga scintigraphy as an index of disease activity in pulmonary sarcoidosis. *Eur J Nucl Med* 6: 205–212, 1981.
6. O'Connell JB, Henkin RE, Robinson JA, Subramanian R, Scanlon PJ, Gunnar RM. Gallium-67 imaging in patients with dilated cardiomyopathy and biopsy proven myocarditis. *Circulation* 70: 58–62, 1984.
7. Tajima T, Naito T, Dohi Y, Miyamae T. Ga-67 and Tl-201 imaging in sarcoidosis involving the myocardium. *Clin Nucl Med* 6: 120–121, 1981.
8. Bulkey BH, Rouleau JR, Whitaker JQ, Strauss HW, Pitt B. The use of thallium for myocardial perfusion imaging in sarcoid disease. *Chest* 72: 27–32, 1977.
9. Mikami R, Sekiguchi M, Ryujin Y, Kobayashi F, Hiraga Y, Shimada Y, et al. Changes in the peripheral vasculature of various organs in patients sarcoidosis—Possible role of microangiopathy. *Heart & Vessels* 2: 129–139, 1986.
10. Sehwell AM, McKillop JH, Milroy R, Sayed MA, Ziada G, Banham SW. Tl scintigraphy in the staging of lung cancer, breast cancer, and lymphoma. *Nucl Med Comm* 11: 263–269, 1990.
11. Stoffey RD, Leckie RG, Buckner AB. Incidental finding of pulmonary sarcoidosis during stress thallium imaging. *Clin Nucl Med* 17: 910–912, 1992.
12. Ando A, Ando I, Katayama M, Sanada S, Hiraki T, Mori H, et al. Biodistributions of ^{201}Tl in tumor bearing animals and inflammatory lesion induced animals. *Eur J Nucl Med* 12: 567–572, 1987.
13. Merz T, Malmud L, Mc Kusick K, Wagner HN. The mechanism of Ga association with lymphocytes. *Cancer Research* 34: 2495–2499, 1974.