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Detection of denervated but viable myocardium in cardiac sarcoidosis with I-123 MIBG and Tl-201 SPECT imaging

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A 58-year-old man, who had biopsy-proven cardiac sarcoidosis, underwent Tl-201 and I-123 MIBG cardiac scintigraphy. Although no perfusion defect was identified by Tl-201, mild heterogeneity of I-123 MIBG uptake was present in the myocardium. The denervated but viable myocardium was demonstrated in the heart with sarcoidosis. Cardiac sympathetic nerve function was impaired in cardiac sarcoidosis, slightly improved with steroid therapy. I-123 MIBG scintigraphy may be useful to assess extent of myocardial involvement and response to therapy.

Key words: sarcoidosis, I-123 MIBG, Tl-201

INTRODUCTION

SARCOIDOSIS is a multisystem disorder of unknown etiology and pathogenesis which can involve almost any organ in the body due to the presence of noncaseating granulomas.[1] The granulomas are composed of epitheloid cells, probably modified macrocyte. No more than 5 percent of patients of cardiac sarcoidosis have clinical signs of heart disease.

We report scintigraphic findings of a patient with biopsy-proven cardiac sarcoidosis. Tl-201 and I-123 MIBG scintigraphy were used to demonstrate the denervated but viable myocardium in the heart.

CASE PRESENTATION

A 58-year-old man was referred to our hospital for dyspnea. On physical examination, his blood pressure was 126/80, his temperature was 36.5°C, his pulse was 72 per minute and regular. There was no pretibial edema and venous distension. A chest x-ray suggested an enlargement of the bilateral hila. Cardio-thoracic ratio in the chest x-ray was 50.3%. A CT scan showed bilateral hilar adenopathy. Laboratory evaluation revealed a hemoglobin of 15.1 g/d*l*, a hematocrit of 44.3%, a white blood cell count of 7,300 and platelet count of 23,000 per mm^3. His serum chemistry was normal. His serum angiotensin converting enzyme was 25.4 IU/*l* (normal range 7.7–29.4 IU/*l*). An electrocardiogram showed right bundle branch block. Echocardiography showed diffuse hypokinesis of the left ventricle; intraventricular septum thickness was 8.9 mm and left ventricular posterior wall thickness was 9.0 mm. The ejection fraction was 39.2%. This patients was diagnosed as having cardiac sarcoidosis documented by cardiac biopsy. The biopsy specimen showed disarray, giant cell, and granuloma, which were compatible with cardiac sarcoidosis. A coronary angiogram showed normal coronary artery. A right heart catheterization showed a mean pulmonary artery pressure of 12 mmHg, a mean pulmonary capillary wedge pressure of 4 mmHg, a mean right atrial pressure of 5 mmHg, and a pulmonary vascular resistance of 150.2 dyne $s^{-1}cm^5$. Left ventricular end-diastolic pressure was 9 mmHg. He underwent Tl-201 and I-123 MIBG cardiac scintigraphy. Tl-201 at a dose of 74 MBq was injected intravenously, and a SPECT image show in Figure 1 was obtained 20 minutes after the injection. I-123 MIBG at a dose of 111 MBq was injected slowly through the antecubital cannula and flushed with 10 m*l* saline at rest after a 3-hour fast. The planar and SPECT views were obtained approximately 15 minutes and 180 minutes after the injection with wide field-of-

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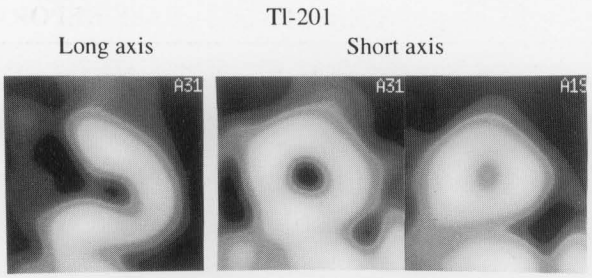

Fig. 1 Rest Tl-201 SPECT imaging shows no perfusion abnormality.

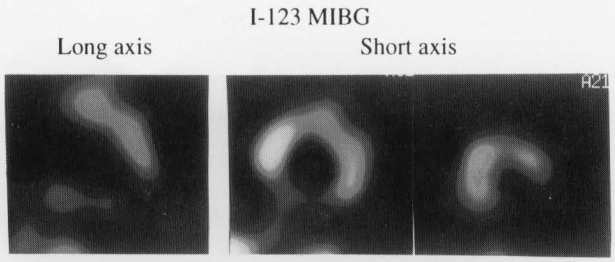

Fig. 2 The defects in inferior and apex, and the reduced uptake in the anterior and lateral segments on resting I-123 MIBG myocardial scintigraphy were noted. The denervated but viable myocardium was demonstrated in the heart with sarcoidosis.

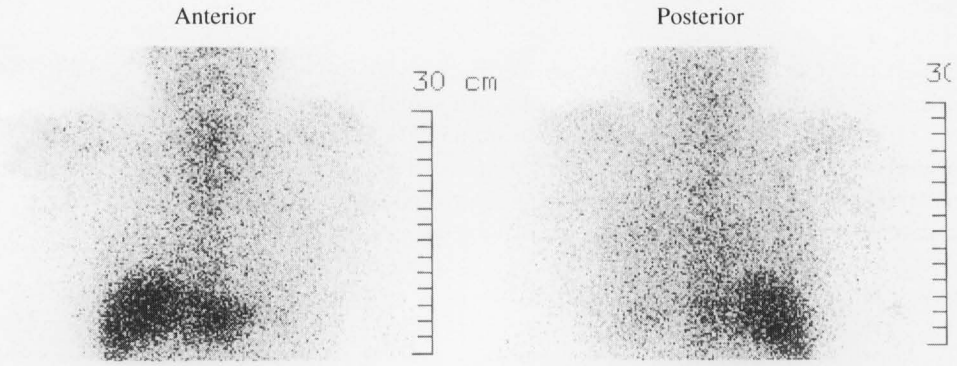

Fig. 3 Rest Ga-67 scintigraphy does not show significant increased uptake in the heart after the treatment with prednisolone.

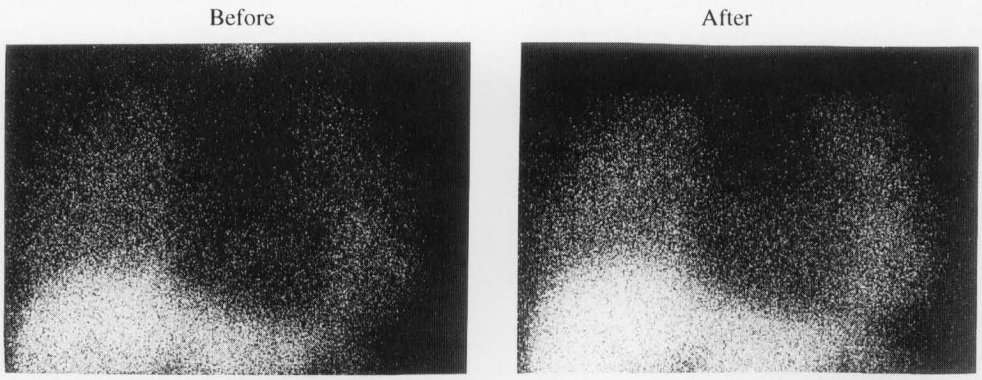

Fig. 4 The planar images before and after treatment with prednisolone are shown. Heart/mediastinum count ratio before treatment with prednisolone was 1.76, and that after treatment was 2.17.

view gamma camera (GCA-930, Toshiba Medical). Although no perfusion defect was identified by Tl-201, mild heterogeneity of the MIBG uptake was present in the myocardium, which is shown in Figure 2. The denervated but viable myocardium was demonstrated in the heart with sarcoidosis.

The patient was treated with oral prednisolone 30 mg/day for 2 weeks, followed by the administration of prednisolone 15 mg/day for a week. The patient's dyspnea were alleviated after 2 weeks' administration of prednisolone. Rest Ga-67 scintigraphy was performed at two weeks after starting prednisolone, and this is shown in Figure 3. Repeated I-123 MIBG myocardial scintigraphy was performed one month after the treatment with prednisolone. The planar imaging before and after the treatment are shown in Figure 4. Cardiac innervation was improved, the ratio of heart/mediastinum in the delayed image was 2.17 and the washout rate was 28.1% with the therapy (H/M was 1.76, washout rate was 32.2% before the treatment).

DISCUSSION

The clinical usefulness of myocardial Tl-201 and Ga-67 imaging in detecting myocardial involvement has already been reported in patients with suspected sarcoidosis.[2,3] Cardiac sympathetic involvement remains to be elucidated.[4] This case showed that cardiac sympathetic nerve function was impaired in cardiac sarcoidosis, and slightly improved with steroid therapy.

The decreased H/M ratio observed in this study is likely due to impaired uptake-1, since the absent uptake soon after cardiac alograft suggests that the uptake-2 (extraneuronal uptake) is low in human. Several mechanisms might be involved in the abnormal uptake of I-123 MIBG in patients with cardiac sarcoidosis. One possibility is that local myocardial inflammation or ischemia may play an important role in reduced MIBG uptake.[5,6] It was reported that myocardial sympathetic denervation were caused by myocarditis inflammation.[7] Myocardial inflammation in cardiac sarcoidosis was documented by Ga-67 imaging.[3] Sympathetic neuronal damage measured by MIBG scintigraphy may be related to the area of inflammation or ischemia, since neuronal damage is highly sensitive to inflammation or ischemia, compared with myocardial cells.[6] Neuronal damage may be induced by the involvement of cytokines, including tumor necrosis factor-alpha or interleukin-10 which are high in the active phase of cardiac sarcoidosis.[8,9] Another possibility is that autonomic innervation to the cardiac conduction system was severely impaired due to marked degeneration of the autonomic nerves secondary to sarcoid infiltration.[10] Finally, the impairment of sympathetic nerve function may be due to uneven ventricular hypertrophy or due to myocardial damage.[11,12] In patients with left ventricular dysfunction, decreased uptake-1 function has been found and related to both myocardial overexposure to norepinephrine and decreased myocardial β-receptors. This indicates that cardiac neuronal dysfunction of decreased MIBG uptake is related to the myocardial damage. And it also indicates a total reduction in the number of sympathetic nerve terminals or the amount of damage to the affected sympathetic neurons in the heart, due to the degeneration or hypertrophy of the myocardium.[13]

The sudden and unexpected deaths of patients with cardiac sarcoidosis is a rare but tragic event.[14] It was reported that patients with ventricular tachycardia in the absence of coronary artery disease have abnormal cardiac sympathetic innervation.[15] This noninvasive scintigraphic method might represent the most suitable approach to investigating cardiac sympathetic function. I-123 MIBG scintigraphy may be more sensitive in detecting sarcoidosis than Tl-201 scintigraphy and useful to assesing the extent of myocardial involvement and response to therapy.

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