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Noninvasive identification of myocardial sympathetic and metabolic abnormalities in a patient with restrictive cardiomyopathy —In comparison with perfusion imaging—

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A 42-year-old man had the insidious onset of heart failure, and was diagnosed as having restrictive cardiomyopathy. Doppler echocardiography study showed short deceleration time of the E wave and short isovolumic relaxation time on transmitral Doppler flow. He underwent Tl-201, I-123 beta-methyl-iodophenyl pentadecanoic acid (BMIPP) and I-123-metaiodobenzylguanidine (MIBG) cardiac scintigraphy. Tl-201 studies showed normal uptake in the left ventricle indicating normal blood perfusion. I-123 BMIPP and I-123 MIBG showed reduced uptake in the inferior segment of the myocardium, indicating impairment of fatty acid metabolism and sympathetic abnormalities.

Key words: restrictive cardiomyopathy, MIBG, BMIPP

INTRODUCTION

RESTRICTIVE CARDIOMYOPATHY can be idiopathic or secondary to a heart muscle disease that manifests as restrictive physiology.[1,2] The most common hemodynamic disturbance is impairment of ventricular filling due to the thickening and increased rigidity of the endocardium and myocardium secondary to infiltration by amyloid tissue or by fibrosis. We present a case of restrictive cardiomyopathy in which sympathetic and metabolic abnormalities and normal perfusion imaging were demonstrated.

CASE PEPORT

A 42-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 irregular. There was no pretibial edema or venous distension. A chest x-ray suggested an enlargement of the bilateral hila. The cardio-thoracic ratio in the chest x-ray was 56.2%. A CT scan showed bilateral hilar adenopathy. Laboratory evaluation revealed a hemoglobin of 16.0 g/d*l*, a hematocrit of 47.7%, a white blood cell count of 5,300 and platelet count of 179,000 per mm^3. His serum chemistry was normal. Brain natriuretic peptide was 262 pg/m*l*. An electrocardiogram showed atrial fibrillation. Echocardiography showed normal movement of the left ventricle and atrial enlargement; intraventricular septum thickness was 9.5 mm and left ventricular posterior wall thickness was 11 mm. The ejection fraction was 56.8%. A small amount of pericardial effusion was seen. Doppler echocardiography study showed short deceleration time of the E wave (90 ms) and short isovolumic relaxation time (64 ms) on transmitral Doppler flow. This patient was diagnosed as having restrictive cardiomyopathy documented by cardiac biopsy and cardiac catheterization. The biopsy specimen showed fibrosis, which was compatible with restrictive cardiomyopathy. No inflammation or amyloid deposit was seen. Coronary angiogram showed normal coronary arteries. A right heart catheterization showed a mean pulmonary artery pressure of 25 mmHg, a mean pulmonary capillary wedge pressure of 20 mmHg, and a mean right atrial pressure of 18 mmHg. Left ventricular end-diastolic pressure was 28 mmHg. Left ventricular pressure and right ventricular pressure showed dip and plateau configuration of the diastolic portion of the ventricular pressure pulse.

On the 12th day of admission, BMIPP SPECT images were obtained. Under fasting and resting conditions, 111

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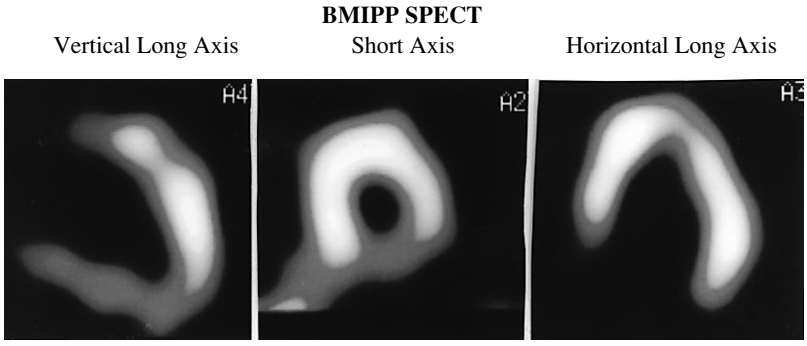

Fig. 1 The defects in inferior and apex on resting BMIPP myocardial scintigraphy were noted.

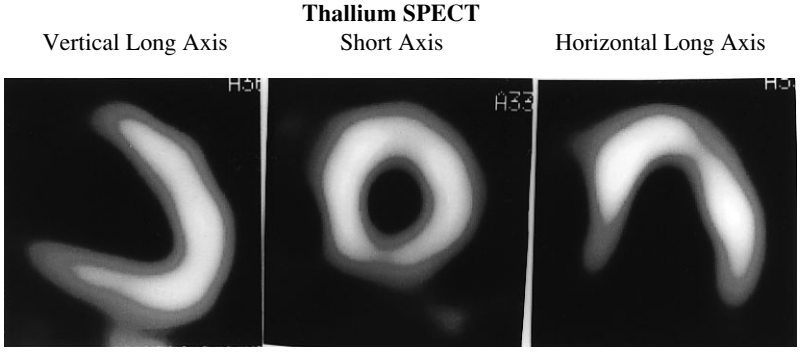

Fig. 2 Rest thallium SPECT imaging showed no perfusion abnormality.

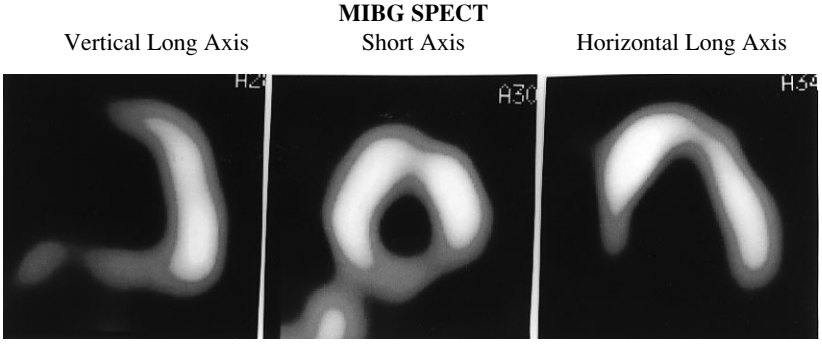

Fig. 3 The defects in inferior and apex on resting MIBG myocardial scintigraphy were noted.

MBq (1.5 m*l*) of ^{123}I-BMIPP administrated intravenously and immediately flushed with 10 m*l* of saline. A wide field-of-view gamma camera (GCA-930, Toshiba Medical) equipped with a low-energy, general-purpose collimator was rotated.[3,4] ^{123}I-BMIPP myocardial SPECT showed decreased uptake of the inferior segment in an early image (Fig. 1). He underwent ^{201}Tl scintigraphy on the 17th hospital day. ^{201}Tl at a dose of 74 MBq was injected intravenously, and the SPECT image shown in Figure 2 was obtained 20 minutes after the injection. Rest thallium SPECT imaging shows no perfusion abnormality. He underwent ^{123}I-MIBG cardiac scintigraphy on the 48th day of admission. ^{123}I-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 injection as previously reported.[3] Although no perfusion defect was identified by ^{201}Tl, mild heterogeneity of the MIBG uptake was present in the myocardium, which is show in Figure 3. According to the scintigraphic findings, the cardiac sympathetic and metabolic abnormalities were demonstrated in restrictive cardiomyopathy

DISCUSSION

In this report, the abnormalities of cardiac sympathetic nerve function and metabolism were demonstrated in a

patient with restrictive cardiomyopathy. To the best of our knowledge, this is the first case report to examine the myocardial characteristics of restrictive cardiomyopathy in terms of the sympathetic nerves and metabolism.

^{123}I-BMIPP scintigraphy has been established as an important technique for studying change in myocardial fatty acid metabolism, because BMIPP is metabolically trapped in the myocardium due to its methyl branching.[5,6] The disparity between BMIPP and thallium is frequently observed in coronary artery disease and tends to show increased fluorodeoxyglucose uptake in a positron emission tomography study, as shown in a previous report.[7] In such ischemic regions, fatty acid metabolism may be easily suppressed in mild ischemia and the source of ATP production may be switched from fatty acid to glucose. And the ratio of phosphocreatine to ATP was significantly altered in transient ischemia. Recent report showed that ^{123}I-BMIPP detects not only present ischemia but also past ischemia in patients with vasospastic angina. In hypertrophic cardiomyopathy or hypertensive heart disease, metabolic abnormalities of non-ischemic myocardium were also reported as non-ischemic metabolic abnormality.[4,8,9] Therefore, reduced ^{123}I-BMIPP uptake compared to a ^{201}Tl image suggests that the inferior wall may suffer fibrotic changes or myocardial damage in extreme cardiac wall stress with diastolic dysfunction, resulting in impaired fatty acid utilization and metabolism.

MIBG imaging of normal subjects, MIBG uptake in the inferior segments is sometimes reduced.[3] Nevertheless the possibility still remains that sympathetic neuronal damage measured by MIBG scintigraphy is closely related to the area of ischemia, since neuronal damage is highly sensitive to ischemia compared with myocardial cells.[10] MIBG abnormalities persisted much longer than regional wall motion abnormalities. In a laboratory animal study, temporal sympathetic nervous denervation from myocardial ischemia lasted from 8 to 17 weeks after myocardial ischemia. In various kinds of cardiomyopathies, including dilated, hypertrophic or diabetic cardiomyopathy, abnormal sympathetic nerve functions with normal perfusion were previously reported.[4,11–15] In restrictive cardiomyopathy, diastolic abnormalities are essentially myocardial. It was reported previously that autonomic abnormality was related with diastolic dysfunction, especially a restrictive ventricular filling pattern, in patients with chronic heart failure.[16] We assume that sympathetic abnormality is related to primary abnormality of diastolic ventricular function, leading to a total reduction in the number of sympathetic nerve terminals or the amount of damage to the affected sympathetic neurons in the heart.[13]

This report showed metabolic and sympathetic abnormalities in a patient with restrictive cardiomyopathy. It was not determined whether these abnormalities were common findings in this disease. Therefore, further studies are needed to clarify the exact characteristic features of restrictive cariomyopathy.

The findings of scintigraphic studies show us that restrictive physiology seems to cause metabolic and sympathetic abnormality with normal perfusion. Combined scintigraphic studies may be useful in providing diagnostic precision, contributing materially to the clinical identification of restrictive cardiomyopathies.

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