**Abstract**

A 72-year-old woman had insidious onset of heart failure, and was diagnosed as multicentric Castleman’s disease. She underwent myocardial imaging with technetium-99m tetrofosmin, I-123 beta-methyl-iodophenyl pentadecanoic acid (BMIPP). Technetium-99m tetrofosmin studies showed almost normal uptake of the left ventricular myocardium indicating normal myocardial perfusion. I-123 BMIPP showed reduced uptake in the apical segment of the myocardium, indicating regional fatty acid metabolic abnormalities.

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**Key words:** multicentric Castleman’s disease cardiomyopathy, BMIPP

**Introduction**

Multicentric Castleman’s disease (MCD) is an uncommon lymphoproliferative disorder which typically presents with constitutional symptoms, multicentric lymphohadenopathy, hepatosplenomegaly, effusions, and ascites (1–3). We present a case of MCD in which metabolic abnormality and normal perfusion imaging were demonstrated.

**Case Report**

A 72-year-old woman was referred to the Cardiovascular and Respiratory Department of Shiga University of Medical Science for dyspnea. Eight months previously, in the Third Department of Internal Medicine, multicentric Castleman's disease had been diagnosed. At that time, she had exhibited multiple peripheral lymphadenopathy, splenomegaly, pleural effusion, and an episode of altered mentality. Biopsy of the enlarged lymph node revealed Castleman’s lymphadeno-pathy. In addition, serum protein immunoelectrophoresis suggested polyclonal gammopathy. Elevated interleukin-2 and IgG were observed. On physical examination, her blood pressure was 128/80 mmHg, her temperature was 36.1°C, her pulse was 102 beats per minute and irregular. She had pretibial edema and venous distension. A chest X-ray suggested an enlargement of bilateral hila. Cardio-thoracic ratio of the chest X-ray was 82.2%. Laboratory evaluation revealed hemoglobin 12.0 g/dl, hematocrit 37.7%, white blood cell count 9,600/μl and platelet count 7,200 per mm³. Her serum chemistry was normal. Plasma brain natriuretic peptide level was 588 pg/ml. An electrocardiogram showed atrial fibrillation. Echocardiography showed reduced wall motion of the left ventricle; intraventricular septum thickness was 11.2 mm and left ventricular posterior wall thickness was 11.2 mm. The ejection fraction of the left ventricle was 41.8%. She underwent technetium-99m tetrofosmin cardiac scintigraphy. Technetium-99m tetrofosmin at a dose of 740 MBq was injected intravenously, and SPECT image was obtained 20 minutes after the injection. Almost normal myocardial perfusion was identified. The quantitative gated SPECT showed reduced left ventricular ejection fraction (41%), which is shown in Fig. 1. The apical wall motion of the left ventricle was mildly reduced.

BMIPP was prepared and provided by Nihon Medi-Physics Co., Ltd. (Hyogo, Japan). The vial of BMIPP contained 74 MBq/ml (0.4 mg/ml) I-123-labeled BMIPP dissolved in ursodeoxycholic acid (7 mg/ml). Under fasting and resting conditions, 111 MBq (1.5 ml) of I-123 BMIPP administrated intravenously and immediately flushed by 10 ml of saline. The BMIPP SPECT images were obtained as previously reported (4–5). I-123 BMIPP myocardial SPECT showed decreased uptake of the apical segment, which is shown in Fig. 2. According to the scintigraphic findings, metabolic abnormalities were demonstrated in MCD.

Cardiac catheterization and cardiac biopsy were perform-
Coronary angiogram showed normal coronary arteries. The biopsy specimen showed fibrosis and mildly atrophic and hypertrophic changes of the myocardium with fatty change.

**Discussion**

Interleukin-6 (IL-6) gene expression is considered to be a primary event that could be related to the etiology of the MCD (1, 5). Recently, Kaposi’s sarcoma virus/human herpes virus 8 has been reportedly associated with a subset of the multicentric type of Castleman’s disease, and a viral homologue of IL-6 encoded by KSHV/HHV-8 has been shown to induce VEGF expression (6). And in the polynephropathy, organomegaly, endocrinopathy, and M protein, skin changes (POEMS) syndrome, IL-6 is reportedly related to this cardiac involvement (7, 8).

Here, cardiac metabolic abnormalities were demonstrated in a patient with MCD. To our knowledge, this is the first case report to examine the myocardial characteristics of MCD in terms of cardiac metabolism. I-123 BMIPP scintigraphy has been established as an important technique for studying the alteration in myocardial fatty acid metabolism, because BMIPP is metabolically trapped in the myocardium due to its methyl branching (4, 9). The disparity of the two tracers is frequently observed in coronary artery disease and tends to show increased fluorodeoxyglucose uptake in the positron emission tomography study, as shown in a previous report (10). 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 is significantly altered in transient ischemia. A recent report showed that I-123 BMI PPP detected not only present ischemia but also past ischemia in patients with vasospastic angina (4, 11). Therefore, reduced I-123 BMIPP uptake compared to myocardial perfusion imaging indicates that myocardial ischemia may play an important role in impaired fatty acid utilization and metabolism (4, 11). Another possibility is that myocardial inflammation causes myocardial damage in patients with MCD, since myocardial inflammation is reportedly documented to be the cause of myocardial damage in patients with myocarditis or sarcoidosis (12–14). It is suggested that myocardial damage may be induced with the involvement of cytokines, including tumor necrosis factor-alpha or IL-6 which are elevated in the active phase of MCD (5). It is reported that metabolic abnormality often occurs before the occurrence of abnormalities in myocardial blood flow distribution (4). Myocardial damage may be induced by the involvement of cytokine interleukin-6, and any viral infection including herpesvirus type-8, a γ2-herpetovirinae, hepatitis B virus, and human immunodeficiency virus. I-123 BMIPP scintigraphy may be useful in evaluating myocardial metabolic abnormality and cardiac involvement related to the inflammation or ischemia in this disease.

The findings of scintigraphic studies suggest that the pathological condition in MCD causes cardiac metabolic abnormality, which could be detected by I-123 BMIPP scintigraphy.

*Figure 1. Quantitative gated SPECT with technetium-99m tetrofosmin showed reduced left ventricular ejection fraction (41%).*
Figure 2. The defects in the apex on resting BMIPP myocardial scintigraphy were noted, and almost normal perfusion of the left ventricle was shown by technetium-99m tetrofosmin SPECT.

References