CASE REPORT

Triglyceride Deposit Cardiomyovasculopathy with Massive Myocardial Triglyceride which Was Proven Using Proton-magnetic Resonance Spectroscopy

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Abstract:
The patient was a 73-year-old man with a history of hypertension, diabetes mellitus, dyslipidemia, rheumatoid arthritis, repeated percutaneous coronary intervention and percutaneous peripheral intervention procedures. He was frequently admitted to our hospital for congestive heart failure with orthopnea. The myocardial washout rate of iodine-123-β-methyl iodophenyl-pentadecanoic acid was defective on scintigraphy. He was diagnosed with triglyceride deposit cardiomyovasculopathy (TGCV). Proton magnetic resonance spectroscopy (^1H-MRS) indicated the level of myocardial triglyceride (TG) content to be extremely high (4.92%). This is the first report to confirm a massive accumulation of TG in the myocardium of a patient with TGCV using ^1H-MRS noninvasively.

Key words: triglyceride deposit cardiomyovasculopathy, proton magnetic resonance spectroscopy

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Introduction

Triglyceride deposit cardiomyovasculopathy (TGCV) is a newly identified heart disease characterized by excessive triglyceride (TG) accumulation in both myocardium and coronary arteries (1-3). This report is the first case of a patient with TGCV who was confirmed to have a massive accumulation of TG in the myocardium using proton magnetic resonance spectroscopy (^1H-MRS).

Case Report

The patient was a 73-year-old man with a past medical history of percutaneous coronary intervention (PCI) because of effort-induced angina pectoris at the age of 50. He had been treated for type 2 diabetes mellitus with oral medical therapy, such as sulfonylureas, glinides and/or dipeptidyl-peptidase-4 inhibitors for the past 9 years. Two years after undergoing PCI, he underwent percutaneous peripheral intervention (PPI) due to the onset of bilateral claudication.

At 69 years of age, he had undergone PPI of the right superficial femoral artery as well as PCI of the mid left anterior descending artery and mid left circumflex artery with drug-eluting stent implantation, followed by an occlusion in the middle segment of the right coronary artery (Fig. 1). In the same year, he had been admitted to our hospital due to congestive heart failure (CHF) for the first time, followed by six subsequent readmissions for CHF with orthopnea triggered by infection and a progression of diabetic nephropa-
He was readmitted because of worsening dyspnea on exertion, orthopnea with jugular venous distention, and edema in both his lower extremities. On admission, he was 150 cm tall and weighted 58 kg. His pulse rate was 84 beats/min, and blood pressure was 104/52 mmHg. Coarse crackles were heard at both lower lung fields. A laboratory analysis was notable for elevated levels of serum creatinine of 3.3 mg/dL, and brain natriuretic peptide of 716 pg/mL. His glucose profile showed a serum glucose level of 103 mg/dL and hemoglobin A1c of 5.9 %. Lipid profile revealed high-density-lipoprotein cholesterol of 31 mg/dL, low-density-lipoprotein cholesterol of 36 mg/dL, and serum TG of 109 mg/dL. A chest X-ray demonstrated pulmonary congestion and pleural effusion. An electrocardiogram showed atrial fibrillation with ventricular rate of 67 beats/min, and complete right bundle branch block. In addition, ultrasound cardiography revealed a normal left ventricular (LV) ejection fraction (63%) and severe tricuspid valve regurgitation.

His condition improved immediately after the repeated intravenous injection of furosemide at 40 mg per day and increased dose of tolvaptan from 3.75 mg to 7.5 mg per day. Iodine-123-β-methyl iodophenyl-pentadecanoic acid (BMIPP) single-photon emission computed tomography (SPECT) indicated a normal myocardial uptake of BMIPP in all areas in the initial phase and a decrease in the washout rate (WOR) of BMIPP to 3.5%. He was diagnosed with TGCV (Fig. 2). Cine imaging using the steady-state free precession technique demonstrated normal LV contraction. 1H-MRS was performed to measure TG accumulation in the myocardium, which appeared to be 4.92% (Fig. 3). After the initiation of optimal medical therapy such as β-blocker, angiotensin II receptor blocker, tolvaptan and oral furosemide 60 mg per day, he was discharged from our hospital.

**Discussion**

TGCV is a rare heart disease in patients requiring cardiac transplantation; it was newly identified in 2008 (1-3). In a normal condition, long chain fatty acids (LCFAs) are taken up through LCFAs transporters and receptors such as CD36, and some of them are transported to the mitochondria for β-oxidation. The remaining LFCAs are utilized as a source for TG and hydrolyzed by intracellular lipases such as adipose triglyceride lipase (ATGL). However, in TGCV, LFCAs are taken up and used to synthesize TG that cannot be hydrolyzed due to ATGL insufficiency, leading to energy failure and lipotoxicity with massive TG accumulation. Therefore, TGCV is characterized by excessive TG accumulation in both the myocardium and coronary arteries, and the sub-

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**Figure 1.** Coronary angiography. (A) Right anterior oblique (30°) view. (B) Cranial (45°) view. (C) Right anterior oblique (30°) and caudal (30°) views.

**Figure 2.** Washout rate of iodine-123-β-methyl iodophenyl-pentadecanoic acid. (A) Quantitative polar map displays with early phase. (B) Quantitative polar map displays with delay phase. (C) Washout rate, WOR=3.5%
types are classified into primary TGCV with ATGL mutations and idiopathic TGCV without ATGL mutations (4, 5).

The criteria for TGCV include three essential and three major items (6). The essential items are an impaired LCFA metabolism or TG deposition in the myocardium, which is the metabolic basis of TGCV. Myocardial TG deposition is demonstrated by biopsy specimens, computed tomography, $^1$H-MRS, or a decreased WOR (<10%) of BMIPP. Major items include a reduced cardiac function, diffuse narrowing of the coronary arteries documented by coronary angiography or computed tomography angiography, or Jordans’ anomaly of polymorphonuclear leucocytes in a peripheral blood smear. Both essential and major items with one or more indicate definite TGCV. Diabetes mellitus and hemodialysis are included as supportive items.

The patient reported herein had a history of diabetes mellitus with repeated PCI procedures because of diffuse narrowing coronary lesions. Furthermore, the WOR of BMIPP-SPECT was 3.5%, indicating a remarkable decrease as compared to the normal level (19.4%±3.2%) (7). The patient fulfilled the criteria of TGCV (6) and was subsequently diagnosed with definite TGCV.

It has been reported that the myocardial TG content is associated with metabolic disorders such as diabetes mellitus. Additionally, increasing the myocardial TG content has been reported to cause LV diastolic and systolic dysfunction along with LV remodeling (8-10). The patient suffered from multiple underlying metabolic disorders, including obesity, hypertension, and several metabolic disorders such as diabetes mellitus and dyslipidemia. McGavock et al. demonstrated that the levels of myocardial TG content in nonglycemic obese subjects and patients with diabetes mellitus as 0.81%±0.46%, and 1.06%±0.62%, respectively (8). The myocardial TG content in the present case was measured to be 4.92% using $^1$H-MRS, which is extremely high even in the context of these metabolic disorders.

In addition, we previously reported the levels of myocardial TG content in apparently healthy subjects without coronary heart disease, endurance athletes, and healthy subjects with fitness habits as 0.85%±0.40%, 0.60%±0.20%, and 0.89%±0.41%, respectively (11, 12). On the other hand, the levels of myocardial TG content in patients with hypertrophic cardiomyopathy (HCM) and hypertensive heart disease were 1.09%±0.72% and 2.14%±1.29%, respectively (13). The myocardial TG content detected in the current case was thought to be high in comparison with these data.

Moreover, Liao et al. reported that the level of myocardial TG content of patients who were admitted for acute heart failure with low LV ejection fraction (EF), those with normal LVEF, and controls without cardiovascular disease were 0.79%, 0.21%, and 0.14%, respectively (14). The myocardial TG content in the present case was extremely high compared with these data regarding the myocardial TG content although not equal to our sequence regarding the procedures and equipment. In conclusion, $^1$H-MRS may be helpful for assessing the myocardial TG pool and establishing a diagnosis of TGCV noninvasively (15).

The authors state that they have no Conflict of Interest (COI).

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