CASE REPORT
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A Case of Mitochondrial Myopathy With Cardiac Involvement

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ABSTRACT

Mitochondrial myopathy is a disease caused by structural, biochemical or genetic disturbance of the mitochondria and this affects many organs, and it may also involve the cardiac muscles. We experienced a case of myocardial involvement in a 21 years old male patient with mitochondrial myopathy. **(Korean Circ J 2008;38:491-494)**

KEY WORDS: Mitochondrial myopathies; Cardiomyopathies.

Introduction

Mitochondrial myopathy is a group of diseases that includes the diverse diseases caused by structural, biochemical or genetic disturbance of the mitochondria, and these pathological changes generally appear in muscles.[1-3] It has the characteristic of functional impairment of primarily the brain and muscles; nonetheless, it may ultimately involve all the organ systems.[4-6] Numerous treatment protocols have recently been proposed, the effectiveness of these treatment methods is not yet known.[7] We experienced a case of myocardial involvement in a patient who was diagnosed with mitochondrial myopathy.

Case

A 21 years old patient was transferred to our hospital for the evaluation of his chest discomfort, chronic fatigue, hypercapnia and hypoxemia. 2 weeks prior to his transfer, the patient had experienced a mild head laceration and he was unconsciousness after a traffic accident. He was transported to a local hospital and there he was treated by tracheal intubation and mechanical ventilation. No abnormal findings were detected on the magnetic resonance imaging of the brain that was performed at that time. He regained consciousness afterward and spontaneous breathing was possible, but he showed continuously hypercapnia and hypoxemia on the arterial blood gas analysis, and he also displayed chronic fatigue. Sleep apnea was suspected, and he was then transferred to our hospital.

Prior to admission, the patient was relatively healthy, but from a young age his motor ability was lower than his peers; he had difficulty with climbing slopes, and he could not perform even a single push-up. Genetic diseases or neuromuscular diseases were not detected in this family history.

His vital signs at the time of admission were a blood pressure of 110/70 mmHg, a pulse rate of 78 times/minute, a respiration rate of 20 times/minute, a temperature of 36.8℃, his height was 161 cm and his weight was 52 kg. He was conscious, and a trace of mild trauma to the head was detected. On the chest examination, his breathing and the cardiac auscultation were normal, and no specific findings were detected on the abdominal and limb examinations. On the neurological examination, the cranial nerve function was normal, the limb muscular force was generally weakened and his sensation was normal.

The complete blood count was normal. On the blood chemistry tests, the aspartate aminotransferase (AST) was 18 IU/L, the alanine aminotransferase (ALT) was 9 IU/L, the creatine phospho kinase (CPK) was 162 IU/L and the lactate dehydrogenase (LDH) was 309 IU/L. On the arterial blood gas analysis, the pH was 7.366, the PaO_2 was 58.9 mmHg, the $PaCO_2$ was 64.9 mmHg and the HCO_3 was 36.3 mmol/L. Cardiac enlargement was not detected on the simple chest X-ray and distinct lesions were not detected in both lung fields. Any special findings were not detected on the electrocardiography (ECG).

Polysomnography was performed, and he was diag-

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nosed with central apnea. The anti-nuclear antibody, rheumatoid factor and anti-acetylcholine receptor antibody tests were all negative; there were no electrodiagnostic findings on the electromyogram that could be diagnosed as myopathy or peripheral neuropathy. Muscle biopsy was performed on the left gastrocnemius muscle for making the definite diagnosis of muscular diseases. Ragged red fibers were detected under the light microscope with the muscle tissue stained by odified Gomori-trichrome staining, and a strong response to succinate dehydrogenase was shown. Paracrystalline structures and an abnormal increase of the number of mitochondria were observed on the electron micrographs; these findings were compatible to mitochondrial myopathy (Fig. 1). Ophthamological and neurological examinations were performed to assess the involvement of other organs, and these exams were normal. On the echocardiography, the left ventricular diastolic internal dimension (LVIDd) was 37 mm, the left ventricular systolic internal dimension (LVIDs) was 21 mm, the left ventricular end-diastolic volume (LVEDV) was 72 mL, the left ventricular endsystolic volume (LVESV) was 30 mL and the left ventricular ejection fraction (LVEF) was 58%.

The patient's symptoms improved and so he was discharged. After discharge, the patient was well without special symptoms, However, on the electrocardiogram performed for follow up observation at the outpatient clinic after 6 months, inversion of the T wave was developed newly in the limb leads II and aVF and in the chest leads V1-V4 (Fig. 2). Chest pain, deterioration of his dyspnea or any distinct history of medication was not shown upon re-examination of the patient's disease history. On the blood biochemistry tests that were done at this time, the AST was 31 IU/L, the ALT was 38 IU/L, the CPK was 403 IU/L (55-215 IU/L), the LDH was 393 IU/L, the creatine kinase MB (CK-MB) was 8.16 ng/mL (0-3.6 ng/mL) and the troponin I was 0.2 ng/mL (0-0.1 ng/mL). On the arterial blood gas analysis, the pH was 7.347, the PaO_2 was 98.4 mmHg, the $PaCO_2$ was 48.7 mmHg and the HCO_3 was 26.1 mmol/L. On the echocardiography, the LVIDd and LVIDs were 41 mm and 23 mm, respectively. The LVEDV was 102 mL and the LVESV was 36 mL. The LVEF was 65%. There was no significant interval change compared to the previous echocardiography. CT coronary angiography showed normal coronary arteries and the Holter monitor revealed no specific findings. Although abnormal findings were shown on the electrocardiographs, the patient was asymptomatic and any findings suggesting coronary artery disease were not detected; thus, he was discharged and is currently under follow up at our outpatient clinic.

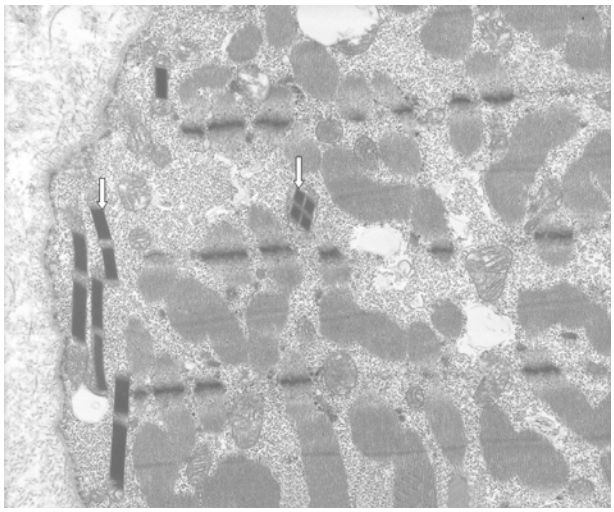

Fig. 1. Electron micrograph showed an increased number of abnormal mitochondria that contained paracrystalline structures (white arrow) in the subsarcolemmal area.

Discussion

Mitochondrial myopathy is group of diverse pathological diseases that involves many organs and systems,[1] and it includes chronic progressive external ophthalmoplegia (CPEO), myoclonus epilepsy with ragged red fibers (MERRF), mitochondrial myopathy, encephalopathy, lactic acidosis and stroke like episodes (MELAS) and Kearns-Sayre syndrome (KSS) etc.[3][8] An important part of the spectrum of this disease is that it is induced by mutations of the mitochondrial deoxyribonucleic acid (DNA).[1] Pathologic mitochondria DNA mutation is caused by deletion, duplication or point mutation, and the mixture of mutated genes and normal genes is present in each cell.[9] Therefore, the mutation load of the pathologic mitochondrial DNA that is developed at the cellular level determines the presence or absence of symptoms. In addition, different mutation loads appear not only among individuals, but also within an individual between the cells as well as between organs, and so the symptoms can be quite diverse.[10]

Mitochondria have been shown to be a major site for synthesizing adenosine triphosphate (ATP) through the oxidative phosphorylation process and so this organelle plays an important role in cellular metabolism.[1] The heart, the central nervous system and the skeletal muscles are all highly dependent on the energy generated by the oxidative process of mitochondria,[11][12] and thus, the inappropriate energy generation caused by defects of the mitochondria may induce heart failure.[13]

The major clinical characteristic of mitochondrial diseases is the gradual increase of the number of involved tissues or organs. These patients gradually develop diabetes, hearing loss, adult onset cardiomyopathy etc. As was the case for our patient, if other common causes of changes of the heart such as hypertension and myocarditis are absent, if there is no history of exposure to toxic drugs and if the coronary angiogram is normal,

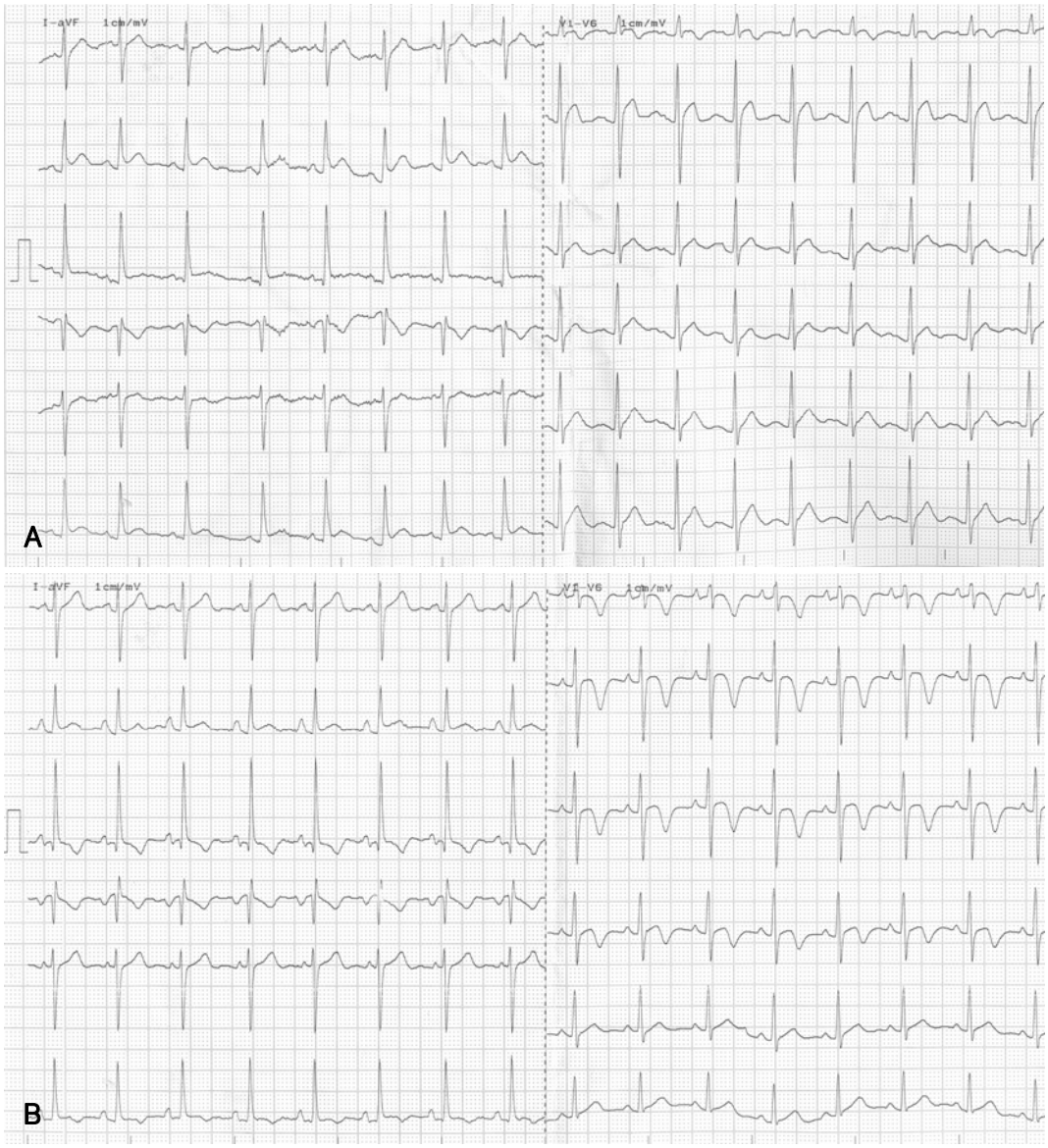

Fig. 2. Change of the electrocardiogram during 6 months. A: the initial electrocardiogram showed non-specific findings. B: 6 months later, the follow-up electrocardiogram showed newly developed T-wave inversion in the limb leads (III, aVF) and the precordial leads (V1-V4).

then mitochondrial myopathy may be the most plausable cause that could explain the gradual changes of the heart of these patients.[4)]

Mitochondrial cardiomyopathy frequently shows an elevated creatinine kinase level, the noticeable deterioration of the mobility of the left ventricle on echocardiography and a resultant decrease of the ST segment. Additionally, Papadimitrion et al.[14)] and Yokoyama et al.[15)] have reported the inversion of the T wave and the prolongation of the PR interval in patients with mitochondrial cardiomyopathy. Our case also displayed elevated creatinine kinase and troponin I levels, and newly developed inversion of the T wave was observed on the electrocardiogram performed at 6 months of follow-up.

Anan et al. have reported that the clinical characteristic of myocardiac involvement were different depending on the subgroups of mitochondrial diseases. In KSS, impairment of the arterioventricular conduction was primarily observed in patients with KSS; further, in patients with MERRF, asymmetric septal enlargement presenting as ventricle wall motion abnormality might be characteristically seen. In addition, regardless of the presence of abnormality of the ventricular wall motion, symmetric left ventricular enlargement is the characteristic of the myocardiac involvement in patients with MELAS.[13)]

The symptoms of mitochondrial myopathy patients generally appear in childhood or during the juvenile period in most cases, and it is rare to observe mild weakness of all the limb muscles and the feature of the chronic hypoventilation syndrome in adults, as was seen in our case. Although there has been a report on a Korean case for whom the cardiac muscles were involved by myopa-

thy and so a permanent pacemaker was inserted, it was the Emery-Dreifuss type myopathy.[16)17)] There have been no reports on Korean cases with the involvement of mitochondrial myopathy in the cardiac muscles.

The functional impairment of mitochondria could influence all the organ systems, and so clinicians in various fields could encounter mitochondrial myopathy patients.[4)] When unexplained cardiomegaly or myocardial hypertrophy on echocardiography is detected or there are unexplained changes on the electrocardiogram such as left ventricular hypertrophy, inversion of T-waves, prolongation of the PR interval and a prolonged QTc, mitochondrial myopathy should be considered in the differential diagnosis of idiopathic cardiomyopathy. Particularly, as in our case, mitochondrial myopathy should be considered for the diagnosis of patients who have symptoms in organs other than the heart, such as the past history of muscle weakness or they exhibit hypoventilation syndrome.

Endomyocardial biopsy confirms the diagnosis for patient with suspected mitochondrial cardiomyopathy. Biopsy shows mitochondrial DNA mutation or the abnormal structure of the mitochondria, yet no effective treatment has yet been reported.

The limitation of this case report is that the analysis of mitochondria by histological testing of the cardiac muscle of the patient was not actually performed. Another limitation is that we did not check other predominant enzymes of the skeletal muscle, such as aldolase, to rule out striated muscle as the primary source of the elevated CK-MB level.

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