

[CASE REPORT]

Hemodynamic Collapse Caused by Cardiac Dysfunction and Abdominal Compartment Syndrome in a Patient with Mitochondrial Disease

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Abstract:

We herein report a case of mitochondrial disease with heart and intestinal tract involvement resulting in hemodynamic collapse. A 66-year-old woman was transferred to our hospital because of cardiogenic shock. Vasopressors were administered, and a circulatory support device was deployed. However, her hemodynamics did not improve sufficiently, and we detected abdominal compartment syndrome caused by the aggravation of chronic intestinal pseudo-obstruction as a complication. Insertion of a colorectal tube immediately decreased the intra-abdominal pressure, improving the hemodynamics. Finally, we diagnosed her with mitochondrial disease, concluding that the resulting combination of acute heart failure and abdominal compartment syndrome had aggravated the hemodynamics.

Key words: shock, mitochondrial disease, abdominal compartment syndrome, chronic intestinal pseudo-obstruction

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Introduction

Mitochondria generate adenosine triphosphate that in turn supports most cellular functions. Mitochondrial disease is a heterogeneous group of multi-organ disorders caused by dysfunctional mitochondria (1, 2). Organs with a high energy demand, including the muscles, brain, and heart, are frequently damaged by mitochondrial disease.

Recently, gastrointestinal involvement in mitochondrial disease, which can cause chronic intestinal pseudo-obstruction (CIPO), has also been reported (3, 4). The aggravation of CIPO is clinically important because its progression complicates abdominal compartment syndrome (5).

We herein report a patient with mitochondrial disease and severe cardiac dysfunction in whom CIPO caused abdominal compartment syndrome, which then accelerated the circula-

tory failure.

Case Report

A 66-year-old woman (height, 150 cm; body weight, 36 kg) with complaints of gradually aggravating dyspnea, disturbance of consciousness, distal muscle weakness, and lower limb hypoesthesia was transferred to our hospital. She had a medical history of diabetes mellitus requiring insulin therapy with poor control (HbA1c, 9.0%) and no diabetic neuropathy since 50 years old and sensorineural deafness from adolescence.

On arrival at our hospital, her systolic blood pressure was 90 mmHg, indicating cardiogenic shock. Her heart rate was 86 bpm, and her respiratory rate was 24 breaths/min. Her consciousness level was II-10 on the Japan Coma Scale. Chest radiography revealed cardiomegaly and pulmonary

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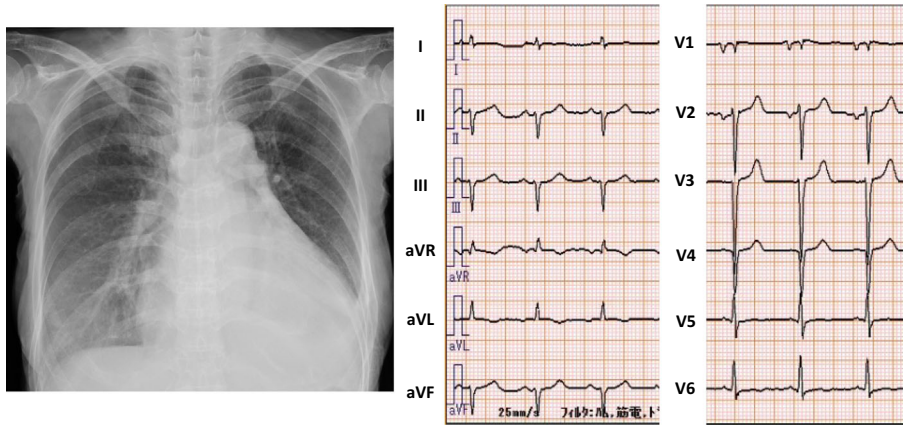


Figure 1. Chest radiograph and electrocardiogram findings on admission.

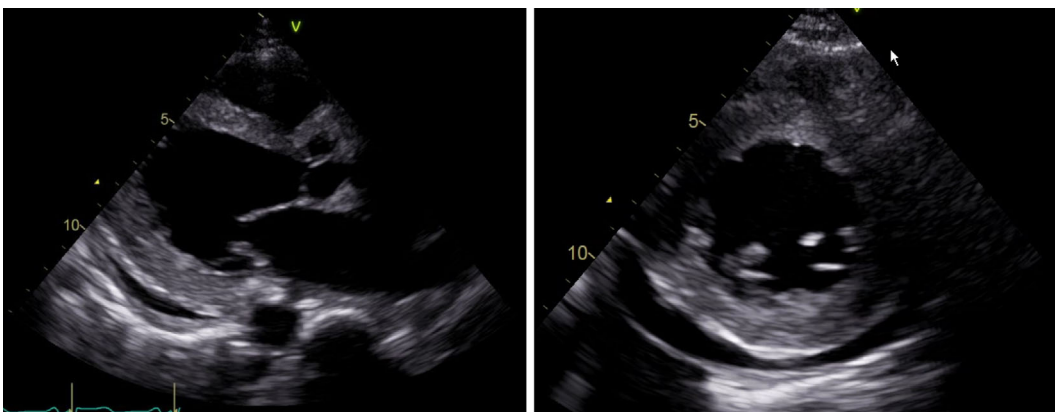


Figure 2. Echocardiography findings on admission. Echocardiography demonstrated a severely reduced left ventricular (LV) ejection fraction (30%), LV hypertrophy (interventricular septum thickness, 12 mm; posterior LV wall thickness, 13 mm) without chamber dilatation (diastolic diameter, 55 mm), pericardial effusion, and a slightly elevated right heart load (tricuspid regurgitation pressure gradient, 35 mmHg) without right ventricular dilatation. LV end-diastolic diameter, 49 mm; LV end-systolic diameter, 42 mm; interventricular septum thickness, 12 mm; posterior wall thickness, 13 mm; ejection fraction, 30%.

congestion. Left-axis deviation and left atrial load were observed on a 12-lead electrocardiogram (Fig. 1). Echocardiography demonstrated severely reduced left ventricular (LV) ejection fraction (30%), LV hypertrophy (interventricular septum thickness, 12 mm; posterior LV wall thickness, 13 mm) without chamber dilatation (diastolic diameter, 55 mm), pericardial effusion, and slightly elevated right heart load (tricuspid regurgitation pressure gradient, 35 mmHg) without right ventricular dilatation (Fig. 2).

A blood examination on admission revealed elevated N-terminal pro-brain natriuretic peptide (5,577 pg/mL), creatine kinase (549 U/L), creatine kinase myocardial band (21 U/L), and high-sensitive troponin T (0.213 ng/mL) (Table). Based on these findings, we diagnosed her with cardiomyopathy from unknown origin complicating cardiogenic shock. Coronary angiography was performed to rule out acute coronary syndrome, and no stenotic or occlusive lesion was observed.

The patient's hemodynamics did not improve despite the

administration of dobutamine (max 4.0 $\mu\text{g}/\text{kg}/\text{min}$). We introduced respiratory support with mechanical ventilation and deployed a circulatory support device (Impella[®]; Abiomed, Danvers, USA) because the right heart function was considered to be maintained based on the results of right heart catheterization (pulmonary artery pressure, 50/26 mmHg; and pulmonary artery pulsatility index, 1.5). We selected the Impella 2.5[®] because of her small physique. The mechanical assistance slightly improved her blood pressure (90/60 mmHg to 110/70 mmHg) and respiratory condition. However, an elevated blood lactate level suggested persistent circulatory failure. Enhanced computed tomography (CT) was performed in response to liver dysfunction (total bilirubin, 2.53 mg/dL; aspartate transaminase, 2,426 IU/L; alanine transaminase, 1,929 IU/L; alkaline phosphatase, 471 IU/L) (Table) and intestinal dilation observed on an abdominal radiograph.

CT showed a congested liver indicated by hepatomegaly and dilatation of hepatic vein, and markedly dilated colon

Table. Laboratory Analysis on Admission.

Arterial blood gas (room air)		Blood coagulation			
pH	7.38	PT-INR	2.78	γ -GT	78 U/L
PaCO ₂	24.1 mmHg	APTT	33.1 s	Na	135 mEq/L
PaO ₂	107 mmHg	D-dimer	23.4 μ g/mL	K	4.3 mEq/L
HCO ₃ ⁻	13.9 mEq/L	Biochemistry			
Base excess	-9.3 mEq/L	TP	6.3 g/dL	Cl	102 mEq/L
Lactate	7.1 mmol/L	Alb	3.7 g/dL	BUN	36.3 mg/dL
Glucose	404 mg/dL	T-Bil	2.53 mg/dL	Cre	0.52 mg/dL
Hematology		AST	2,426 U/L	CRP	0.52 mg/dL
WBC	9,400 / μ L	ALT	1,929 U/L	NT-proBNP	5,577 pg/mL
RBC	397 / μ L	LDH	3,299 U/L	Troponin T	0.213 ng/mL
Hb	12.2 g/dL	CK	549 U/L		
Ht	37.5 %	CKMb	21 U/L		
Plt	10.8 \times 10 ⁴ / μ L	ALP	471 U/L		

WBC: white blood cell, RBC: red blood cell, Hb: hemoglobin, Plt: platelet, PT-INR: prothrombin time-international normalized ratio, APTT: activated partial thromboplastin time, TP: total protein, Alb: Albumin, T-Bil: total-bilirubin, AST: aspartate transaminase, ALT: alanine transaminase, LDH: lactate dehydrogenase, CK: creatine kinase, CKMb: creatinine kinase myocardial band, ALP: alkaline phosphatase, γ -GT: γ -glutamyltransferase, BUN: blood urea nitrogen, Cre: creatinine, CRP: C-reactive protein, NT-pro BNP: N-terminal pro-brain natriuretic peptide

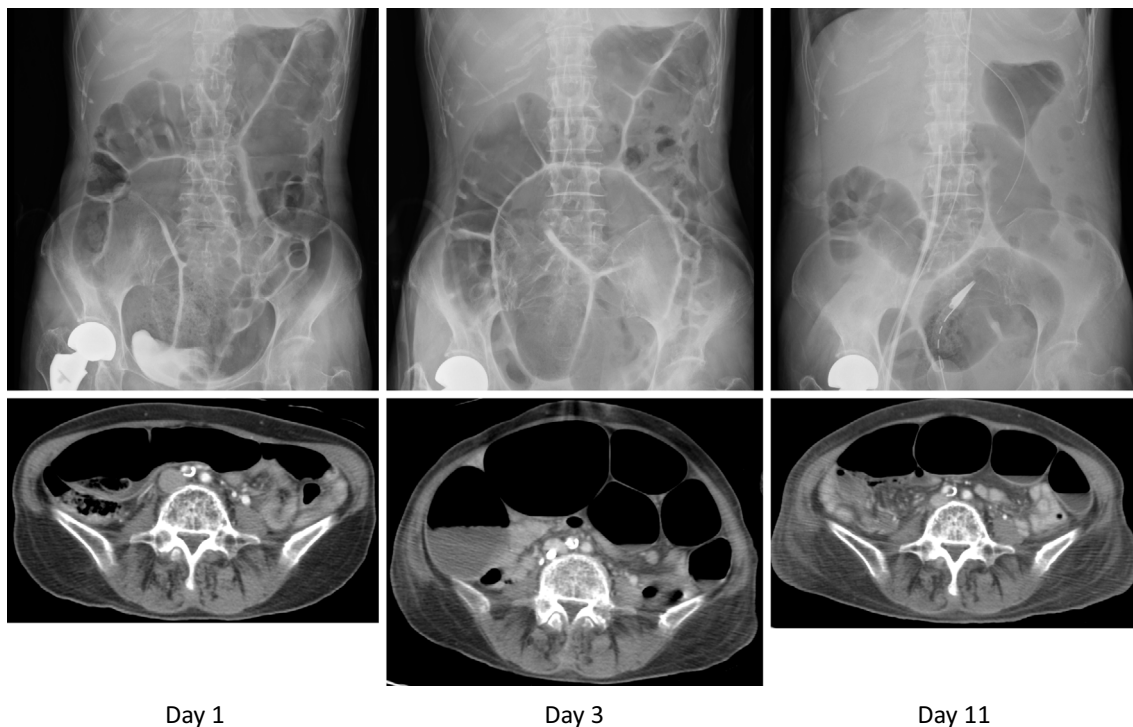


Figure 3. Abdominal radiograph and computed tomography image during the clinical course. Both images show dilatation of the colon on day 1, which was aggravated on day 3. After the insertion of a colorectal tube, dilation of the colon had improved by day 11. Obstructive lesions of the colon were not found on abdominal computed tomography.

without organic occlusion (Fig. 3). Furthermore, the intra-abdominal pressure increased to 40 mmHg, as measured by intra-bladder pressure. Her renal function did not decrease during the clinical course.

At this point, she had developed abdominal compartment syndrome due to CIPO, and an elevated intra-abdominal pressure restricted venous return. We considered that the

combination of severe LV dysfunction and reduced venous return induced by abdominal compartment syndrome caused the circulatory collapse. A colorectal tube was inserted into the colon through the rectum to reduce the intra-abdominal pressure.

With the decrease in intra-abdominal pressure from 40 to 12 mmHg at 3 hours after the insertion of the colorectal

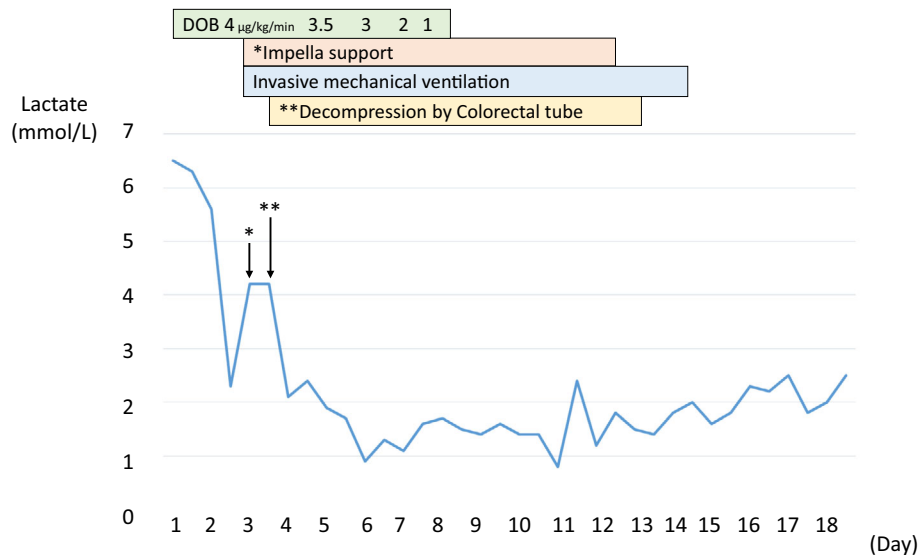


Figure 4. The clinical course of the patient. On day 3, the Impella 2.5[®] device was introduced under intubation and maintained until day 11. The lactate level decreased after colorectal tube insertion. The patient was extubated on day 13.

tube, the cardiac index increased from 1.8 L/min/m² to 2.1 L/min/m². The mean pulmonary capillary wedge pressure decreased from 36 mmHg to 13 mmHg, and the mixed venous oxygen saturation increased from 48% to 60%. Colon dilatation observed on abdominal radiography and CT improved gradually (Fig. 3). The blood lactic acid level decreased after the insertion of the colorectal tube. Impella 2.5[®] was carefully weaned because of the extremely low cardiac function. Finally, the patient was successfully withdrawn from the Impella 2.5[®] device on day 10 and extubated on day 13 (Fig. 4).

We ultimately diagnosed her with mitochondrial disease based on LV hypertrophy, a high level of lactic acid in the blood and cerebrospinal fluid, and a 3,243 A>G mutation in *MT-TL1* detected from a blood sample. Since there was no stroke-like episode, we did not diagnose mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes syndrome. Informed consent for a genetic analysis and the publication of the present case report was obtained from the patient and her family.

Discussion

We herein report a case of mitochondrial disease with both cardiac and gastrointestinal involvement resulting in hemodynamic collapse. We considered that the combination of cardiac dysfunction and reduced venous return, induced by abdominal compartment syndrome, caused circulatory failure. Treatments of both cardiac dysfunction and abdominal compartment syndrome were thought to be effective: a circulatory support device (Impella 2.5[®]) increased cardiac output and insertion of the colorectal tube reduced intra-abdominal pressure resulting in the recovery of venous return. In the clinical course, we utilized catecholamine and a circulatory support device before inserting the colorectal

tube, as we initially assumed that cardiac dysfunction was the only reason for circulatory failure. The Impella[®] device can properly augment cardiac output under sufficient LV preload. Thus, a reduction in the intra-abdominal pressure to increase the cardiac preload was required for the effective operation of the device. However, whether or not the reduction in intra-abdominal pressure alone was sufficient to recover circulatory failure and whether the high lactate value in this patient indicated circulatory failure (the lactate value in a patient with mitochondrial disease is usually high) was still unclear.

LV hypertrophy and reduced cardiac dysfunction were documented in the present case of mitochondrial disease. Although 20-40% of mitochondrial diseases have been reported to be complicated cardiomyopathies, the diagnosis of mitochondrial cardiomyopathy is often overlooked (6). In contrast, the frequency of abdominal compartment syndrome in patients with mitochondrial syndrome has not been reported. Mitochondrial cardiomyopathy produces various types of cardiomyopathy, such as hypertrophic, dilated, or restrictive cardiomyopathies. Although an endomyocardial biopsy for the differentiation of secondary cardiomyopathy, such as amyloidosis, was not performed, we concluded that the heart failure was due to mitochondrial cardiomyopathy based on the evidence with a diagnosis of mitochondrial disease, cardiac ultrasound findings, clinical course (e.g., no history of hypertension), and lack of any specific family history of dilated or hypertrophic cardiomyopathy. The hypertrophic type is the most common cardiomyopathy, and in the clinical course, it often shifts to the dilated phase with LV systolic dysfunction. The next-most frequent type is dilated cardiomyopathy. The restrictive type is rare and leads to a poorer prognosis than other types (7). For any type of cardiomyopathy, heart failure complications, severe arrhythmia (including ventricular arrhythmia), sick sinus syndrome,

and complete atrioventricular block worsen the prognosis (7).

Mitochondrial disease in this patient involved the gastrointestinal tract to the extent that she developed CIPO (8). CIPO is a severe functional digestive syndrome characterized by a disturbance in gastrointestinal motility (9, 10). In patients with mitochondrial disease, deficiency of fatty acid cyclooxygenase is thought to diminish the peristaltic motion of the gastrointestinal tract (11). Furthermore, a colon dilated by CIPO can cause physical compression in the abdomen and consequently increase the intra-abdominal pressure. When the intra-abdominal pressure exceeds 20 mmHg, it potentially causes the failure of several organs, producing respiratory and renal failure, circulatory insufficiency, and intestinal ischemia (12, 13). This clinical condition is defined as abdominal compartment syndrome. Furthermore, the low cardiac output due to mitochondrial cardiomyopathy progression may have led to a decrease in intestinal blood flow and contributed to the exacerbation of abdominal compartment syndrome in this case.

In conclusion, a combination of cardiac dysfunction and abdominal compartment syndrome caused hemodynamic collapse in a patient with mitochondrial disease. Mitochondrial disease can be associated with CIPO. However, abdominal compartment syndrome and hemodynamic collapse caused by intestinal dysfunction with mitochondrial disease has been scarcely reported.

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

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