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【 CASE REPORT 】

Transient Left Ventricular Contractile Dysfunction during the Treatment of Rhabdomyolysis: A Case Report and Literature Review

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Abstract:
Transient left ventricular contractile dysfunction (TLVCD) is often observed as a result of stress-related cardiomyopathy; however, recent reports suggest that rhabdomyolysis and eating disorders can also induce the development of TLVCD. We report a 52-year-old malnourished man who developed acute heart failure on day 4 of treatment for rhabdomyolysis. Transthoracic echocardiogram revealed severe hypokinesis at the apical and mid-ventricular segments, except for the basal segments of the left ventricular wall, which recovered within one week. We discuss the pathogenesis of TLVCD with sympathetic nerve activation in association with rhabdomyolysis or refeeding syndrome.

Key words: echocardiography, refeeding syndrome, cardiomyopathy

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Introduction

The pathogenesis of transient left ventricular contractile dysfunction (TLVCD) remains uncertain. Acute emotional or physical stress is suggested to cause TLVCD, with the possible involvement of sympathetic nerve activation on coronary microvessel spasms (1). TLVCD is a synonym of "ampulla (Takotsubo) cardiomyopathy", as the left ventricular (LV) shape mimics an octopus pod, showing abnormal left ventricular wall motion, typically at the apical and/or mid-ventricle walls, except for the basal segments. Recent reports have shown that a number of medical conditions are also associated with the development of TLVCD (2, 3). Furthermore, anorexia nervosa in eating disorders leads to TLVCD in patients with severe hypoglycemia (4-7).

We herein report a malnourished man who developed TLVCD during the treatment of rhabdomyolysis. Our case raises awareness that a predisposed electrolyte imbalance and refeeding after a long period of malnutrition may be involved in the pathophysiology of TLVCD.

Case Report

A 52-year-old Japanese man with a height of 172 cm and weight of 51.4 kg (body mass index 17.5 kg/m^2) was admitted to our emergency room due to a disturbance of consciousness. He had abused alcohol and had frequent diarrhea for two weeks, and he had not eaten anything for at least three days before admission. He had never been prescribed any sort of medications. His blood pressure was 117/81 mmHg, pulse rate 100 beats/min and regular, respiratory rate 30 breaths/min, and body temperature 37.7°C. A physical examination revealed a Glasgow coma scale score of 14 (E4 V4M6), but there were no apparent signs of heart failure or focal neurological deficits except for muscular grasping pain. As shown in (Table 1), blood testing revealed a glucose level of 168 mg/dL and increased aspartate transaminase and alanine transaminase levels of 247 and 134 U/L, respectively, but decreased ion concentrations of potassium (1.1 mmol/L; normal range 3.6-4.8), phosphate (2.0 mg/dL; normal range 2.7-4.6), magnesium (1.4 mg/dL; nor-

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Table 1. Laboratory Data on Admission.

White blood cell	12.5 $\times 10^3$/uL
Red blood cell	3.3 $\times 10^6$/uL
Hemoglobin	12.1 g/dL
Hematocrit	31.9 %
Platelet	280 $\times 10^3$/uL
Total protein	5.30 g/dL
Albumin	2.87 g/dL
Urea nitrogen	10.0 mg/dL
Creatinine	0.68 mg/dL
Total bilirubin	3.7 mg/dL
Direct bilirubin	1.7 mg/dL
Glucose	168 mg/dL
Sodium	139 mmol/L
Potassium	1.1 mmol/L
Chloride	79 mmol/L
Calcium	7.5 mg/dL
Magnesium	1.4 mg/dL
Phosphate	2.0 mg/dL
AST	247 U/L
ALT	134 U/L
LD	770 U/L
ALP	185 U/L
ChE	165 U/L
Creatine kinase	11,064 U/L
CK-MB	28 IU/L
Amylase	72 U/L
Folic acid	1.6 ng/mL
Aldosterone	6.1 ng/dL
ACTH	62.8 pg/mL
Cortisol	19.8 ug/dL
BNP	47.3 pg/mL
C-reactive protein	1.55 mg/dL

AST: aspartate transaminase, ALT: alanine transaminase, LD: lactate dehydrogenase, ALP: alkaline phosphatase, ChE: cholinesterase, ACTH: adrenocorticotropic hormone, BNP: brain natriuretic peptide

mal range 1.8-2.3), and albumin-corrected calcium (8.63 mg/dL; normal range 8.8-10.1). Blood testing also showed an elevated creatine kinase level (11,064 U/L; normal range 59-248) with 28 IU/L for the MB isoform (creatine isozyme BB, 0%; MB, 0%; MM 100%), and metabolic alkalosis (pH 7.62, carbon dioxide partial pressure (pCO_2) 46.5 mmHg, HCO_3^- 47.7 mmol/L). Chest X-ray showed a 47% cardiothoracic ratio without pulmonary congestion (Fig. 1A), and a 12-lead surface electrocardiogram demonstrated a sinus rhythm at 100 beats/min and prolongation of the corrected QT interval (654 ms) without ST elevation (Fig. 2A). To prevent refeeding syndrome, electrolytes, minerals and vitamins were corrected intravenously with frequent monitoring, and he was started on 300 kcal/day of enteral alimentation (Fig. 3).

On day 4 after admission, he complained of shortness of breath after drinking a large amount of water, and chest X-ray revealed bilateral pulmonary congestion (Fig. 1B). A 12-lead electrocardiogram revealed a prolongation of the corrected QT interval (626 ms) and T-wave symmetrical inversion at the precordial leads $V_{2\text{-}4}$ (Fig. 2B). Blood testing showed re-elevation of the creatine kinase level (14,123 U/L) accompanied by increased MB isoform (60 IU/L) and troponin-T levels (0.1 ng/mL; normal range <0.02). In addition, the brain natriuretic peptide level had elevated from 47.3 pg/mL on the day of admission to 361 pg/mL, but the magnesium (5.1 mg/dL) and potassium (4.8 mmol/L) ions were corrected to the normal ranges. Transthoracic echocardiogram revealed severe hypokinesis of the apical and midventricular segments, except for the basal segments of the LV wall (ejection fraction of 35%) (Fig. 4A, B). Ten milligrams of furosemide was administered intravenously, leading to relief of his symptoms. The patient refused to undergo coronary angiography. Thallium-201 myocardial scintigraphy performed on day 7 suggested a preserved perfusion, but ^{123}I-metaiodobenzylguanidine scintigraphy showed a 34% increased washout rate. Follow-up chest X-ray showed improved pulmonary congestion on day 8 (Fig. 1C), and a trend toward improvement in the T-wave inversion at the precordial leads was noted on his electrocardiogram on day 12 (Fig. 2C). Transthoracic echocardiogram performed on day 12 revealed a dramatic improvement in the LV systolic function (ejection fraction of 55%) (Fig. 4C, D). He was transferred to the rehabilitation hospital 15 days after admission.

Discussion

In the present case, we posited three hypotheses regarding the cause of TLVCD: [1] rhabdomyolysis, [2] refeeding syndrome, and [3] coronary multivessel vasospasm.

The cause of rhabdomyolysis was initially presumed to be hypokalemia and hypophosphatemia due to a shortage of food intake, chronic diarrhea, or alcohol abuse (8). The patient exhibited metabolic alkalosis, and his pCO_2 level remained high despite tachypnea. pCO_2 increases at 0.6-0.7 mmHg per 1-mmol/L increase in HCO_3^-, and the pCO_2 level was expected to be 55-64 mmHg (normal range 42-50 mmHg) under 47.7 mmol/L of HCO_3^- (normal range 23-27 mmol/L) in venous blood. We speculate that the tachypnea and pCO_2 value of 46.5 mmHg were a result of compensation. Several reports have described the relationship between rhabdomyolysis/myopathy and TLVCD (Table 2) (9-15). We did not assess the echocardiogram on the admission day, but the patient did not show any physical signs, chest X-ray findings, or brain natriuretic peptide levels suggestive of heart failure, despite severe hypokalemia and marked elevation of creatine kinase. This implies that rhabdomyolysis is unlikely to have played a major role in the development of TLVCD in this case.

The LV ejection fraction is usually maintained within normal limits in patients with anorexia nervosa (16); however, anorexic patients are susceptible to TLVCD if they have severe hypoglycemia on the day of admission (4-6). An exces-

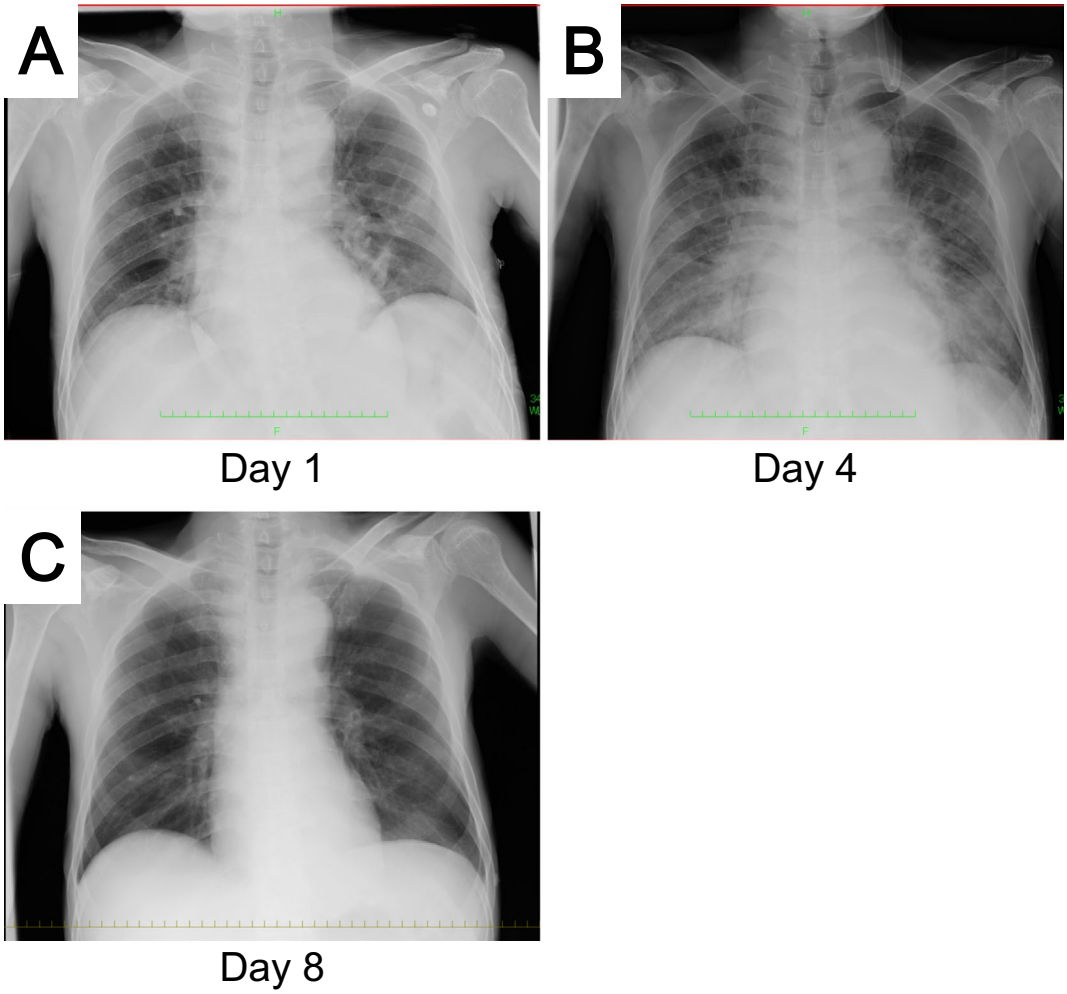

Figure 1. **Chest X-ray on the day of admission (A) and days 4 (B) and 8 (C) after admission.**

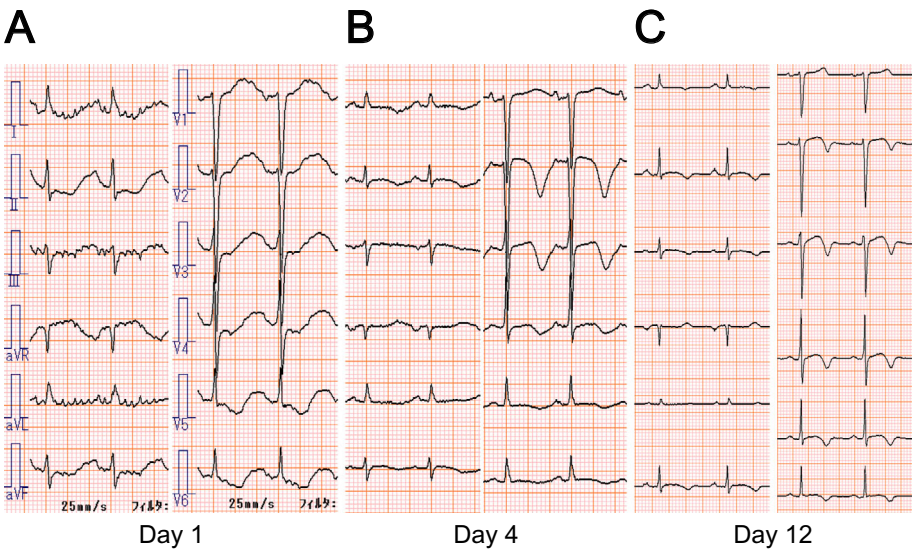

Figure 2. **Surface electrocardiogram on the day of admission (A) and days 4 (B) and 12 (C) after admission. The corrected QT interval was calculated using Bazett's formula.**

sive catecholamine release against hypoglycemia is postulated to result in coronary microvessel spasms. Artificial feeding (either enteral or parenteral) in malnourished/cachectic patients can lead to multisystem organ failure due to a shortage of phosphate, potassium, magnesium, calcium, and vitamins, known as "refeeding syndrome" (17, 18). This failure usually occurs 2-5 days after the beginning of nutritional repletion. Cardiovascular failure includes sudden

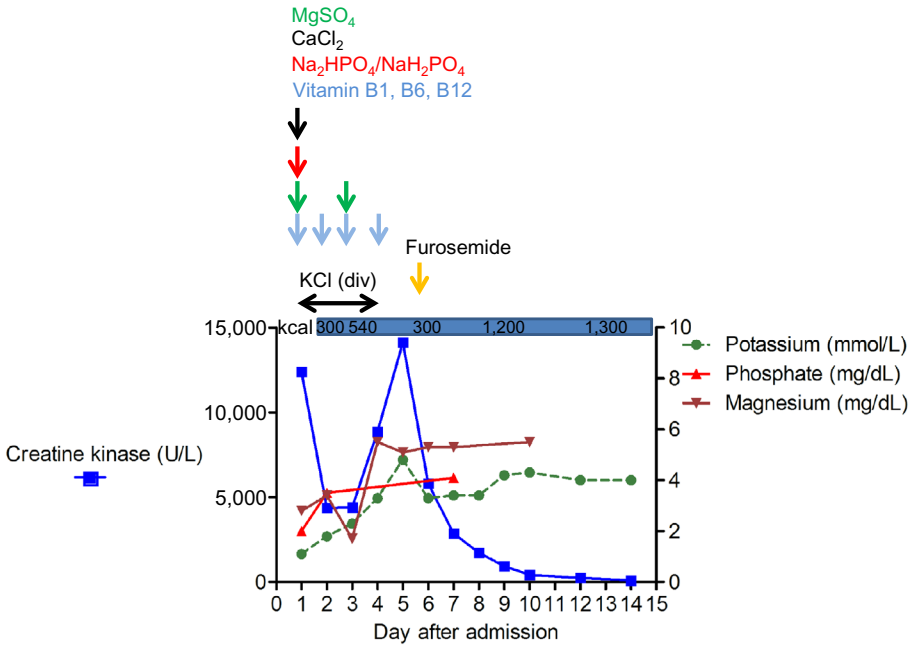

Figure 3. **Laboratory data and treatment after admission.**

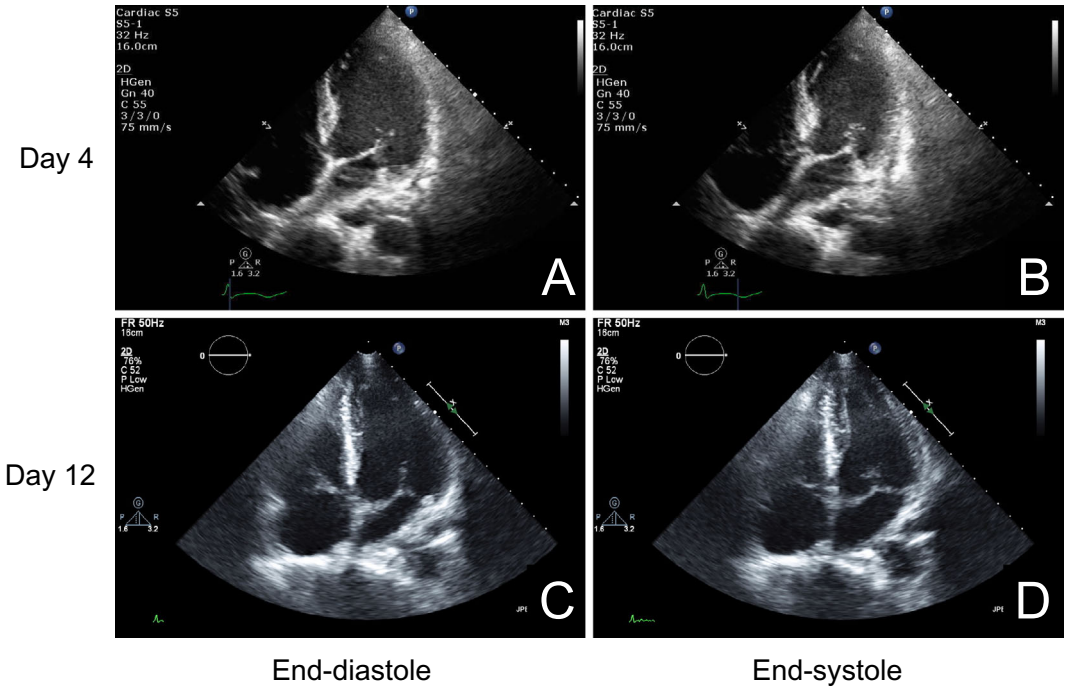

Figure 4. **Apical four-chamber views of transthoracic echocardiography on day 4 (A and B) and day 12 (C and D) after admission. A and C, end-diastole; B and D, end-systole.**

death, arrhythmias, hypertension, and congestive heart failure. Consistent with these previous findings, heart failure occurred four days after starting alimentation in this case, accompanied by re-elevation of the creatinine kinase levels. This was comparable to TLVCD associated with rhabdomyolysis, which usually exhibits left ventricular dysfunction on the day of admission (Table 2). The LV morphology mimicked a Takotsubo-like configuration, which is rarely recognized as a form of acute heart failure in this setting (19, 20) (Table 3). Of additional note, hypoglycemia appears to be a trigger for the development of TLVCD in these cases.

The mechanisms underlying the development of TLVCD in the present patient remain unclear. We acknowledge that the patient did not show hypoglycemia as observed in previous reports (21, 22). Similarly debatable is whether or not hypophosphatemia itself causes left ventricular dysfunction (8). Our case supports the notion that exaggerated sympathetic nerve activity may be involved in accelerating the form of Takotsubo-like configuration. We speculate that the depletion of myocardial energy production by a series of

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Table 2. **Takotsubo Cardiomyopathy Complicating Rhabdomyolysis/Myopathy.**

Reference	Age	Sex	Symptom (s)		Possible trigger (s)	Manifestation of LV dysfunction	CPK max (U/L)	Creatinine (mg/dL)	Phosphate (mg/dL)	Potassium (mmol/L)	Glucose (mg/dL)	LV wall motion	LVEF (%) at onset	LVEF (%) at recovery
[9]	73	M	general fatigue	dysbasia	rouvastatin	on the day of admission	16,538	1.4	nd	3.4	226	apical ballooning	52	65
[10]	61	F	retrosternal chest pain diaphoresis lighteaedness	shortness of breath fever	inflammatory myopathy	on the day of admission	31,241	nd	nd	nd	nd	apical ballooning	28	63
[11]	58	F	burn		burn injury emotional and physical stress	on the day of admission	nd	nd	nd	nd	nd	apical ballooning	5 to 10	55 to 70
[12]	39	M	collapse		heat stroke	on the day of admission	4,517	2.7	nd	nd	nd	apical ballooning	40	65
[13]	78	M	fall		anxiety	on the day of admission	5,342	nd	nd	nd	nd	apical ballooning	15	45
[14]	55	F	general fatigue weakness of extremities	vomiting	nd	on the day of admission	7972	nd	nd	nd	nd	apical ballooning	41	nd
[15]	67	F	chest discomfort		rouvastatin fenofibrate	on the day of admission	19,000	3.6	nd	nd	nd	apical ballooning	25	47
Our case	52	M	shortness of breath		malnutrition alchohol abuse	4th day of admission	14,123	0.68	2.0	1.1	168	apical ballooning	35	55

We searched the reports in PubMed using the following key words; "takotsubo", "myopathy", "rhabdomyolysis", and "cardiomyopathy". nd indicates "not described", LVEF, left ventricular ejection fraction assessed by transthoracic echocardiogram or magnetic resonance image. "Apical ballooning" indicates hypokinesis to akinesis (aneurymal apex) of the left ventricle, except in the basal region.

Table 3. Takotsubo Cardiomyopathy Complicating Refeeding Syndrome.

Reference	Age	Sex	Symptom (s)	Possible trigger (s)	Manifestation of LV dysfunction	CPK max (U/L)	Creatinine (mg/dL)	Phosphate (mg/dL)	Potassium (mmol/L)	Glucose (mg/dL)	LV wall motion	LVEF (%) at onset	LVEF (%) at recovery
[19]	54	F	impaired consciousness palpitation malnutrition	urge to ingest a coppius dinner	1 day after coppius dinner	80	nd	2.2	2.7	19	Inverted apical ballooning	25	nd
[20]	18	F	apetite loss anorexia nervosa	enteral nutrition	2nd day of admission	nd	nd	6.2	4.7	21	apical ballooning	nd	nd
[20]	58	F	drowsy anemia	administration of a vitamin with saline	4th day of admission	nd	nd	2.9	3.4	19	apical ballooning	nd	nd

We searched the reports in PubMed using the following key words; "takotsubo" , "myopathy" , "refeeding", and "cardiomyopathy". nd indicates "not described", LVEF, left ventricular ejection fraction assessed by transthoracic echocardiogram. "Apical ballooning" indicates hypokinesis to akinesis (aneurymal apex) of the left ventricle, except in the basal region. Inverted apical balooning indicates dyskinesia of basal and mid-ventricular segment, with hyperkinesia of the left ventricular apex.

electrolyte derangements as well as food intake after long-term malnutrition may have resulted in the reduced left ventricular contractile force, leading to overt heart failure following excessive water intake. We did not perform coronary angiography; therefore, we were unable to distinguish the multivessel coronary spasm from ampulla (Takotsubo) cardiomyopathy based solely on scintigraphy with ^{123}I-metaiodobenzylguanidine (23, 24). Under the National Institute for Health and Care Excellence (NICE) guidelines, our patient was identified as being at high risk of developing refeeding syndrome given his chronic alcoholism, low nutritional intake for more than 10 days, and low levels of serum potassium, phosphate, and magnesium before feeding. Accordingly, the patient was administered vitamins and minerals, phosphate, potassium, and magnesium intravenously, followed by low-calorie enteral alimentation, and he eventually recovered.

In conclusion, the present case reminds us that TLVCD can be associated with rhabdomyolysis or refeeding syndrome, and meticulous care may help prevent the development of life-threatening events in such patients.

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

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