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/m²) 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 V4 M6), 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.

| Test                        | Value          |
|-----------------------------|----------------|
| White blood cell            | 12.5 x10^9/μL  |
| Red blood cell              | 3.3 x10^9/μL   |
| Hemoglobin                  | 12.1 g/dL      |
| Hematocrit                  | 31.9%          |
| Platelet                    | 280 x10^9/μL   |
| Total protein               | 5.50 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      |
| Phosphatase                 | 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 mg/mL      |
| Aldosterone                 | 6.1 mg/dL      |
| ACTH                        | 62.8 pg/mL     |
| Cortisol                    | 19.8 ug/mL     |
| 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

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 pCO2 level remained high despite tachypnea. pCO2 increases at 0.6-0.7 mmHg per 1-mmol/L increase in HCO3- (normal range 23-27 mmol/L). In the present case, the patient refused to undergo coronary angiography. Thallium-201 myocardial scintigraphy performed on day 7 suggested a preserved perfusion, but 123I-metaiodobenzylguanidine scintigraphy showed a 34% increased washout rate. Follow-up chest X-ray revealed 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

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 asymmetrical inversion at the precordial leads V1-V4 (Fig. 2B). Blood testing showed re-elevation of the creatine kinase level (14,123 U/L) accompanied by increased MB isofrom (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 123I-metaiodobenzylguanidine scintigraphy showed a 34% increased washout rate. Follow-up chest X-ray revealed 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.

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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.

Dissipative 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
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
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 | dysasia             | rouvastatin                     | on the day of admission | 16,538           | 1.4              | nd                | 3.4               | 226            | apical ballooning | 52              | 65               |
| [10]      | 61  | F   | retrosternal chest pain | 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 alcohol 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 keywords: "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 (aneurysmal apex) of the left ventricle, except in the basal region.
We searched the literature for the following key words: “takotsubo”, “miyopathies”, “refeeding”, and “cardiomyopathy”, and identified cases in which the left ventricle balloonled or showed akinesis. Apical balloonning indicates dyssynergia of the left ventricular apex. Inverted apical balloonning indicates dysfunction of the basal and mid-left ventricular segment, with hypokinesis of the left ventricular apex.

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

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| Reference | Takotsubo Cardiomyopathy | Complicating Refeeding Syndrome. |
|-----------|--------------------------|----------------------------------|
| [19]      | F                        | 54                               |
| [20]      | F                        | 18                               |
| [20]      | F                        | 58                               |

**Table 3.** Takotsubo Cardiomyopathy Complicating Refeeding Syndrome.
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