PATIENT - CENTRED FOCUSED REVIEW

Raise vigilance against refractory distributive shock due to severe wet beriberi

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ABSTRACT

Differentiating the type and cause of shock is crucial for intensive care. The rapid aggravation of lactic acidosis in patients often indicates a severe impairment of oxygen uptake in tissues. Herein, we presented a rare case of refractory distributive shock with severe wet beriberi. A 40-year-old male was admitted to the emergency department (ED) with recurrent chest tightness and lower extremity edema. The condition of the patient continued to deteriorate after symptomatic treatments. After several turnovers, the medical history of the patient was requested again and finally obtained. Our emergency management team hypothesized that the thiamine-deficient diet caused an aerobic metabolism disorder in the patient. Overall, we aimed to alert clinicians to unusual causes of distributive shock and further discussed the application of thiamine supplementary therapy in critical care.

Keywords: Distributive shock; Lactic acidosis; Wet beriberi; Thiamine; Hemodynamic disturbance; Emergency management.
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INTRODUCTION

Thiamine deficiency and subsequent severe metabolic acidosis can contribute to the development of complications in intensive care units (ICUs).[1] Wet beriberi (soshin beriberi) is a severe situation that can cause hemodynamic disturbance and refractory distribution shock.[2] Thus, clinicians should pay more attention to life-threatening diseases caused by metabolite deficiency. Herein, we presented a rare case of refractory distributive shock with severe wet beriberi. Further, we discussed thiamine supplementary therapy in critical care.

CASE PRESENTATION

A 40-year-old male was admitted to the emergency department (ED) with recurrent chest tightness and lower extremity edema for one month, which have been aggravated for three days. Heart failure was diagnosed at a local hospital, and a diuretic drug was given for symptomatic treatment. He was admitted to the cardiac care unit (CCU) due to “heart failure and cardiogenic shock”. The electrocardiogram (ECG) suggested sinus tachycardia, and no significant abnormalities were observed in the ST-T segment. The blood routine examination showed that the white blood cell (WBC) count was 11.9×10^9 cells/L, the neuter granule percentage was 72.2%, and the levels of procalcitonin and C-reactive protein (CRP) were normal. The blood gas analysis (FiO_2 29%) presented the following results: pH: 7.47; PCO_2: 24 mmHg; PO_2: 109 mmHg; BE: -5.1 mmol/L; cLac: 4.3 mmol/L. The myocardial enzymes were normal, the NT-pro BNP was 170 pg/mL, and the TnI was 0.11 ng/mL. Finally, an emergency coronary angiography was performed, and no clear abnormalities were detected. Thus, the possibility of ”viral myocarditis" was considered. Even after positive inotropic support and diuretic treatments, the tachypnea continued to aggravate, and the urine volume progressively decreased. Then, the physical examination showed a pulse of 139/min, respirations of 39/min, and blood pressure (BP) of 110/66 mmHg. The subsequent blood gas analysis (FiO_2 29%) showed a pH of 7.40, CO_2 of 12.4 mmHg, BE of -15.7 mmol/L, and cLac of 13.1mmol/L. According to the diagnostic criteria (infection, host response, and organ dysfunction) of sepsis 3.0[3] and the patient’s blood routine examination, procalcitonin, and CRP, no signs of infection were detected. Additionally, no abnormal

findings were observed in the chest computed tomography (CT), and the blood culture was negative. The SOFA score was performed after admission to the CCU (SOFA < 2), and the possibility of sepsis was ruled out.

Considering the continuous worsening of the shock, the patient was transferred to the intensive care unit (ICU) for extracorporeal membrane oxygenation (ECMO) treatment. The body examination indicated pulse of 130/min, respirations of 42/min, BP of 74/41 mmHg, and apathy. The patient immediately received vasopressor, intubation, analgesia, sedation, muscle relaxation, acid correction, and hemofiltration. The central venous catheterization revealed a central venous pressure (CVP) of 9 mmHg (5-10 mmHg), CO_2 GAP of 0.9 mmHg (<6 mmHg), $ScvO_2$ of 90.7% (>70%), and cLac of 23 mmol/L (<1.6 mmol/L). The bedside ultrasound showed that the left ventricular ejection fraction (LVEF) was 50%, the width of the inferior vena cava was 2 cm and no variability. Combined with the blood gas results, we excluded cardiogenic shock, hypovolemic shock, and obstructive shock.

The pulse indicator continuous cardiac output (PICCO) revealed a CI of 3.5, GEDI of 463, ELWI of 8.7, GEF of 25%, SVRI of 478, and SVV of 8%. Hence, we considered the possibility of intractable distributed shock. After treatments with noradrenaline (3 ug/kg/min), terlipressin (1 mg/6 h), piperacillin-tazobactam (4.0 g q8h), continuous renal replacement therapy (CRRT), sedation, analgesia, and muscle relaxation, the blood gas analysis still showed a pH of 6.96, PCO_2 of 46.4 mmHg, PO_2 of 136 mmHg, cLac of 30 mmol/L, base excess (BE) of -21.6 mmol/L, GAP of 6.8 mmol/L, and SvO_2 87.3%. Thus, we concluded that the patient had rapidly progressive hemodynamic disturbance, with an oxygen utilization barrier, which could result in multiple organ dysfunction syndrome and death if not timely recognized and promptly treated. Even with all uncertainties, our emergency management team was committed to searching for the primary cause of the persistent hyperlactic disease and refractory distributed shock.

After several turnovers, we inquired about the patient's medical history from his family again and found that he drank about 250 mL of liquor every day supplemented by beer for more than 10 years, and rarely ate staple foods. Given the patient's persistent refractory shock, the lack of significant remission after treatment with norepinephrine (3 ug/kg/min) and terlipressin (1 mg/6 h), high lactic acidosis, $ScvO_2$ above 90%, right ventricular enlargement, lower extremity edema, chronic onset, and worsening outbreak, and alcoholism, we hypothesized that the patient was suffering from refractory distributed shock caused by severe wet beriberi. The patient was immediately treated with vitamin B1 (thiamine) (0.2 g im q12h), and vitamin C (1.5 g q6h). After five hours, the SvO_2 decreased to 79.1%, and, within a day, the lactic acid and $ScvO_2$ returned to normal levels (Fig. 1). The telivasopressin was discontinued and the norepinephrine was downregulated to 1.0 ug/kg/min. Then, the patient's consciousness gradually returned, and the urine volume returned to normal. Next, the intermittent blood purification was stopped. Finally, he was transferred to the department of cardiology and discharged with a full recovery.

DISCUSSION

Herein, we reported a rare case of refractory distribution shock with severe wet beriberi. During shock progression in patients, clinicians should increase their vigilance regarding the primary cause of the disease and search for targeted treatment. Shock syndromes include four distinct subtypes: hypovolemic, obstructive, cardiogenic, and distributive (*e.g.,* septic, anaphylactic, and neurogenic).[4] Distributive shock is caused by abnormal vasodilation or impaired oxygen uptake by tissues. In the present case, the levels of serum lactate reached

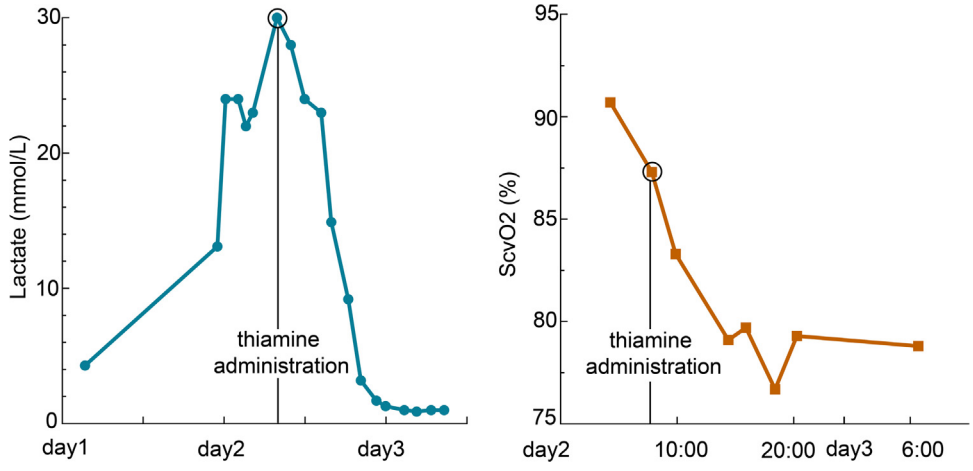

FIG. 1. Changes in the serum lactate and central venous saturation (ScvO2) over time. The patient was admitted to the emergency department (ED) at 3:23 on day 1. Note that both parameters rerecovered soon after the thiamine administration.

30 mmol/L in about 24 h, which suggested hypoxia and metabolic disorder of tissues. However, the average PO_2 level and abnormally high $ScvO_2$ indicated that an intrinsic metabolite deficiency might have led to a peripheral oxygen utilization barrier. This omission could have led to a poor iatrogenic clinical outcome.

The present case has dramatically changed our clinical practice in critical care. It also showed that the possibility of severe wet beriberi, a rapidly treatable hemodynamic disorder, needs to be considered in refractory distributed shock. Patients with severe wet beriberi are prone to thiamine deficiency, and metabolic resuscitation should be considered in the treatment of refractory shock. Clinicians should be alert to shock caused by intrinsic metabolite deficiency, and rapidly determine the type of shock as a prerequisite for emergency management. Additionally, the medical history and physical examination are essential for every physician to obtain meaningful information and correctly treat patients.

LESSONS FROM THE HEMODYNAMIC CRISIS CAUSED BY WET BERIBERI

Wet beriberi is a metabolic disease caused by vitamin B1 or thiamine deficiency, characterized by a history of alcoholism, unbalanced diet, cardiovascular damage, neurological involvement, and response to thiamine with clinical recovery.[5,6] Thiamine is an essential cofactor for pyruvate dehydrogenase, participating in oxidative energy metabolism. Under normal circumstances, it can be converted to thiamine pyrophosphate. As a cofactor of pyruvate dehydrogenase, thiamine pyrophosphate helps catalyze the oxidative decarboxylation of pyruvic acid to acetyl-CoA, which is the entry point of the citric acid cycle. Therefore, thiamine deficiency can lead to an insufficient citric acid cycle rate, and the levels of pyruvate and its metabolite, lactate, can rise.[5] Meanwhile, thiamine pyrophosphate is also a cofactor of transketolase, which participates in the pentose phosphate pathway.[7] (Fig. 2) Therefore, increased levels of serum lactate and severe metabolic acidosis are the basic elements of beriberi,[8] and can further contribute to ICU complications, including heart failure, shock, oxidative stress, delirium, critical care neuropathy, and gastrointestinal dysfunction.[1,9]

Furthermore, wet beriberi is commonly seen in patients with long-term alcoholism, digestive diseases, surgery, imprisonment, and under furosemide.[10] Being aware of the diet pattern in the patient's medical history is an essential clue for beriberi. Most wet beriberi patients also have causal factors. For example, a 17-year-old female was previously reported as severely hypotensive, with a high heart rate, and an absence of urine output. Her cardiogenic shock was associated with wet beriberi and the administration of thiamine led to a quick reversion. Her congenital jejunal atresia and the recent surgical duodenal–jejunal anastomosis due to intestinal sub-occlusion might be the causal factors.[11] Another case of beriberi with multi-organ failure presented a medical history of imprisonment, bodyweight loss (15 kg), and heavy alcohol abuse.[12]

The main cause of our current case was long-term alcohol abuse. However, why it progressed to such a severe shock and lactic acidosis remains unclear. The medical diagnosis deviation and repeated furosemide treatment for a possible "heart failure" also contributed to the deterioration. Hence, rapid determination of the shock type is essential for emergency management. Medical history inquiry and physical examination are essential skills for every physician to obtain meaningful information and correctly treat patients. Besides, the use

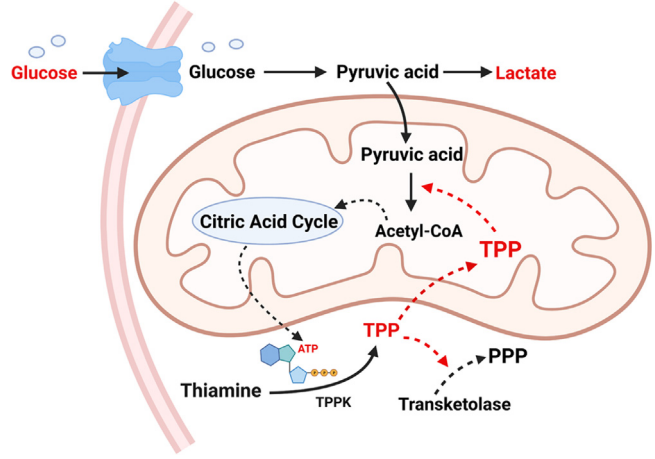

FIG. 2. Impacts of thiamine on cellular metabolic pathways. Thiamine is first converted to thiamine pyrophosphate by the thiamine pyrophosphokinase. Thiamine pyrophosphate is a cofactor of pyruvate dehydrogenase (oxidative decarboxylation of pyruvic acid to acetyl-CoA) and transketolase (a cytosolic enzyme that catalyzes the pentose phosphate pathway). The thiamine deficiency leads to increased levels of pyruvate and lactate. Solid arrows: direct change; Dotted arrows: indirect participation.

Abbreviations: TPP: thiamine pyrophosphate; ATP: adenosine-triphosphate; TPPK: thiamine pyrophosphokinase; PPP: pentose phosphate pathway.

of bedside ultrasound helped us to more rapidly identify the etiology.

The clinical diagnosis of beriberi includes cardiomegaly with normal sinus rhythm; dependent edema; signs of neuritis and/or pellagra; non-specific EKG changes; no other causes of heart disease; at least 3 months of thiamine-deficient diet. These abnormalities can be reversed by thiamine administration.[10] Moreover, hemodynamic data is necessary for diagnosis. Additionally, increases in the pulmonary wedge, pulmonary artery, and right atrial pressures have also been reported. The systemic blood pressure is low despite a marked increase in cardiac output, indicating decreased total peripheral resistance.[13,14] A high $ScvO_2$ might also serve as a predictor of thiamine deficiency in critically ill patients since impaired tissue oxygen extraction can lead to high $ScvO_2$. In the present case, the $ScvO_2$ returned to normal levels within 10 h after thiamine treatment.[15] However, in clinical practice, when lactic acidosis and hemodynamic disorders are confirmed and no other apparent etiology cause is probable, the diagnosis of beriberi should be considered as a cause of non-infection-induced distributed shock, and thiamine should be administered.[2,16]

THIAMINE SUPPLEMENTARY THERAPY IN CRITICALLY ILL PATIENTS

Thiamine has a more comprehensive application for shocks beyond beriberi. For example, a retrospective matched cohort study in 2018 compared 123 patients who received IV thiamine supplementation within 24 h of admission with 246 patients who did not receive thiamine. The thiamine treatment was associated with an improved likelihood of lactate clearance, and a reduction in the 28-day mortality.[17] Recently, Byerly et al. conducted a multicenter study with 146,687 patients from 186 hospitals to evaluate the effects of vitamin C and thiamine on ICU patients. Vitamin C and thiamine were independently associated with increased survival, and the administration of thiamine was associated with significantly increased lactate clearance.[18] Furthermore, thiamine deficiency can develop in critically ill patients secondary to the myriads of pathological states, such as inadequate nutrition, alcohol abuse, increased urinary excretion, acute metabolic stress, and sepsis.[9,19,20]

In the latest management guide for refractory vasodilatory shock, high dose thiamine is recommended as adjunctive therapy when the combination of vasopressor therapy is required. Additionally, thiamine administration (200 mg/12 h) can improve lactate clearance with minimal adverse effects.[21] However, a randomized, double-blind, placebo-controlled trial found that significant decreases in the lactate levels at 24 h and mortality between the thiamine and placebo groups were only identified in the subgroup of thiamine deficiency patients at baseline.[22] Therefore, with increasing studies focused on thiamine deficiency patients and adequate thiamine supplementary treatment, a more standard measurement procedure for thiamine in clinical samples is necessary and remains a challenge.[1]

CONCLUSIONS

The present case represented a typical example of refractory distribution shock with severe wet beriberi. The treatment with thiamine was efficient to bring a quick recovery to the patient. Thus, early differentiation and diagnosis are crucial. Finally, clinicians should be alert to shock caused by intrinsic metabolite deficiency and consider supplementary therapy in critical care.

AUTHORS CONTRIBUTIONS

W.X. conceived the case report and literature review; T.M. collected the clinical data; J.X. conducted the literature review; T.M. and J.X. wrote the paper.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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REFERENCES

1. **Collie JTB, Greaves RF, Jones OAH, et al.** Vitamin B1 in critically ill patients: needs and challenges. *Clin Chem Lab Med*. 2017;55(11):1652–1668. https://doi.org/10.1515/cclm-2017-0054.
2. **Kountchev J, Bijuklic K, Bellmann R, et al.** A patient with severe lactic acidosis and rapidly evolving multiple organ failure: a case of shoshin beri-beri. *Intensive Care Med*. 2005;31(7):1004. https://doi.org/10.1007/s00134-005-2648-7.
3. **Singer M, Deutschman CS, Seymour CW, et al.** The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA*. 2016;315(8):801–810. https://doi.org/10.1001/jama.2016.0287.
4. **Rodriguez R, Fernandez EM.** Role of angiotensin II in treatment of refractory distributive shock. *Am J Health-Syst Pharm: AJHP: Offic J Am Soc Health-Syst Pharmacists*. 2019;76(2):101–107. https://doi.org/10.1093/ajhp/zxy014.
5. **Seta T, Okuda K, Toyama T, et al.** Shoshin beriberi with severe metabolic acidosis. *South Med J*. 1981;74(9):1127–1130. https://doi.org/10.1097/00007611-198109000-00028.
6. **King JF, Easton R, Dunn M.** Acute pernicious beriberi heart disease. *Chest*. May 1972;61(5):512–514. https://doi.org/10.1378/chest.61.5.512.
7. **Depeint F, Bruce WR, Shangari N, et al.** Mitochondrial function and toxicity: role of the B vitamin family on mitochondrial energy metabolism. *Chem Biol Interact*. 2006;163(1-2):94–112. https://doi.org/10.1016/j.cbi.2006.04.014.
8. **Platt BS, Lu GD.** Studies on the metabolism of pyruvic acid in normal and vitamin B(1)-deficient states: the accumulation of pyruvic acid and other carbonyl compounds in beri-beri and the effect of vitamin B(1). *Biochem J*. 1939;33(10):1525–1537. https://doi.org/10.1042/bj0331525.
9. **Attaluri P, Castillo A, Edriss H, et al.** Thiamine deficiency: an important consideration in critically ill patients. *Am J Med Sci*. 2018;356(4):382–390. https://doi.org/10.1016/j.amjms.2018.06.015.
10. **Meurin P.** [Shoshin beriberi. A rapidly curable hemodynamic disaster]. *Presse Med*. 1996;25(24):1115–1118. Jul 6-13. Le shoshin béribéri. Une catastrophe hémodynamique rapidement curable.

11. **Cottini M, Ranucci M, Facciolo C, et al.** An unusual case of cardiogenic shock in which thiamine administration led to reversal of lactic acidosis and heart function recovery: Shoshin beriberi in an adolescent. *Int J Cardiol*. 2016;222:401–403. https://doi.org/10.1016/j.ijcard.2016.07.248.
12. **Lei Y, Zheng MH, Huang W, et al.** Wet beriberi with multiple organ failure remarkably reversed by thiamine administration: a case report and literature review. *Medicine (Baltimore)*. 2018;97(9):e0010. https://doi.org/10.1097/md.0000000000010010.
13. **Richard C, Fond B, Auzepy P.** Shoshin beriberi. *Lancet (London, England)*. 1982;2(8291):215. https://doi.org/10.1016/s0140-6736(82)91060-1.
14. **Richard C, Auzépy P.** Shoshin beriberi. *Intensive Care Med*. 1987;13(4):298. https://doi.org/10.1007/bf00265128.
15. **Numata G, Kodera S, Kiriyama H, et al.** Usefulness of central venous saturation as a predictor of thiamine deficiency in critically ill patients: a case report. *J Intensive Care*. 2017;5:61. https://doi.org/10.1186/s40560-017-0255-7.
16. **Oriot D, Wood C, Gottesman R, et al.** Severe lactic acidosis related to acute thiamine deficiency. *JPEN J Parenter Enteral Nutr*. 1991;15(1):105–109. https://doi.org/10.1177/0148607191015001105.
17. **Woolum JA, Abner EL, Kelly A, et al.** Effect of thiamine administration on lactate clearance and mortality in patients with septic shock. *Crit Care Med*. 2018;46(11):1747–1752. https://doi.org/10.1097/ccm.0000000000003311.
18. **Byerly S, Parreco JP, Soe-Lin H, et al.** Vitamin C and thiamine are associated with lower mortality in sepsis. *J Trauma Acute Care Surg*. 2020;89(1):111–117. https://doi.org/10.1097/ta.0000000000002613.
19. **Cruickshank AM, Telfer AB, Shenkin A.** Thiamine deficiency in the critically ill. *Intensive Care Med*. 1988;14(4):384–387. https://doi.org/10.1007/bf00262893.
20. **Donnino MW, Carney E, Cocchi MN, et al.** Thiamine deficiency in critically ill patients with sepsis. *J Crit Care*. 2010;25(4):576–581. https://doi.org/10.1016/j.jcrc.2010.03.003.
21. **Jentzer JC, Vallabhajosyula S, Khanna AK, et al.** Management of refractory vasodilatory shock. *Chest*. 2018;154(2):416–426. https://doi.org/10.1016/j.chest.2017.12.021.
22. **Donnino MW, Andersen LW, Chase M, et al.** Randomized, double-blind, placebo-controlled trial of thiamine as a metabolic resuscitator in septic shock: a pilot study. *Crit Care Med*. 2016;44(2):360–367. https://doi.org/10.1097/ccm.0000000000001572.

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