Shoshin beriberi in a patient with oral and cutaneous graft-versus-host disease

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Key words: bone marrow transplantation; cardiac beriberi; cutaneous graft-versus-host-disease; graft-versus-host disease; heart failure; hematopoietic cell transplantation; nutritional deficiencies; oral graft-versus-host disease; Shoshin beriberi; thiamin deficiency; thiamine deficiency; vitamin B1 deficiency; vitamin deficiency; wet beriberi.

INTRODUCTION

Thiamine (vitamin B1) deficiency affects multiple organ systems and may present with waxy edematous skin, vesicular oral eruptions, oral ulcerations, oral hyperesthesia, burning tongue, fatigue, nausea, vomiting, abdominal pain, anorexia, sensory or motor neuropathies, Korsakoff amnestic-confabulatory syndrome, Wernicke encephalopathy, or beriberi.[1-4] Shoshin beriberi is a fulminant form of cardiac beriberi that features rapidly progressive heart failure and distributive shock.[1] Hematopoietic cell transplant patients are at increased risk for nutritional deficiencies caused by graft-versus-host disease, comorbid renal dysfunction, and cytotoxic conditioning regimens.[5] We report a case of Shoshin beriberi identified during dermatologic evaluation of oral and cutaneous graft-versus-host disease.

CASE REPORT

A 68-year-old man with myelodysplastic syndrome underwent allogeneic hematopoietic cell transplant complicated by heart failure and acute tubular necrosis, leading to intensive care unit stay for 40 days. Echocardiogram showed severe biventricular dilatation with left ventricular ejection fraction of 19%. His heart failure was attributed to cyclosporine-induced acute kidney injury and iron-overload cardiomyopathy from repeated transfusions. However, magnetic resonance imaging revealed only mild iron deposition in his myocardium.

Five months later, the patient was hospitalized again for fulminant heart failure and acute kidney failure, despite receiving maximum-dose torsemide at home. Repeated echocardiogram showed a left ventricular ejection fraction of 9.4%. Lactate level was elevated, at 3.2 mmol/L (normal <2.0 mmol/L). He had scaly pink to purple plaques on his trunk and extremities (Fig 1) and lacy white plaques on his buccal mucosa (Fig 2). Skin biopsies from his upper arm and abdomen showed lichenoid interface dermatitis with individually necrotic keratinocytes at the dermal-epidermal junction and occasional eosinophils, compatible with lichenoid graft-versus-host disease.

For his fulminant heart failure, he urgently began receiving high doses of intravenous dobutamine, bumetanide, and eplerenone. He received oral prednisone 1 mg/kg and topical steroids for graft-versus-host disease affecting his skin and oral mucosa. Although his cutaneous lesions improved, he remained hypotensive and tachycardic for 16 days, with minimal improvement of his left ventricular ejection fraction, and his dysgeusia persisted.

Dermatologic evaluation for persistent dysgeusia led to consideration of steroid-refractory oral graft-versus-host disease and nutritional deficiency.[6] Nutritional evaluation revealed thiamine deficiency (15 nmol/L; normal 70-180 nmol/L). There were no deficiencies of zinc, iron, riboflavin, niacin, pyridoxine, biotin, folate, or cobalamin. Given the newly discovered thiamine deficiency in a background of dysgeusia, fulminant heart failure, and volume overload requiring treatment with high doses of diuretics,

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Funding sources: None.
Conflicts of interest: None disclosed.
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JAAD Case Reports 2020;6:420-1.
2352-5126

https://doi.org/10.1016/j.jdcr.2020.02.031

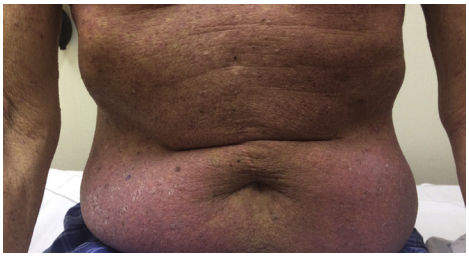

Fig 1. Trunk and upper extremities with erythematous to violaceous scaly papules coalescing into thin plaques.

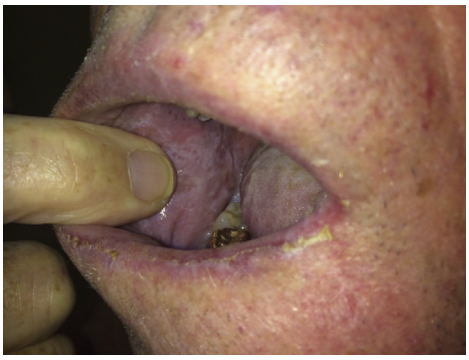

Fig 2. Buccal mucosa with lacy white plaques and edematous maceration.

Shoshin beriberi was considered. Supplementation with thiamine 300 mg daily led to rapid resolution of his heart failure and oral symptoms, and his dobutamine was gradually tapered to discontinuation. His left ventricular ejection fraction increased from less than 10% to 28% in 13 days and to 36% in 30 days, and he has remained stable for more than 11 months.

DISCUSSION

Patients with allogeneic hematopoietic cell transplant are at high risk for nutritional deficiencies.[5,7] Acute and chronic graft-versus-host disease occurs in an estimated 45% and 70% of such patients, respectively,[5] which can reduce oral intake by affecting the oral mucosa and gastrointestinal tract and can reduce absorption of thiamine from the jejunum.[5] Comorbid renal dysfunction decreases expression of vitamin transporters in the intestine, liver, and heart and also leads to accumulation of oxythiamine, a competitive inhibitor of thiamine.[5,8] Diuretics in the setting of renal dysfunction exacerbate thiamine deficiency by increasing urinary excretion of thiamine.[4] Even before the actual hematopoietic cell transplant, cytotoxic conditioning regimens can precipitate thiamine deficiency from prolonged mucositis, nausea, vomiting, and diarrhea.[5]

When thiamine pyrophosphate, the active form of thiamine, is depleted, pyruvate and lactate accumulate in tissues, leading to vasodilation, edema, and biventricular heart failure.[1,9] Blood flow increases in peripheral tissues while decreasing to the kidneys and brain, leading to distributive shock of Shoshin beriberi.[10]

Given the multiorgan consequences of untreated thiamine deficiency and the simple treatment with thiamine supplementation, dermatologists should maintain a high index of suspicion for thiamine deficiency in patients with oral or cutaneous graft-versus-host disease who have any relevant symptoms, many of which overlap with those caused by graft-versus-host disease itself.

REFERENCES

1. Dabar K, Harmouche C, Habr B, Moussa R, Jaber B. Shoshin beriberi in critically-ill patients: case series. *Nutr J*. 2015;14:51.
2. Lee LW, Yan AC. Skin manifestations of nutritional deficiency disease in children: modern day contexts. *Int J Dermatol*. 2012; 51:1407-1418.
3. Tolkachjov SN, Bruce AJ. Oral signs of nutritional disease. In: Fazel N, ed. *Oral Signs of Systemic Disease*. Cham, Switzerland: Springer Nature Switzerland AG; 2019:63-89.
4. Pachariyanon P, Thakolwiboon S, Motes A, Payne JD, Nugent K. Atypical presentation of a forgotten disease: refractory hypotension in beriberi. *Eur J Clin Nutr*. 2019;73: 1598-1600.
5. Levavi H, Park D, Tannenbaum J, Steinberg A. Retrospective analysis of thiamine deficiency in allogeneic stem cell transplant patients. *Ann Hematol*. 2019;98:1499-1500.
6. Scordo M, Shah GL, Peled JU, et al. Unlocking the complex flavors of dysgeusia after hematopoietic cell transplantation. *Biol Blood Marrow Transplant*. 2018;24:425-432.
7. Steinberg A, Gorman E, Tannenbaum J. Thiamine deficiency in stem cell transplant patients: a case series with an accompanying review of the literature. *Clin Lymphoma Myeloma Leuk*. 2014;14:S111-S113.
8. Elias IM, Sinclair G, Blydt-Hansen TD. Acute Shoshin beriberi syndrome immediately post-kidney transplant with rapid recovery after thiamine administration. *Pediatr Transplant*. 2019;23:e13493.
9. Vedder EB. The pathology of beriberi. *JAMA*. 1938;110:893-896.
10. Witte KKA, Clark AL. Nutritional abnormalities contributing to cachexia in chronic illness. *Int J Cardiol*. 2002;1:23-31.