Research Letter

Clinical Correlates and Outcome of Shoshin Beriberi

Manifestations of Shoshin beriberi in the form of shock, severe metabolic acidosis, and multiorgan failure can be misleading and challenging, especially in individuals who are not considered high risk. Because of rarity in the occurrence, lack of standardized laboratory tests and atypical presentation, the diagnosis is often not entertained. The rationale of this study is to describe the clinical correlates and outcome of a series of cases of Shoshin beriberi that was encountered in a tertiary care center of coastal South India. Among six cases with features of Shoshin beriberi, five were nonalcoholics and none had signs of overt malnutrition. A prompt reversal of acidosis and shock in 24-48 hours and full recovery was observed in three cases in which thiamine infusion was used. Shoshin beriberi can mimic sepsis with multiorgan failure and a high index of suspicion is required to diagnose this rapidly reversible condition. In a patient with unexplained metabolic acidosis, a therapeutic trial of thiamine infusion is a reasonable option especially since it is inexpensive, safe, and can be lifesaving. The occurrence of several such cases in this geographical region raises the suspicion of an alternative precipitating factor, the confirmation of which needs further research.

The institutional ethical committee clearance was taken before undertaking the study. This was a retrospective study of hospital records conducted at K.S. Hegde Medical College Hospital, Deralakatte, Mangalore, Karnataka, India. On encountering three cases with similar clinical presentation of severe shock, acidosis, and right heart failure that had fatal outcomes, a clinical diagnosis of Shoshin beriberi was considered in the subsequent three cases with dramatic response to intravenous thiamine and this is a retrospective review of all the six cases. A thorough search was done in the medical records section for all the cases admitted with the diagnosis of shock, right heart failure, metabolic acidosis, and multiorgan failure. We excluded cases with an alternative explanation for such a clinical presentation.

The diagnostic criteria included for beriberi heart disease are as follows: (1) enlarged heart with normal sinus rhythm, (2) edema and elevated venous pressure, (3) shock without any other obvious cause, (4) nonspecific ST-T changes in electrocardiography (ECG), (5) metabolic acidosis on arterial blood gas (ABG) analysis, (6) no other evident cause, (7) response to thiamine.[1] Complete blood count, renal and hepatic functions, serum electrolytes, urine analysis, prothrombin time (PT), activated partial thromboplastin time (aPTT), arterial blood gas analysis, chest X-ray, ECG, and echocardiography of all six cases who met the inclusion criteria were tabulated and analyzed. The serial ABG readings and the medications used were also tabulated.

All had presented with dyspnoea, oligo-anuria, edema, and none had fever. Three cases had vomiting and two were in altered mentation on admission. One case (case 6) was alcoholic in this series. Shock was refractory to fluid replacement and all were treated with combination inotropes, broad-spectrum antibiotics, sodium bicarbonate infusion, assisted ventilation, and four of them needed renal replacement therapy. All patients were young and were in the third or fourth decade. Three cases in whom thiamine deficiency was suspected and treated recovered completely in this series. The baseline hemoglobin, total leucocyte count, platelet count, and serum albumin on admission were normal in all [Table 1]. Blood urea and serum creatinine (maximum) ranged between 60-141 mg/dl and 1.9-6 mg/dl, respectively. Creatinine phosphokinase-MB (CPK-MB) was done in three cases and was elevated in all of them. Viral markers for hepatitis B, C, and human immunodeficiency virus; dengue and leptospira serology were negative in all. Echocardiography evidenced dilated right atrium and ventricle with moderate-to-severe pulmonary hypertension and normal left ventricular ejection fraction [Table 2]. ECG showed sinus tachycardia in all, ST depression in leads V3 to V6 in one case. Ultrasonography in two cases showed mild ascites and minimal right-sided pleural effusion. Chest X-ray showed cardiomegaly and CT angiography done in one case did not show evidence of pulmonary embolism [Figure 1].

One case (case 4) had a protracted hospital stay of 3 weeks due to hospital acquired methicillin resistant *staphylococcus aureus* (MRSA) pneumonia with a new onset of chest X-ray opacity; however he recovered completely and was discharged from the hospital after treatment with antibiotics. There was worsening acidosis in the first three cases [Table 1] in whom thiamine deficiency was not suspected and all of them succumbed due to refractory shock and acidosis. The remainder of three cases in whom thiamine replacement was given had a dramatic response to intravenous thiamine and acidosis improved over 24-48 hours with normalization of blood pressure.

Table 1: Characteristics of study subjects

Case no.	1	2	3	4	5	6
Age/sex	23/M	20/F	26/F	35/M	36/M	36/M
Hb (g/dl)	17.1	13.7	12.8	14.87	12.3	13.2
TLC* (on admission)/mm^3	8700	9400	10,000	10,400	6700	8,200
Platelet count/mm^3	1,82,000	5,02,000	2,83,000	3,32,000	2,63,000	2,08,000
Creatinine (max) in mg/dl	4.4	2.4	1.9	6	2.62	4.2
Albumin (on admission), mg/dl	4.1	4.4	3.9	4.2	5	4.2
CPK†/CPK-MB‡ in U/L	-	-	726/110	1116/114	-	- /144
Renal replacement therapy	Yes	No	Yes	Yes	Yes	No
pH (*N* = 7.35-7.45): on admission	7.236	7.428	7.518	6.911	6.992	6.933
pH (*N* = 7.35-7.45): on second day	7.1	6.92	7.16	7.404	7.429	7.529
HCO_3: on admission	6.1	13.5	13.9	7.5	5	2.5
HCO_3: on second day	11.8	7	6.3	18.5	12.2	25.9
Thiamine use	No	No	No	Yes	Yes	Yes

TLC*: Total leucocyte count; CPK†: Creatinine phosphokinase; CPK-MB‡: Creatinine phosphokinase-MB

Table 2: Echocardiographic data of study subjects

Case no.	1	2	3	4	5	6
RA*/RV† dilatation	Yes	Yes	Yes	Yes	Yes	Yes
PASP‡	45 mm of Hg	65 mm of Hg	40 mm of Hg	65 mm of Hg	50 mm of Hg	35 mm of Hg
TR§	Moderate	Severe	Moderate	Severe	Severe	Moderate
LVEF‖	60%	55%	60%	64%	62%	65%

RA*: Right atrium; RV†: Right ventricle; PASP‡: Pulmonary artery systolic pressure; TR§: Tricuspid regurgitation; LVEF: Left ventricular ejection fraction

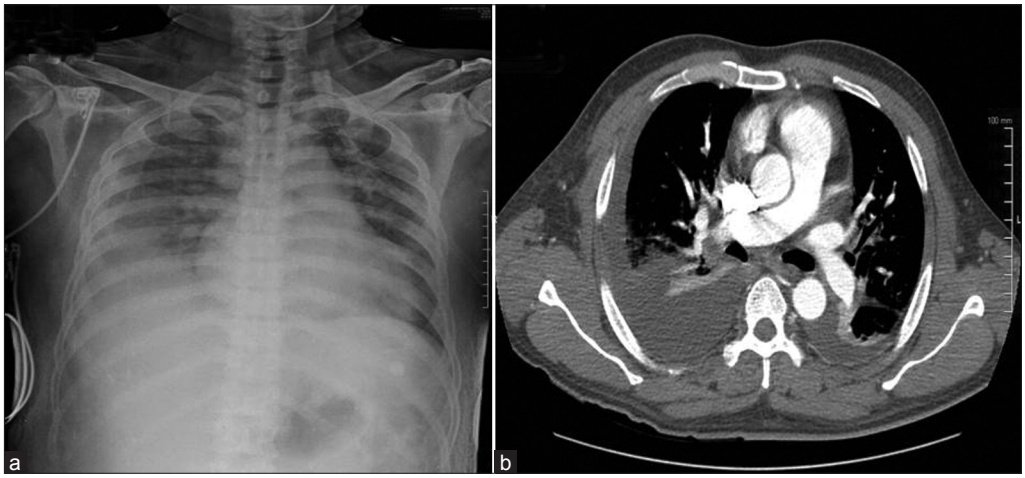

Figure 1: (a) Chest radiograph AP view shows cardiomegaly and moderate right-sided pleural effusion. (b) Axial postcontrast CT section of the thorax showing bilateral pleural effusion with no evidence of thrombus in the pulmonary arteries

Beriberi is the clinical disease associated with thiamine deficiency and people affected by subacute thiamine deficiency will have symptoms of peripheral edema and mixed motor and sensory neuropathy. Wet beriberi is the term used for thiamine deficiency with cardiovascular involvement. There has been a long association of rice consumption with beriberi in Asia and other parts of the world.[2-5] Consumption of highly milled rice grain and white rice in the diet has replaced coarser and more traditional grains over the time all over the world. Many factors are important in the etiology of beriberi but overall current outbreaks usually occur where people are restricted as in prisons[6,7] or abuse alcohol as it reduces absorption of thiamine.[8] More recent studies in the western literature have described beriberi almost exclusively occurring in alcoholics with poor nutritional status.

A more rapid form of wet beriberi is termed acute fulminant cardiovascular beriberi/Shoshin beriberi, or acute pernicious beriberi. The occurrence of high-output heart failure in classical beriberi is due to excessive vasodilatation in the muscles and a fall in the peripheral vascular resistance with resultant increase

in venous return and stroke volume. Either progressive vasodilatation or damage to the myocardium or both may disturb the equilibrium, and a falling blood pressure will signal circulatory breakdown.[9] Direct impairment of myocardial energy production has been proposed as one possible mechanism of the heart failure seen in beriberi as thiamine is required as a cofactor for energy production. In Shoshin beriberi, in addition to falling blood pressure and shock the clinical picture includes evidence of vasoconstriction in skin and kidney, leading to cyanosis and acute renal shutdown.

All the patients in our series had severe metabolic acidosis with clinical and echocardiographic evidence of right heart failure. All of them had multiorgan failure as evidenced by acute renal shutdown and elevated liver enzymes possibly as a result of ischemic injury. In the absence of pulmonary embolism or clinical evidence of sepsis, acute thiamine deficiency was considered in the last three cases and all have recovered completely. Elevation of the serological markers of myocardial injury and multiple organ failure is known to occur in this setting.[10-13] Reversible severe pulmonary hypertension is due to an increased pulmonary arterial blood flow and elevated left ventricular end-diastolic pressure.[14,15] ECG changes were nonspecific with sinus tachycardia and ST depression. CPK-MB was elevated in three cases and such a presentation may be mistaken for acute coronary syndrome with cardiogenic shock.[11,16] ST depression in ECG with T wave inversion and elevated troponin-I as well as profound myocardial edema on cardiac magnetic resonance imaging (MRI) in wet beriberi have also been reported.[17] The above-mentioned ECG changes, acute onset of pulmonary hypertension with right atrium/right ventricular dilatation, and shock may require a differential diagnosis of pulmonary embolism. One of the most striking clinical features in our patients was the development of severe metabolic acidosis. Such exceptionally severe acidosis has been described in other studies as well.[12] The reversal of shock and the striking improvement in acidosis in 24-48 hours of treatment with thiamine was obvious in the last three cases, which highlights the importance of this simple modality of treatment in this rapidly reversible condition.

Increased metabolic consumption of thiamine can result from high carbohydrate intake, increased physical exercise, severe infection, and hyperthyroidism. Increased thiamine depletion can result from diarrhea, diuretic therapy, and in patients on hemodialysis. Chronic intestinal disease, alcoholism, malabsorption syndrome, and folate deficiency can lead to decreased absorption of thiamine. All the above patients were young, without any medical illness or overt malnutrition and the laboratory parameters of hemoglobin and serum albumin were normal on admission. Thiamine deficiency could result either from inadequate intake of thiamine or consumption of food containing antithiamine factors. The west coastal belt of southern India consumes boiled rice as staple food and fish as the additional diet. Thiaminase has been found in some Indian salt water and brackish water fish.[18] Betel nut has also been shown to possess antithiamine activity.[19] Both fish and betel nut are consumed widely in this region. The reporting of such cases necessitates the need for a larger study to explore the role of such dietary ingredients in precipitating such devastating manifestations in apparently healthy individuals.

Laboratory diagnosis of thiamine deficiency can be made on the basis of an increase in thiamine pyrophosphate effect, a decrease in blood thiamine levels, reduced red cell transketolase activity, and increased serum pyruvate and lactate levels. Apart from the elevated lactate levels, the availability of the rest of the investigations is limited to a few research laboratories and these tests are often not standardized. Diagnostic tests for thiamine deficiency are rarely performed in the acute care setting since their result is often delayed beyond the period of acute illness. Diagnosis is commonly based on monitoring the therapeutic response to thiamine replacement in the appropriate clinical setting.[20] The only definitive treatment of beriberi is intravenous administration of thiamine, which improves the adverse hemodynamic situation within minutes to hours, and is considered diagnostic of this rare disease.[12,13]

In conclusion, Shoshin beriberi can mimic sepsis with multiorgan failure or massive pulmonary embolism and in the absence of readily available laboratory tests; a high index of suspicion is required to diagnose this rapidly reversible condition. In a patient with unexplained metabolic acidosis, a therapeutic trial of thiamine infusion is a reasonable option especially since it is inexpensive, safe, and can be lifesaving. The occurrence of several such cases in people without obvious risk factors for thiamine deficiency in this geographical region raises the suspicion of an alternative precipitating factor, the confirmation of which needs further research.

Rama Prakasha Saya, Shashidhar Baikunje[1], Parampalli Suryanarayana Prakash, Kodangala Subramanyam[2], Vikram Patil

Departments of General Medicine, [1]Nephrology, and [2]Cardiology, K. S. Hegde Medical Academy, Deralakatte, Mangalore, Karnataka, India
E-mail: dr_prakashbhat@yahoo.co.in

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