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RESEARCH LETTER

Thiamine Deficiency-Related Rhabdomyolysis: an Exploration Through a Case Series

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INTRODUCTION

Thiamine, also known as vitamin B1, is a vital B-complex vitamin that is essential for energy metabolism and the functioning of key organ systems. Thiamine pyrophosphate, its active form, acts as a co-enzyme in mitochondrial oxidative decarboxylation processes and likely offers the most accurate indication of thiamine's nutritional status.[1]

Thiamine deficiency (TD) was prevalent worldwide among rice-consuming populations, but its incidence has declined with time due to food fortification initiatives. However, it still persists in some South Asian countries and is being reported increasingly from Kashmir, where the primary dietary staple is polished white rice.[2] In countries with food security, and where obesity is prevalent, it is challenging to associate TD with this framework, except in special situations such as bariatric surgery. Although a diet deficient in thiamine is the primary cause of TD, the percentage of calories derived from carbohydrates has been shown to directly increase the requirement of thiamine in the body.[3] TD presents as wet and dry beriberi, Wernicke's encephalopathy, Korsakoff's encephalopathy, gastric beriberi, and high-output heart failure, categorized by affected organs. Wet beriberi relates to high-output heart failure and edema, whereas dry beriberi involves peripheral neuropathies, Wernicke's encephalopathy, and muscle discomfort. In regions with high TD prevalence, other variants such as gastric beriberi and TD during pregnancy have been noted.[4–6] TD prompts a decline in adenosine triphosphate (ATP) synthesis, thereby disturbing the availability of ATP for energy supply; and ATP depletion is one of the primary pathogenic mechanisms of rhabdomyolysis. Barring a few case reports of rhabdomyolysis associated with TD, the data in this regard is scanty. Herein, we present some atypical cases of TD associated with rhabdomyolysis.

RESULTS

In a series of distinct clinical cases of rhabdomyolysis (Table 1), TD emerged as a common denominator, contributing to a range of severe symptoms and complications. In the first case, a laborer with occasional alcohol consumption and dietary intake of polished rice presented with rhabdomyolysis with acute kidney injury. The initial laboratory tests showed hyperkalemia (potassium 6.1 mEq/l), hyperlactatemia (lactate >15 mmol/l), and azotemia (urea 105 mg/dl; creatinine 7.74 mg/dl). Following catheterization, the patient passed 100 ml of cola-colored urine, and the serum creatine phosphokinase (CPK) and lactate dehydrogenase (LDH) levels were elevated (CPK ≥42,670 U/l) (LDH ≥1995 U/l) levels. Whole-blood thiamine on admission was 0.65 ng/ml. The echocardiogram showed an ejection fraction of 65% with right ventricular systolic pressure = 23 + right atrial pressure. The lactate levels returned to normal after administration of

Table 1. Biochemical investigations and radiological findings of the patients

Characteristics	Case 1			Case 2			Case 3			Case 4	
	50			18			35			70	
Age, years	Initial	Final		Initial	Final		Initial	Final		Initial	Final
Hemoglobin, g/dl	13.6	9.0		12.7	10.4		13.5	10		12.6	11.1
Urea, mg/dl	105	77		115	109		96	24		55	41
Creatinine, mg/dl	7.74	3.1		3.06	1.67		1.08	0.51		1.03	0.79
Uric acid	20.1	16.5		11.94	10.40		3.9	2.9		7.1	4.9
Sodium, mmol/l	130	138		133	142		122	140		133	140
Potassium, mmol/l	6.1	3.0		5.1	3.3		4.1	3.9		4.5	3.6
Calcium, mg/dl	9.01	8.4		8.55	7.85		9.4	8.0		7.0	8.6
Phosphate, mg/dl	6.41	4.3		2.42	4.96		2.7	1.7		3.8	4.1
Alanine transaminase (ALT), U/l	1233	989		572	46		63	165		>942	103
Aspartate transaminase (AST), U/l	>4500	2324		1950	33		98	69		>913	47
Alkaline phosphatase (ALP), U/l	48	72		76	44		308	144		83	168
Albumin	3.4	3.0		3.5	3.8		2.5	3.1		2.8	2.5
pH	7.0	7.48		7.25	7.47		7.49	7.48		7.26	7.44
pCO_2	12	30		40	36		20	35		50	56
pO_2	12	62		33	82		95	32		14	265
Lactate, mmol/l	>15	0.5		5.5	0.6		2.5	1.3		6.7	0.9
Lactate dehydrogenase (LDH), U/l	≥1995	800		≥1995	853		801	345		>1995	398
Whole-blood thiamine (μg/dl)	0.65	3.2		1.05	4.10		1.01	3.01		0.95	3.31
Creatine phosphokinase (CPK), U/L	≥42,670	≥34,183	1311	>8450	546	303	3500	4992	47	2188	353
Other investigations	Echocardiography EF = 65% RVSP = 23+RAP			Echocardiography EF = 60% RVSP = 46+RAP			Echocardiography EF = 63% RVSP = 35+RAP NCV Axonal motor polyneuropathy involving lower limbs				

EF, ejection fraction; NCV, nerve conduction velocity; RAP, right atrial pressure; RVSP, right ventricular systolic pressure.

thiamine 600 mg i.v. once daily leading to clinical improvement. The second case involved a young male with opioid ingestion who presented with reduced consciousness and rhabdomyolysis. He displayed a small bruise on the left side of the chest, an abrasion on the right elbow, and a tea-colored urine of 200 ml in urobag. The initial assessments revealed hyperkalemia (potassium 6.0 mmol/l) and hyperlactatemia (lactate 3.9 mmol/l); however, within a short span of time, the creatinine increased to 7.20 mg/dl, blood urea nitrogen elevated to 170 mg/dl, urinary output decreased to 100 ml/24h, the LDH level exceeded 1995 U/l whereas whole-blood thiamine levels were 1.05 μg/dl. In addition to the standard treatment care, the patient received i.v. thiamine at a dose of 600 mg twice daily. The patient exhibited a positive response to the thiamine supplementation, characterized by a reduction in lactate levels to 0.7 mmol/l and notable clinical improvement, which was indicative of primary TD. In the third case, a 25-year-old female postpartum presented with recurrent vomiting followed by muscle tenderness, generalized body swelling, muscle edema, reduced urine output, breathlessness, and weakness in both lower limbs. She had a history of hyperemesis gravidarum during her pregnancy. Neurological examination showed absent reflexes in the lower limbs with the nerve conduction velocity documenting peripheral neuropathy. Echocardiography revealed an ejection fraction of 63% and right ventricular systolic pressure = 35 + right atrial pressure, whereas brain natriuretic peptide was normal. The initial whole-blood thiamine level was reported to be 1.01 μg/dl. After supplementation with i.v. thiamine (400 mg), creatinine decreased to 0.51 mg/dl from 1.08 mg/dl, the final CPK levels decreased to 47 from 3500 U/l, LDH reduced to 345 from 801 U/l, and lactate level normalized to 0.7 mmol/l along with symptom resolution. In the fourth case, an elderly male who was bedridden because of Pott's spine, presented with a urinary tract infection, muscle tendernesss, and evidence of rhabdomyolysis (CPK = 2188 U/l). The urine output was recorded at 1.6 l/24h. The baseline thiamine levels were 0.95 μg/dl and lactate was 6.7 mmol/l. Thiamine supplementation, in conjunction with standard care, led to improved clinical status and the lactate levels decreased to 0.9 mmol/l on day 2, creatinine decreased to 0.79 mg/dl from an initial level of 1.03 mg/dl, sodium levels increased to 140 mmol/l from 133 mmol/l, potassium levels decreased to 3.6 mmol/l from 4.5 mmol/l, and CPK levels reduced to 353 U/l from 2188 U/l. TD featured prominently in all cases, and timely thiamine supplementation played a pivotal role in the positive clinical

outcomes observed. Ethical approval for this study was provided by the Institutional Ethical Committee of Government Medical College, Srinagar (No: 138/ETH/GMC/ICM dated May 28, 2019).

DISCUSSION

Rhabdomyolysis involves the disintegration of skeletal muscle cells, releasing intracellular constituents, including myoglobin, creatine kinase, LDH, and enzymes, into circulation. TD exacerbates this process primarily through the central mechanism of ATP depletion, which disrupts ion-exchange pumps, increases intracellular calcium levels, and triggers the degradation of muscle proteins, consequently resulting in an elevation of CPK levels.[7] The pivotal role of thiamine as a cofactor for transketolase in ATP production establishes a direct link between TD and ATP depletion, potentially contributing to rhabdomyolysis. In thiamine-deficient states, disruption of oxidative metabolism occurs, blocking the Krebs cycle and shifting from aerobic to anaerobic metabolism. This causes an accumulation of lactate with an associated decrease in ATP synthesis. In our region of Kashmir, known for endemic TD and a rising incidence of TD-related disorders, we have encountered instances of spontaneous rhabdomyolysis, marked by elevated lactate levels. We have documented cases of rhabdomyolysis where there was no apparent evidence of direct muscle injury or any known precipitating drug intake, except for 1 instance involving opioid consumption with minor injury in a young male patient. Consequently, it is worth noting that even minor injuries can precipitate rhabdomyolysis in patients experiencing thiamine depletion. In addition, in all our cases, lactic acidosis was present and a prompt response to thiamine supplementation was noted as indicated by the normalization of lactate levels. This could again be attributed to the low thiamine status because inadequate thiamine results in the failure of pyruvate to enter the tricarboxylic acid cycle, thus preventing aerobic metabolism, which may lead to profound lactic acidosis through anaerobic metabolism. We observed a positive response in both clinical and biochemical parameters following the administration of thiamine.

Previous studies have documented a high mortality rate in rhabdomyolysis, especially when associated with acute kidney injury; however, in our cases, no mortality was observed.[8] Prior research has shown that thiamine has renoprotective effects in a rat model of glycerol-induced rhabdomyolysis, by its antiinflammatory and antioxidant properties. These findings suggest that thiamine may be efficaciously employed in circumstances associated with both traumatic and nontraumatic muscle injuries to prevent the onset of acute kidney injury and its subsequent progression into chronic renal disease.[9] Therefore, prompt thiamine supplementation may improve survival by aiding ATP production and its antioxidant effects in rhabdomyolysis, with or without acute kidney injury. Several studies have previously documented that patients presenting with signs and symptoms of heart failure linked to TD may also exhibit myopathic symptoms, including rhabdomyolysis (S1 and S2 – see supplementary references).

In conclusion, TD may play a role as a causative or contributory factor in the development of rhabdomyolysis, and the high lactate levels and subsequent reduction following thiamine supplementation are closely linked to favorable outcomes, including full recovery and improved prognosis.

DISCLOSURE

All the authors declared no competing interests.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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AUTHORS CONTRIBUTIONS

All authors contributed equally to this work.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplemental References.

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