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Dry Beriberi Due to Thiamine Deficiency Associated with Peripheral Neuropathy and Wernicke's Encephalopathy Mimicking Guillain-Barré syndrome: A Case Report and Review of the Literature

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female, 56
Final Diagnosis: Dry Beri Beri
Symptoms: Anasarca • ascending paralysis • hypotension • unresponsiveness
Medication: —
Clinical Procedure: —
Specialty: Neurology

Objective: Challenging differential diagnosis

Background: Beriberi due to thiamine (vitamin B1) deficiency has two clinical presentations. Patients with dry beriberi present with neuropathy, and patients with wet beriberi present with heart failure, with or without neuropathy. Dry beriberi can mimic the most common form of Guillain-Barré syndrome (GBS), an acute inflammatory demyelinating polyradiculoneuropathy (AIDP). Severe thiamine deficiency results in Wernicke's encephalopathy. This report of a case of dry beriberi and Wernicke's encephalopathy due to thiamine deficiency includes a review of the literature.

Case Report: A 56-year old woman with a history of gallstone pancreatitis and protein-calorie malnutrition was treated six months previously with total parenteral nutrition (TPN). She initially presented at another hospital with paresthesia of the lower limbs, arms, and neck, and symptoms of encephalopathy. Initial diagnosis of GBS was made, based on magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) findings. Despite five days of intravenous immunoglobulin (IVIG) treatment, her encephalopathy worsened, requiring transfer to our hospital, where she required intubation and treatment with vasopressors. A repeat MRI of her brain showed changes consistent with Wernicke's encephalopathy. Following treatment with high-dose intravenous thiamine, her mental status improved within 48 hours, and by the third hospital day, she no longer required intubation.

Conclusions: Symptoms and signs of dry beriberi due to thiamine deficiency can mimic those of acute or chronic GBS. However, thiamine repletion leads to rapid clinical improvement and can prevent irreversible neurologic sequelae, including Korsakoff syndrome. Clinicians should consider thiamine deficiency in malnourished patients presenting with symptoms and signs of GBS.

MeSH Keywords: Beriberi • Guillain-Barre Syndrome • Polyradiculoneuropathy • Thiamine Deficiency • Wernicke Encephalopathy

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Background

Thiamine (vitamin B1) is a water-soluble vitamin that has a vital role in cell metabolism, specifically in the tricarboxylic acid cycle (Krebs's cycle) [1]. An average adult requires approximately 330 mcg of thiamine per 1,050 calories metabolized, with a recommended daily thiamine intake of 1–1.5 mg [2]. There is limited storage capacity for thiamine in the human body, with an average amount of 25–30 mg stored at any one time [3]. Therefore, thiamine depletion can occur within 14 days in the setting of reduced thiamine intake [4].

Thiamine deficiency can resultingfrom reduced thiamine intake can occur due to alcohol abuse, anorexia nervosa, dieting, or malabsorption following bariatric surgery [2]. Malabsorption may also occur in patients with diarrhea, celiac disease, tropical sprue, or dysentery [5]. Other less common causes of thiamine deficiency are burns, pregnancy, dialysis, and malignancy [2].

Thiamine deficiency leads to beriberi, which has both dry and wet manifestations [6]. Dry beriberi is characterized by neuropathy, which has a severity that correlates with the degree and duration of thiamine deficiency and can be associated with Wernicke's encephalopathy and Korsakoff syndrome. Wet beriberi is characterized by cardiomyopathy, cardiomegaly. Patients present with symptoms of heart failure, including dyspnea and peripheral edema. Shoshin beriberi is a fulminant form of wet beriberi in which patients develop cardiogenic shock, lactic acidosis, and subsequent multi-organ failure if left untreated [6].

Wernicke's encephalopathy is associated with thiamine deficiency and can also occur due to chronic alcohol abuse [6]. Wernicke's encephalopathy commonly presents as a triad of altered mental status (confusion and mild memory impairment), ataxia, and ocular symptoms (ophthalmoplegia or nystagmus) [6]. However, this classic clinical triad is not always present. If left untreated, Wernicke's encephalopathy can lead to irreversible cognitive impairment and can be fatal. Although Wernicke's encephalopathy is a clinical diagnosis, magnetic resonance imaging (MRI) and serum thiamine levels may assist with confirmation of diagnosis in some cases [2,6]. Also, severe thiamine deficiency may lead to axonal abnormalities and impaired acetylcholine transmission [7,8]. These axonal injuries may result in ataxia, areflexia, and painful sensory or sensorimotor polyneuropathy, accompanied by variably severe degrees of muscle weakness [7].

Guillain-Barré syndrome (GBS), or an acute inflammatory demyelinating polyradiculoneuropathy (AIDP), is commonly preceded by infection [9]. The distinction between dry beriberi and GBS can be difficult as there is overlap in the presenting symptoms, signs, and diagnostic features. GBS and its variants can be diagnosed using through electromyography, but the features overlap with those of dry beriberi [9]. Both GBS and dry beriberi can lead to sensorimotor polyneuropathy as well as albuminocytologic dissociation within the cerebrospinal fluid. Albuminocytologic dissociation is an increase in CSF protein (>0.55 g/L) that occurs without an increase in white blood cells. Also, cases of severe dry beriberi can be associated with axonal injury, mimicking the ascending motor paralysis that is usually associated with GBS.

This report is of a patient who presented with ascending neuropathy and paralysis who was initially empirically treated for GBS and who was later diagnosed with dry beriberi and Wernicke's encephalopathy due to severe thiamine deficiency. This report includes a review of the literature characterizing the overlap between these syndromes.

Case Report

A 56-year-old woman presented to a community hospital with a history of weakness. One month prior to admission, she reported numbness and weakness in her lower extremities, which progressed to her hands and neck over the course of a few days. At this time, she had a presumptive diagnosis of Guillain-Barré syndrome (GBS), or acute inflammatory demyelinating polyradiculoneuropathy (AIDP). Her past medical history included type 2 diabetes mellitus, and hypertension. A year previously, she had an episode of necrotizing pancreatitis due to gallstones, which was complicated by severe protein-calorie malnutrition requiring total parenteral nutrition (TPN). Six months prior to her recent presentation, TPN was discontinued and she was able to return to a normal diet.

On admission to the community hospital, a lumbar puncture was performed, which showed albuminocytologic dissociation in the cerebrospinal fluid (CSF), consistent with the initial presumptive diagnosis of GBS. A brain magnetic resonance imaging (MRI) scan initially showed small vessel ischemic changes. She received five days of empiric intravenous immunoglobulin (IVIG) treatment, but without clinical response. She then developed worsening pancytopenia and encephalopathy, which prompted her transfer to a specialist center.

On arrival at our institution, the patient was hypotensive, with a blood pressure of 64/48 mmHg. She was unresponsive to verbal stimuli, minimally responsive to painful stimuli, and had a Glasgow Coma Scale (GCS) score of 6. On examination, she was anasarcic with flaccid paralysis of all four extremities. The results of laboratory investigations indicated a malnourished and septic state with a calcium of 6.7 mg/dL, hemoglobin of 9.4 g/dL, white cell count of 2.1×10^9/L, phosphorus of 1.1 mg/dL, creatinine <0.2 mg/dL, albumin <1.5 gm/dL, and lactate of 4 mmol/L. Nutritional risk screening (NRS-2002) resulted

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Table 1. Previously published reports of cases of thiamine deficiency mimicking Guillain-Barré syndrome (GBS) or acute inflammatory demyelinating polyneuropathy (AIDP)*.

Reference	Age	Sex	Clinical presentation	Diagnosis	Treatment	Outcomes
Faigle et al. [11]	62	F	Acute sensory and motor neuropathy. Numbness, paresthesia and ascending lower extremity weakness	Dry beriberi	Thiamine IV (Dose not reported)	Slow resolution of clinical symptoms, MRI lesions and nerve conduction abnormalities
Murphy et al. [23]	44	M	Confusion and flaccid quadriparesis evolving over three weeks	Dry beriberi	High doses (not specified) of thiamine for one week	Mobile with a Zimmer frame and steady progress in rehabilitation
Koike et al. [14]	46	M	Weakness in lower limbs. Decreased consciousness on day 27 of hospitalization, and diuretic-resistant heart failure on day 28	Wet beriberi	Fursultiamine (disulfide thiamine derivative) 100 mg IV once	Consciousness and heart failure recovered over several days. Walking independently after six months
Koike et al. [14]	33	M	Numbness for two weeks, weakness in lower limbs for five days progressing to upper limbs and bedridden on admission	Dry beriberi	Fursultiamine (disulfide thiamine derivative) 100 mg IV once	Gradual improvement from day 1 of treatment. Walking with a cane one month later
Riahi et al. [24]	14	F	Numbness and lower limbs weakness for one month. Leg cramps and upper limbs weakness for two weeks. Dysphagia and unable to walk on the day of admission	Dry beriberi	Thiamine 300 mg IV BID for 1 week. At discharge, 300 mg IM BID for 4 weeks then oral tabs daily	Walking with foot drop at one month. Normal gait and deep tendon reflexes at six months

* Restricted to English language case reports. MRI – magnetic resonance imaging; IV – intravenous; BID – twice daily.

in a score of 5 points and a malnutrition universal screening (MUST) score of 5, with both results supporting the presence of malnutrition [9,10]. She was intubated to protect her airway and resuscitated with intravenous fluids and eventually required an intravenous infusion of norepinephrine. Due to concerns regarding sepsis, meropenem, vancomycin, and anidulafungin treatment was initiated. Her provisional diagnosis was AIDP complicated by septic shock. Given her nutritional status and laboratory findings, empirical treatment with high-dose intravenous thiamine was commenced with a dose of 500 mg every 8 hours.

An electroencephalogram (EEG) did not show seizure activity but showed diffuse slow waves consistent with severe metabolic encephalopathy. On hospital day 3, a brain magnetic resonance imaging (MRI) scan was performed which showed hyperintensity of the bilateral medial thalamus on T2-weighted and fluid-attenuated inversion recovery (FLAIR) axial images, consistent with Wernicke's encephalopathy. Her serum thiamine level was 104 nmol/L (reference range, 70–180 nmol/L) after four doses of high-dose thiamine therapy. On hospital day 4, her mental status markedly improved and she became able to understand simple commands. Norepinephrine and antimicrobial treatment were discontinued with resolution of her hemodynamic stability and with negative blood and urine cultures. On hospital day 5, the patient was successfully extubated. On hospital day 7, she underwent electromyography (EMG), which showed severe sensorimotor polyneuropathy. Her mentation and weakness continued to gradually improve, and she was transferred out of the intensive care unit (ICU) after 14 days. Thiamine supplementation was continued throughout her hospital stay.

Discussion

The patient described in this report initially presented with encephalopathy, ascending lower extremity weakness, and cerebrospinal fluid (CSF) findings consistent with Guillain-Barré syndrome (GBS), prompting initial treatment with intravenous immunoglobulin (IVIG). However, it was only after initiation of thiamine supplementation that the patient gradually recovered both central and peripheral neurologic function.

Dry beriberi has been previously described as a mimic for GBS mimic in several case reports (Table 1). Faigle et al. described

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a patient present who presented with three weeks of progressive sensory and motor function deterioration, which failed to improve despite typical GBS treatment, which was similar to the patient described in the present report [11]. While IVIG therapy may take 2–4 weeks to show an effect for the treatment of GBS, patients with thiamine deficiency-associated neuropathy typically demonstrate a more rapid clinical improvement following thiamine supplementation [12,13]. The neuropathy of both GBS and thiamine deficiency are peripheral and ascending in nature, making initial clinical differentiation quite difficult. The magnetic resonance imaging (MRI) features that suggest thiamine deficiency include bilateral involvement of the medial thalamus, which may take some time to develop. The pathophysiologic effect of thiamine deficiency on the peripheral nervous system is likely to be responsible for the overlap of presentations between dry beriberi and GBS. Neuronal biopsies from affected tissues from patients with dry beriberi have been reported to show predominantly axonal degeneration and progression to demyelination in end-stage disease [14,15]. However, nerve histology requires expert interpretation, which is not always readily available. A further factor that may make it difficult to diagnose dry beriberi is that the CSF in patients with beriberi can show a mild elevation in protein that mimics the albuminocytologic dissociation commonly observed in GBS [6]. The mechanism for albuminocytologic dissociation in beriberi has not been fully elucidated.

Both acute inflammatory demyelinating polyneuropathy (AIDP) and chronic inflammatory demyelinating polyneuropathy (CIDP) were also considered in this case, as the patient's symptoms progressed over nearly six weeks. CIDP includes a spectrum of acquired inflammatory sensory and motor polyneuropathies with relapsing and remitting clinical features [16,17]. Similar to our patient, CIDP typically involves more motor than sensory deficits and can involve cranial and bulbar nerves in 10–20% of cases [17]. CIDP was ultimately thought to be less likely in this case given the initial presence of autonomic instability and the patient's rapid improvement with thiamine supplementation. Also, the clinical history and diagnostic testing did not identify a viral or bacterial pathogen that could have provoked an inflammatory response, which is usually a diagnostic feature of the majority of cases of CIDP.

Due to the underlying severe protein-calorie malnutrition and duration of critical illness in this patient, primary neuromuscular disorders, specifically critical illness myopathy and critical illness polyneuropathy were also considered in the differential diagnosis. These disorders, typically acquired by patients in the intensive care unit (ICU), present with symptoms of flaccid limb weakness and neuropathic pain. Sepsis is a well-established risk factor for the development of both critical illness myopathy and critical illness polyneuropathy [18]. Critical illness myopathy can occur within days of hospitalization, whereas critical illness polyneuropathy typically requires weeks to develop. Both disorders can be complicated by encephalopathy and delirium, which may cause difficulty in weaning the patient from mechanical ventilation, resulting in a prolonged stay in ICU with a cycle of worsening neuromuscular and cognitive impairment. In critical illness myopathy, the EMG demonstrates normal to low motor amplitudes with minimally reduced sensory responses [19]. In critical illness polyneuropathy, the EMG demonstrates an axonal sensorimotor polyneuropathy with diminished sensory and motor potentials, which more closely resembles thiamine deficiency [19,20]. In this case report, given the patient's relatively rapid clinical improvement with thiamine supplementation, if these disorders were present, they only minimally contributed to her overall weakness. In the case presented, the absolute thiamine levels at presentation were unknown as thiamine levels were measured only after rapid repletion with intravenous thiamine had begun.

Conclusions

Thiamine deficiency resulting in beriberi can present as dry or wet forms. As discussed in this case report, the dry form of beriberi results in ascending flaccid neuropathy that can closely mimic Guillain-Barré syndrome (GBS). It is important to identify thiamine deficiency as the cause of the neurologic symptoms, as high-dose thiamine supplementation is inexpensive and rapidly effective. As this case has shown, magnetic resonance imaging (MRI) of the brain and electrophysiological studies may assist in the clinical diagnosis of thiamine deficiency. It is important that physicians consider the possibility of thiamine deficiency in patients with a history of alcohol abuse, severe protein-calorie malnutrition, bariatric surgery, dependence on total parenteral nutrition (TPN), or any disease state complicated by malabsorption and increased caloric requirements [15,21,22]. Given the prevalence of the factors that can lead to thiamine deficiency, the prevalence of beriberi is likely to be greater than previously reported. Therefore, thiamine deficiency resulting beriberi should be considered in the differential diagnosis for any patient presenting with neuropathy, weakness, cardiomyopathy, or autonomic instability when in the appropriate clinical context.

Conflict of interest

None.

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