CLINICAL VIGNETTE

Thiamine Deficiency in a Patient with Severe Alcohol Use Disorder

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Case Presentation

A 37-year-old female with alcohol use disorder and cirrhosis, presented with progressively worsening bilateral lower extremity weakness, numbness, and tingling for 2 weeks. Her symptoms started during an outside hospitalization for generalized weakness, abdominal pain, and non-bloody vomiting thought to be caused by alcohol withdrawal. She had been drinking 6-8 shots of vodka, 48 oz beer, and two 4 oz glasses of wine per day and had been attempting to abstain for one month. During this outside hospitalization, she had 4 L of serosanguineous fluid drained from abdominal ascites, an MRCP liver without contrast which showed moderate hepatosplenomegaly and a serrated liver surface suggestive of sclerosis and heterogeneous steatosis, MRI of her brain, cervical and thoracic spine were unremarkable. She was discharged home after declining transfer to a skilled nursing facility. Nine days following her discharge, she presented to the emergency department at this hospital with worsening lower extremity weakness, numbness, and burning tingling pain, causing her to be bedbound.

She was afebrile and normotensive upon presentation. On physical exam, she was jaundiced but in no acute distress. She was alert and fully oriented. Cranial nerves II – XII were intact. There was limited range of motion and significant muscular atrophy in her bilateral lower extremities. Strength was 3/5 proximally and 4+/5 distally in bilateral lower extremities. Sensation was intact to pinprick in bilateral upper extremities except at the distal fingertips bilaterally, absent below T8 anteriorly, and absent below L4 posteriorly. Patellar and Achilles reflexes were absent bilaterally and plantar reflexes were downgoing bilaterally with severe burning pain when performed. Finger to nose testing was normal. Admission labs were notable for a white blood cell count of 28,900/µL, Hgb of 9.7 g/dL, and elevated liver enzymes with AST of 100 U/L, ALT of 95 U/L, and total bilirubin of 5.9 mg/dL.

Initial testing for a central neurologic process included lumbar puncture and MRI with and without contrast of the C-, T-, and L-spine were unremarkable. She was admitted and neurology was consulted. Subsequent electromyography was notable for length-dependent axonal denervation without evidence of demyelination. Infectious testing was negative for meningoencephalitis, West Nile virus, HIV, hepatitis, syphilis, Lyme disease, as well as negative bacterial and fungal cultures. A positive ANA, mildly elevated CA-125, and elevated CRP and ESR raised concern for an autoimmune, malignant, or paraneoplastic etiology, and Rheumatology was consulted. Follow-up studies for SLE, Sjogren's syndrome, scleroderma, and monoclonal gammopathy were negative except for a +ß2 glycoprotein, and she did not meet diagnostic criteria for autoimmune causes. The possibility of a hepatocellular or gynecologic malignancy was investigated with abdominal ultrasound, which revealed an irregular hypervascular lesion and hypoechoic lesion in the left hepatic lobe; which were not noted on a follow-up CT of the abdomen and pelvis. AFP was normal. A pelvic ultrasound was notable only for fibroids. Metabolic etiologies for peripheral neuropathy revealed low thiamine levels (<7 nmol/L), confirming a diagnosis of thiamine deficiency and dry beriberi likely due to chronic, heavy alcohol use with poor nutrition. She had received oral thiamine during her hospital course, and was repleted with IV thiamine 500 mg for 2 days, followed by IV thiamine 250 mg for 5 days, and ongoing oral thiamine 100 mg three times daily. She improved significantly but had residual ongoing motor and sensory deficits. She was placed at a long-term acute care facility upon discharge for ongoing physical therapy and rehabilitation.

Discussion

Thiamine (vitamin B1) is a water-soluble vitamin that is an important cofactor in cell and carbohydrate metabolism.[1] Humans cannot synthesize thiamine, and thiamine must be obtained through diet, intestinal absorption, and renal reabsorption.[2] Among healthy adults, the recommended dietary allowance of thiamine is 1.1-1.2 mg of thiamine per day.[3] In most industrialized and food-secure countries, this dietary requirement is easily met due to enrichment and fortification of food products.[3]

Despite the advent of fortified food products, thiamine deficiency remains prevalent in susceptible populations. Thiamine deficiency occurs due to poor oral intake, inadequate supplementation in enteral or parenteral nutrition therapy, reduced gastrointestinal absorption due to disease or surgery, increased metabolic requirements, or increased gastrointestinal or renal losses.[4] Thiamine reserves can be depleted following as few as 20 days of inadequate oral intake.[4] Hence, three weeks of protracted vomiting, chronic diarrhea, or anorexia can result in symptoms of thiamine deficiency.[5] Susceptible populations include individuals with chronic alcoholism, pregnancy, renal failure on hemodialysis, eating disorders, elderly, critically ill,

and bariatric surgery.[4] Chronic alcoholism not only predisposes to poor nutrition but also causes inhibition of thiamine intestinal absorption and renal reabsorption, resulting in a net negative impact on thiamine balance in the body.[4,6]

Clinical manifestations of early thiamine deficiency are highly variable and nonspecific.[4] As a result, conventional descriptions focus on later stage manifestations of thiamine deficiency: Wernicke encephalopathy, Korsakoff's syndrome, and dry or wet beriberi.[7] Wernicke encephalopathy is characterized by the classic neurological triad of mental confusion, ocular abnormalities, and ataxia. However, this triad is completely present in a minority of patients.[3,5] Korsakoff's syndrome presents as a more severe progression of Wernicke encephalopathy with confabulation, psychosis, and significant memory deficits.[3] Dry beriberi presents as a symmetrical peripheral neuropathy characterized by both sensory and motor impairment that typically affect the distal extremities, whereas wet beriberi manifests with cardiac involvement with cardiomegaly, cardiomyopathy, heart failure, peripheral edema, and tachycardia, in addition to neuropathy.[3,5] Symptoms of dry beriberi develop gradually over weeks to months and typically begin with fatigue, irritability, and muscle cramps at onset of thiamine deficiency. Distal sensory loss, burning pain, paresthesias, and muscle weakness in the lower extremities are common. If untreated, the neuropathy will cause ascending weakness, eventually leading to sensorimotor neuropathy in the hands.[8] The ascending, peripheral, sensorimotor polyneuropathy seen in dry beriberi has often been described as a mimic for Guillain-Barré syndrome, making initial clinical differentiation difficult.[9]

Confirming diagnosis of thiamine deficiency involves either testing serum thiamine diphosphate levels or a functional assay testing erythrocyte transketolase activity, a marker for thiamine function within red blood cells.[4,7,8] Testing should be performed prior to thiamine replacement. Serum testing of thiamine deficiency is not a reliable indicator of thiamine status, and a normal level does not exclude the diagnosis of thiamine deficiency.[4,8] An individual is said to be thiamine deficient when a thiamine level or functional activity test is below a population-based standard.[7] Given that these tests are often not readily available, test results can be delayed. The clinician should act on clinical judgment and initiate treatment without waiting for laboratory confirmation.[4] Additional testing can be helpful, and include electrodiagnostic testing, which will typically show an axonal polyneuropathy worse in the lower extremities, and nerve biopsies, which will demonstrate axonal degeneration.[8]

Treatment of thiamine deficiency is thiamine replacement. Thiamine is very safe, regardless of route of administration.[4,8] Given the safety and affordability of thiamine, a high degree of clinical suspicion and prompt treatment is recommended in high-risk populations.[7] When administering thiamine, route of administration should be considered – orally administered thiamine is less effective at increasing blood thiamine compared to intravenous doses.[7] For patients with high suspicion or proven thiamine deficiency, thiamine is recommended to be administered intravenously at a dose of 200 mg, three times a day.[4] After clinical improvement, thiamine can be given orally at a maintenance dose of 50-100 mg daily.[4] Clinical improvement can be slow, and neurological improvement may take 3-6 months with motor manifestations responding better than sensory symptoms. In patients with severe neuropathy, permanent deficits may persist, and ongoing physical therapy is important.[8] Treatment of thiamine deficiency also involves addressing the underlying cause, when possible. Patients with chronic alcohol use disorder should be counseled and instructed to abstain from alcohol.

Conclusion

Thiamine deficiency is uncommon but can be quickly precipitated in high-risk groups, such as individuals with chronic alcohol use disorder. The signs and symptoms of thiamine deficiency are nonspecific and overlap with signs and symptoms of unrelated disorders. Dry beriberi manifests with an ascending, peripheral, sensorimotor polyneuropathy. Testing involves serum assays that are often readily unavailable which can delay diagnosis. Treatment is thiamine replacement; however, oral thiamine may be insufficient for clinical improvement. High clinical suspicion is important and prompt treatment, even in the absence of confirmed laboratory diagnosis, is critical in high-risk patients.

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