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CLINICAL QUIZ

An adolescent on peritoneal dialysis with acute encephalopathy: Answers

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Answers

1. Thiamine deficiency presenting as Wernicke's encephalopathy and depressed cardiac function.
2. Serum thiamine level.
3. Intravenous thiamine boluses.

Total parenteral nutrition (TPN) was started on hospital day 7 as the patient was still intubated and stuporous. Prior to initiation of TPN, serum thiamine and cobalamin levels were obtained given the patient's history of malnutrition and chronic peritoneal dialysis (PD). On hospital day 11, the patient began to improve. She was extubated, able to respond to basic questions but remained withdrawn and taciturn and not back to baseline. A repeat echocardiogram showed resolution of abnormal left ventricular function. TPN was discontinued as the patient began to tolerate small amounts of food. The patient was then transferred back to the Nephrology service for further care.

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On the Nephrology service, she continued to act withdrawn and minimally responsive. On hospital day 15, results for serum thiamine levels came back as 28 nMol/l (reference range 70 – 180 nMol/l). Cobalamin levels were within normal limits. She was given a 25 mg bolus of intravenous (IV) thiamine. Within several hours after this bolus, the patient showed a dramatic improvement in her neurological status. She became more responsive and was able to sit up on a chair at the bedside, order a meal on her own from the hospital menu and text her mother. She was later seen to be ambulating with assistance and interacting with her family members. Thiamine was continued at a dose of 50 mg IV for 1 week, and then continued orally at the same dose. Repeat measurements of the thiamine level obtained after 4 days of thiamine replacement therapy was shown to be >2,000 mMol/l. The patient required physical and occupational therapy services for deconditioning. On hospital day 29, she was discharged home in a much improved condition. Since then the patient has been doing well with no permanent neurological deficit.

Discussion

Thiamine (vitamin B1) is a water-soluble vitamin that is absorbed in the small intestine [1]. Its derivative, thiamine pyrophosphate, is an important cofactor for enzymes involved primarily in carbohydrate metabolism. Thiamine's half-life is short (10–20 days), and it is minimally stored [2]; therefore tissues with a high metabolic demand, such as the nervous system, can quickly become deficient [3], and daily supply is necessary.

Water-soluble vitamins have been reported to be low in adults on chronic PD. This is presumed to be secondary to inadequate intake, peritoneal losses and increased needs [4–6]. Although there have been no studies of serum levels of water-soluble vitamins in children not taking supplements, studies of children on dialysis have shown a low intake of water-soluble vitamins, including thiamine [7, 8]. The Kidney Diseases Outcomes Quality Initiative guidelines on nutrition suggest that children on dialysis receive water-soluble vitamin supplements [9]. It is known that children with chronic kidney disease have a decreased intake of food in general [10] and that this deteriorates with declining glomerular filtration rate [11]. Poor appetite, abnormal taste sensation and chronic inflammation contribute to poor dietary intake [12] and place the pediatric dialysis patient at risk for vitamin deficiencies. Our patient had a history of behavioral food restriction and had experienced vomiting and diarrhea for a few days. This, together with the potential thiamine losses on PD, probably precipitated development of symptomatic thiamine deficiency.

Thiamine deficiency may be clinical or subclinical. The classical clinical disorders include wet and dry beriberi and the Wernicke–Korsakoff syndrome. Our patient presented with acute Wernicke's encephalopathy (WE) which is classically described as a triad of oculomotor dysfunction, ataxia and encephalopathy that deteriorates if not treated to coma and death. It can also present with peripheral neuropathy that typically involves the lower extremities. Although WE is most commonly seen in chronic alcoholics, it can develop in patients with poor nutrition (prolonged fasting or anorexia [13] and bariatric surgery [14]), and it has also been described in adults on dialysis [15]. Central nervous system lupus was less likely in our patient in view of a normal electroencephalogram, normal cerebrospinal fluid immunoglobulin G index and a normal magnetic resonance imaging (MRI) scan. The low serum thiamine level and clinical presentation with ophthalmoplegia, peripheral neuropathy and encephalopathy support thiamine deficiency as the etiology of her neurological impairment. Her impressive response to the first bolus of thiamine then confirmed the diagnosis in this case. Our patient also had depressed cardiac function which required vasopressors. Wet beriberi is characterized by a high output cardiac failure and edema [16]. Although our patient did not have edema, her depressed cardiac function could also be explained by thiamine deficiency.

Laboratory tests available to detect thiamine deficiency include the measurement of erythrocyte thiamine transketolase before and after the addition of thiamine pyrophosphate . However this is a functional assay that may be influenced by factors other than thiamine deficiency [17]. Direct measurement of thiamine in the blood is currently preferred. Although imaging studies are not necessary to diagnose thiamine deficiency, they may help rule out other diagnostic possibilities. MRI findings include areas of increased T2 and decreased T1 signal around the aqueduct and third ventricle and within the medial thalamus and mammillary bodies [18, 19]. However, results of these tests are not necessary for patient management as the diagnosis can be made by clinical suspicion. Treatment should be started without waiting for laboratory confirmation since WE can progress to irreversible neurological damage, coma and death.

Conclusion

The differential diagnosis of encephalopathy in a child on PD is extensive. Thiamine deficiency should be considered in this differential diagnosis as children on dialysis are at risk for water-soluble vitamin deficiencies. Prompt treatment with intravenous thiamine in patients with a clinical suspicion of thiamine deficiency is recommended as this is associated with dramatic improvement in clinical status.

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