CASE REPORT

Severe lactic acidosis and multiorgan failure due to thiamine deficiency during total parenteral nutrition

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SUMMARY

A 16-year-old perioperative paediatric patient presented with refractory lactic acidosis and multiorgan failure due to thiamine-deficient total parenteral nutrition during a recent national multivitamin shortage. Urgent empiric administration of intravenous thiamine resulted in prompt recovery from this life-threatening condition. Despite readily available treatment, a high index of suspicion is required to prevent cardiovascular collapse and mortality.

BACKGROUND

Lactic acidosis is an ominous sign, especially when it occurs with concomitant cardiovascular collapse. Because of the widespread use of total parental nutrition in critically ill patients and the ongoing shortage of multivitamins, energy failure due to thiamine deficiency should be considered. The objective of this report is to increase the awareness of the potential for harm of thiamine deficiency during times of multivitamin shortage.

CASE PRESENTATION

A 16-year-old man with progressive ulcerative colitis, which was not successfully treated with medical therapy that included steroids and immunosuppressives, underwent a total colectomy, and total parenteral nutrition (TPN) was initiated prior to surgery. An attempt at enteral feeding failed due to ileus and abdominal pain. On the 20th postoperative day he reported general fatigue, knee and ankle joint pain, weakness, ataxia, and visual and auditory hallucinations.

The patient was transferred to our intensive care unit due to significant tachypnoea, hypotension, severe lactic acidosis, thrombocytopenia and acute kidney injury. He was intubated en route due to decompensated shock.

On examination he was hypothermic, tachycardic and vasodilated. His temperature was 35.8°C, pulse 122 bpm and blood pressure 85/35 mm Hg. His abdomen was tense and distended. He had epistaxis with active bleeding.

INVESTIGATIONS

Laboratory investigations revealed arterial blood pH 6.85, pO_2 230 torr, pCO_2 55 torr, HCO_3 9.6 mEq/L and base deficit 24 mEq/L. Serum glucose was 771 mg/dL, and urine sugar and ketones were 1+. The patient's serum lactate level was 35 mmol/L. His blood urea nitrogen and creatinine were 37 and 2.6 mg/dL, respectively. He had a coagulopathy with an International Normalised Ratio of 1.9, he was thrombocytopenic with platelets of 79 K/μL, and he had megaloblastic anaemia. His white cell count and liver function were normal. His lipase was elevated at 1669 units/L.

TREATMENT

Fluid resuscitation, sodium bicarbonate infusion and inotropic support with dopamine and norepinephrine infusion were started. Broad-spectrum antibiotics were initiated after appropriate cultures were obtained. A stress dose of hydrocortisone was administered due to concerns of adrenal insufficiency because of the recent steroid taper postoperatively. Insulin infusion was started to treat his significant hyperglycaemia. Coagulopathy and thrombocytopenia were corrected with fresh frozen plasma and a transfusion of platelets, respectively.

Because of his deteriorating clinical condition, severe lactic acidosis and distended abdomen, intestinal catastrophe could not be excluded. He was taken to the operating room for bowel inspection. A moderate amount of ascitic fluid was observed, but no evidence of an abscess or intestinal ischaemia was found. The patient returned to the intensive care unit (ICU) in critical condition.

The patient was also found to have hyperammonemia (NH_3 >500 μmol/L) and was started on continuous venovenous haemodiafiltration (CVVHDF). An echocardiogram was also obtained and showed hyperdynamic function without pericardial effusion.

After excluding other possible causes of lactic acidosis, the diagnosis of acute thiamine deficiency was considered. Further investigation revealed that the patient's TPN formulation contained no multivitamins for more than 3 weeks at the referring institution. The pharmacy had not included vitamins in the patient's TPN due to a national shortage of intravenous multivitamins.[1] It was believed that a thiamine deficiency was the cause of the metabolic acidosis and energy failure. The patient was empirically given 400 mg of thiamine intravenously. A plasma thiamine level was sent prior to administration of thiamine, which was low at 7 nmol/L (reference range 8–30 nmol/L), but this level did not come back until 3 days after the episode.

OUTCOME AND FOLLOW-UP

Within 2 h, the patient's acidosis dramatically improved and he was weaned off inotropic support and insulin. His hyperammonaemia improved, and CVVHDF was discontinued after 6 h. He was extubated after 48 h. Supplemental thiamine therapy was continued and was included in the subsequent TPN formulas.

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His overall clinical condition improved and he was transferred from the ICU after 5 days. His acute kidney injury slowly resolved over a 10-day period. The last parameter to normalise after thiamine correction in this patient was thrombocytopenia (2 weeks). The patient was discharged home after 2 weeks.

DISCUSSION

The fundamental problem in lactic acidosis during thiamine deficiency is the inability of the mitochondria to process the pyruvate via the aerobic pathway. The oxidative metabolism of pyruvate proceeds through pyruvate dehydrogenase (PDH), the Krebs cycle and the respiratory chain. A defect in any of the pathways of pyruvate utilisation may lead to the accumulation of pyruvate. This excess pyruvate is then converted to lactate by lactate dehydrogenase and results in acidosis.[2]

Under aerobic conditions, pyruvate is converted to acetyl-coenzyme A by PDH, which enters the Krebs cycle. An alternative path for pyruvate is conversion to oxaloacetate by pyruvate carboxylase (PC). Neither PDH nor PC functions properly when there is a thiamine deficiency.[2]

Thiamine (vitamin B_1) is a water-soluble vitamin with body stores of 3–4 weeks. Critically ill patients are prone to thiamine deficiency because of pre-existing malnutrition, increased consumption of high carbohydrate nutrition, and accelerated clearance in renal replacement.[3]

The classic neurological symptoms of thiamine deficiency, referred to as Wernicke's encephalopathy, include a mental status change, ophthalmoplaegia and ataxia; these symptoms are only present in a few patients.[4] Systemic complications, termed Beriberi, include high output heart failure and death.[5 6]

Thiamine deficiency has also been implicated in significant haematological manifestations. These include neutropoenia, thrombocytopenia and anaemia.[7] The latter can be megaloblastic, sideroblastic or aplastic.[8] These findings suggest that thiamine might have a role in the regulation of haematopoiesis at the stem cell level.

Other manifestations include hyperglycaemia resistant to insulin, pancreatitis and hyperammonaemia.[9 10] The pathophysiology of the latter in thiamine deficiency is still unclear despite its prompt response to thiamine supplementation.

Although close observation is required, treatment with thiamine is safe, inexpensive, and currently readily available outside of intravenous multivitamin preparations. Current guidelines on parenteral nutrition recommend a daily intravenous dose of 100–300 mg of thiamine during the first 3 days in the intensive care unit when thiamine deficiency is a possibility.[11] Treatment should continue for 7–14 days. Attention to magnesium levels is important during this period because the symptoms of thiamine deficiency will be aggravated by a concomitant magnesium deficiency.[12]

There is a considerable body of literature in children showing the importance of thiamine supplementation during TPN and the potential harm of its deficiency. In 1985 the first case of acute thiamine deficiency during TPN was reported[13] followed by a cluster of cases in the mid-1990s in the setting of a multivitamin shortage.[6] Thauvin-Robinet reported another series of infants with acute thiamine deficiency during TPN, of whom many had a delayed diagnosis leading to high mortality.[3] Current intravenous multivitamin shortage has been intermittent since 2009 and increasing in severity since 2012. The American Society of Parenteral and Enteral Nutrition provided recommendations for management of the intravenous multivitamin shortage to members and clinicians in May 2012.[14] The Food and Drug Administration and the American Society of Health-Systems Pharmacists maintain their drug shortage websites with up to date drug shortage information. Nutrition support teams and pharmacies providing TPN are continuing to develop strategies to manage intravenous multivitamin and parenteral nutrition product shortages, with an increasing number of short supply products.

This case highlights that despite prior publications and notifications, there remains inadequate awareness of the potential for thiamine deficiency in TPN-dependent patients and opportunities for improved communication during times of vitamin shortage.

Learning points

- Thiamine deficiency should be considered in the differential diagnosis of any paediatric patient with severe metabolic acidosis and shock.
- Despite publication of prior cases of thiamine deficiency in total parenteral nutrition-dependent patients during multivitamin shortages, there remains insufficient awareness of the potential for harm.
- Hospitals and providers should consider establishing formalised monitoring programmes for signs of vitamin deficiency during times of vitamin shortage.

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