Acute Pancreatitis in a Patient with Maple Syrup Urine Disease: A Management Paradox

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Maple syrup urine disease (MSUD) is an inborn error of metabolism that causes elevated leucine in the setting of acute illnesses. We describe an 8-year-old boy with MSUD who developed acute pancreatitis and subsequent leucinosis. This case highlights the complexities of fluid management in patients with MSUD. *(J Pediatr 2018;■■:■■-■■).*

Maple syrup urine disease (MSUD) is caused by deficient activity of the branched-chain alpha-keto acid dehydrogenase complex, which catalyzes the first step in the catabolism of branched-chain amino acids (BCAAs): isoleucine, leucine, and valine. When acutely ill, patients with MSUD develop elevated plasma concentrations of leucine. Leucinosis is typically reversible but if inadequately managed can lead to cerebral edema, long-term neurologic impairment, and death. Given the need for emergent evaluation and treatment, the early management of patients with MSUD often is undertaken by pediatric emergency department (ED) providers and hospitalists.[1] We report the management of a boy with MSUD and acute pancreatitis, a recognized complication of MSUD, to highlight the challenges of fluid resuscitation and the need for multidisciplinary care.

Case Report

An 8-year-old boy with MSUD presented to our ED with acute onset abdominal pain and vomiting. He had been diagnosed with MSUD in infancy. His disease was controlled with a diet of BCAA-free enteral formula, restricted protein intake, and supplements of isoleucine and valine. Since birth, he had been hospitalized multiple times due to metabolic exacerbations, with nearly one-half of those admissions occurring before he was 2 years of age. Over the past 6 months, monthly leucine measurements varied from 34 to 503 μmol/L; the level was 181 μmol/L 8 days before presentation (normal: 61-201).

On arrival to the ED, the patient was lethargic but spontaneously returned to his neurologic baseline. Physical examination revealed a tense and tender abdomen. Laboratory results were notable for anion gap metabolic acidosis (bicarbonate 15 mmol/L [normal: 22-30], anion gap 24 mmol/L [normal: 7.0-14.0]), lactic acidosis (lactate 4.8 mmol/L [normal: 0.5-2.2]), hyperglycemia (glucose 10.2 mmol/L [normal: 4.4-7.8]), leukocytosis (white blood cells 33K cells/μL [normal: 5.7K-9.9K]), elevated aminotransferase levels (aspartate aminotransferase 137 unit/L [normal: 2-40], alanine aminotransferase 177 unit/L [normal: 3-30]), and elevated lipase (4030 unit/L [normal: 7-60]). Leucine was 410 μmol/L (**Figure**). An abdominal ultrasound scan demonstrated an enlarged heterogeneously hypoechoic pancreas, peripancreatic inflammatory changes, and complex ascites. The patient was diagnosed with acute pancreatitis, presumed secondary to MSUD.

Because of the risk of cerebral edema, intravenous fluid (IVF) had not been initiated before the diagnosis of acute pancreatitis. Following diagnosis, 10% dextrose IVF with normal saline (NS) was provided at 1.5 times the maintenance rate.

The patient was admitted to the intensive care unit. Because of his recent lethargy, he received no enteral nutrition. BCAA-free parenteral nutrition (PN) was not immediately available. He continued receiving 10% dextrose IVF with NS at 1.5 times the maintenance rate. He subsequently developed hyperglycemia to 19.8 mmol/L and was placed on an insulin infusion to treat the hyperglycemia and promote anabolism. Eight hours after presentation, serum leucine increased to 660 μmol/L. Twelve hours after presentation, he developed manifestations of shock including hypotension, tachycardia, lactic acidosis, and poor urine output. He required a total of 100 mL/kg in normal saline fluid boluses to maintain hemodynamic stability. Twenty hours after presentation, leucine rose to 1276 μmol/L. At that time, BCAA-free PN, 40% dextrose IVF, and 1.5 g/kg/d of intralipid became available and were initiated.

On hospital day 2, the patient developed worsening abdominal distention, and leucine increased to 1326 μmol/L. A computed tomography scan revealed evolving necrotizing pancreatitis as well as multiple thrombi in the superior mesenteric vein, extrahepatic portal vein, and splenic vein. The patient developed signs of cerebral edema, including intermittent

BCAA	Branched chain amino acid
ED	Emergency department
IVF	Intravenous fluid
MSUD	Maple syrup urine disease
PN	Parenteral nutrition

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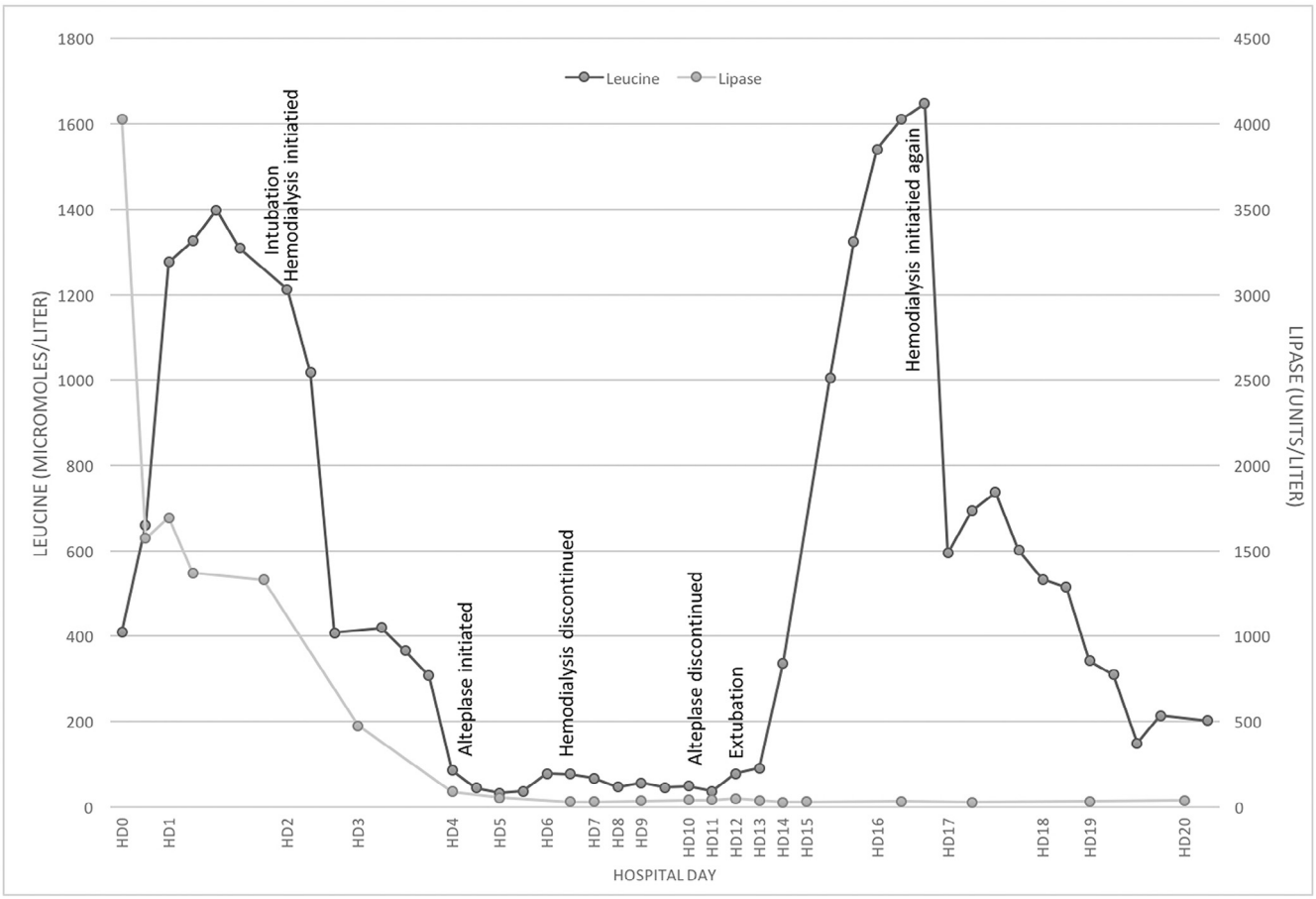

Figure. Leucine and lipase trends over time with significant clinical events noted. On days with multiple laboratory values, each value is placed in order obtained. *HD*, hospital day.

lethargy, slurred speech, tachypnea, and hypertension. His mental status transiently improved with boluses of 3% saline. As the result of his altered mental status, he was intubated. To more effectively treat his leucinosis, hemodialysis was initiated. Following 12 hours of hemodialysis, leucine decreased to 408 μmol/L, whereas other amino acids remained approximately within normal ranges. On hospital day 3, hemodialysis was transitioned to continuous renal-replacement therapy, which continued until hospital day 6.

From hospital day 4 through hospital day 10, the patient also underwent catheter-directed thrombolysis to treat and prevent extension of his vascular thrombi. Leucine reached a nadir of 33 μmol/L on hospital day 5, below the level sufficient for protein synthesis. The patient therefore received intravenous supplementation of BCAA, adjusted daily to maintain sufficient levels.

Despite improvement in both leucine and lipase levels, a repeat abdominal computed tomography scan on hospital day 7 showed a large, loculated peripancreatic fluid collection representing walled-off necrosis compressing the posterior gastric wall, as well as edematous bowel, a large amount of free ascites, and venous thrombosis extending into the inferior vena cava. An ileus of the bowel prevented initiation of enteral feeding.

Following extubation on hospital day 12, enteral nutrition was initiated via BCAA-free formula administered by a nasojejunal tube. As feeding advanced, leucine remained below 100 μmol/L and the patient's neurologic, respiratory, and gastrointestinal examinations remained unchanged.

Unfortunately, on hospital day 15, in the setting of walled-off necrosis and ongoing systemic inflammation, the patient's leucine increased to 1647 μmol/L. Daily hemodialysis was reinitiated on hospital day 16, again with successful resolution of leucinosis. While the patient was receiving hemodialysis, nasojejunal enteral feeding was reintroduced and gradually increased to meet the recommended dietary intake. Hemodialysis was discontinued on hospital day 22, and leucine remained within normal limits thereafter.

The patient was discharged home on hospital day 38. He resumed a diet of enteral BCAA-free formula and low-protein foods. The intact protein allowance was unchanged from the amount prescribed before admission. As the result of persistent hyperglycemia, he continued a subcutaneous insulin regimen after discharge. A fecal elastase level completed 5 months after discharge suggested ongoing pancreatic exocrine insufficiency.

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