Case Report

Methylmalonic acidemia mimicking diabetic ketoacidosis and septic shock in infants

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Abstract

Methylmalonic acidemia (MMA) is most common inherited type of organic acidemia. It has diverse presentation in older infants without any initial apparent symptoms. MMA sometimes present with sudden metabolic decompensation, which may mimics common emergencies like septic shock and diabetic ketoacidosis (DKA) without early recognition can be fatal. In born error of metabolism especially organic acidemia should be suspected in any infant presented with severe high anion gap metabolic acidosis. We report two cases of MMA in infants presented acutely mimicking DKA and septic shock.

Keywords: Anion gap, metabolic acidosis, methylmalonic acidemia

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Introduction

Methylmalonic acidemia (MMA) encompasses a heterogeneous group of disorders that is characterized by impaired metabolism of methylmalonic acid that is generated during the metabolism of certain amino acids (isoleucine, methionine, threonine, or valine).[1] The incidence rate of MMA is 1 in 50,000–80,000 newborns but it is more common in countries with high amount of consanguinity and countries with no systematic newborn screening, like developing countries.[2,3] Patients typically presents at the age of 1-month to 1-year with varied presentations of symptoms ranging from poor feeding, vomiting, dehydration, shock, hypoglycemia, hyperammonemia and hyperglycemias with high anion gap (AG) metabolic acidosis[4,5] if left untreated can lead coma or even death.[6,7] MMA may present suddenly in older infants without initial apparent symptoms, which may mimic septic shock and diabetic ketoacidosis (DKA) and without early recognition can lead fatal consequences. Here we are reporting two cases of MMA in infants presented with severe high AG metabolic acidosis mimicking as DKA in one case and septic shock in an another case even without any initial apparent symptoms.

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Case Reports

Case 1

We report an 8-month-old male child presented in an emergency department with hypotensive shock, respiratory failure and disseminated intravascular coagulation with a short history of nonspecific low grade fever associated with upper respiratory infection and vomiting since 1-day. He was apparently asymptomatic since then. Child was intubated and resuscitated in an emergency department. His initial investigation showed: Hemoglobin (Hb)-6.0 g/dl, total leukocyte count (TLC)-4500 with 55% neutrophil, platelet counts 65/nL, C-reactive protein (CRP)-10 mg/dl, protein thiolation index/activated partial thromboplastin time - no clot, international normalized ratio-9, serum glutamic-oxaloacetic transaminase/prothrombin time - 65/42 and arterial blood gas was PH-7.0, HCO3-2.4, Lactate-2.2, AG-28, blood sugar-122 mg/dl, urine analysis 4 + ketones. Initial diagnosis of septic shock was made and managed accordingly. Blood culture was sterile and cerebrospinal fluid (CSF) examination done after stabilization came normal.

Ketoacidosis remain persisted even after the 24 h of reversal of shock requiring sodium bicarbonate infusion. Hence, underlying metabolic disorder was suspected and was investigated. The child was conservatively managed with fluids, inotropes, fresh frozen plasma, pack cell transfusion, sodium bicarbonate, antibiotics, low protein diet, methylcobalamin, and carnitine. The child responded well to treatment and was extubated after 72 h of admission was shifted out of Pediatric Intensive Care Unit (PICU) on 5th day. Investigation revealed high levels of methyl malonic acids in urine and blood. Neuroimaging revealed bilateral hyperdensities in global pallidus. The child was discharged on 10th day on oral B12 supplementation and low protein diet.

Case 2

We report a 2nd case of previously healthy 1-year-old male child with altered sensorium with a short history of vomiting and low grade fever with no history of seizures. On examination child was comatose with Glasgow coma scale score 9, Kussmaul breathing with signs of dehydration. His initial investigation showed Hb-8.4 g/dl, TLC-15,200/cmm with 70% neutrophils, platelet counts - 720/nL, CRP - 12 mg/dl, blood gas PH - 7.119, HCO3-3.7, AG - 44, lactate 1.04, blood sugar - 485 mg/dl, urine 4 + ketones. An initial diagnosis of DKA was made, and stranded treatment with fluids and insulin infusion was started. After 15 h blood sugar normalized but severe metabolic acidosis persisted. Other causes of poor response to insulin e.g.; dose, administration, and infection were ruled out. Blood culture, CSF examination, and neuroimaging were normal. Persistence of severe high AG metabolic acidosis after 24 h of admission with hemoglobin A1c 4.9%, underlying metabolic disorder was suspected and was investigated to rule out organic acidemia and had high levels of methyl malonic acid. Insulin was discontinued and started on B12, carnitine, low protein diet and sodium bicarbonate and the child responded well to treatment, acidosis was corrected after 24 h and he was shifted out of PICU on 5th day.

Discussion

Methylmalonic acidemia is a rare autosomal recessive disease in which there is a deficiency in conversion of methylmalonic Coenzyme A (CoA) to succinyl CoA. Vitamin B12 is needed to convert the methylmalonyl CoA to succinyl CoA. MMA appears to be more common than other organic academia perhaps because it has several underlying causes.[8-10]

Methylmalonic acidemia can present in the neonatal period. Affected infants present in the first few days of life with vomiting, respiratory distress, feeding intolerance, lethargy, and severe ketoacidosis, which, if not aggressively treated, often progresses rapidly to coma and death.[11,12] A benign variant of MMA is a more frequent form of the disease. It occurs in older children who usually have low levels of methyl malonic acid in blood and urine and have normal growth and development.[8,13] These children present intermittently with acidotic crises and are otherwise normal during crisis-free periods. Increased levels of organic acids including methylmalonic acid can be toxic to various cell types in the body.[14] Metabolic disease must always be considered as possible diagnosis when an infant presents with a severe metabolic acidosis accompanied by an increased AG and other causes of increased AG metabolic acidosis with increased osmolar gap, e.g. drug ingestion should be ruled out.[15]

We report two cases of infants with MMA with sudden decompensation associated with high AG severe metabolic acidosis without any initial signs and symptoms. In first case infant with presented as mimic septic shock responded well to fluid management, but ketoacidosis was persisted even after the shock was corrected. An underlying metabolic disorder was suspected and had very high levels of methylmalonic acids in urine. In another case infant presented with hyperglycemic ketoacidosis with poor response to insulin. Because of persistence of ketoacidosis an underlying metabolic disorder was considered. Hyperglycemia is a rare but fatal manifestation of MMA, which mimics DKA.[16,17] Although hyperglycemia is an unusual presentation for MMA, Boeckx and Hicks, Guven *et al*. and Kumar and Suthar reported cases with severe and persistent metabolic acidosis and hyperglycemia, despite large doses of insulin.[15,18,19] DKA is most common cause of ketoacidosis, but it shows excellent response to standard treatment; therefore other etiologies of acidosis/hyperglycemia should be investigated in poor responders. Organic acidurias (OAs) should be included in the differential diagnosis especially in countries where national newborn screening is not implemented. Determining the etiology of hyperglycemic ketoacidosis is important and can lead to a good outcome.[15] The unusual presentation of our patients, mimicking DKA and septic shock reminds us of the wide spectrum of clinical signs of organic acidemia. In very young patients with severe acidosis and metabolic decompensation, or with atypical clinical course should lead a suspicion of a less common diagnosis such as organic academia to prevent severe morbidities and even death.

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