# Methylmalonic acidemia and diabetic ketoacidosis: An unusual association

Sir,

We read with interest the recently published article "methylmalonic acidemia (MMA) mimicking diabetic ketoacidosis (DKA) and septic shock in infants" by Saini *et al*.[1] and would like to make some important comments.

Methylmalonic acidemia commonly presents as acute metabolic decompensation with hypoglycemia.[2] MMA manifesting as hyperglycemia or DKA is rare, only nine cases have been reported till date including one by Saini *et al*.[1] Boeckx and Hicks[3] for the first time reported a female neonate with severe and persistent metabolic acidosis and hyperglycemia, despite large doses of insulin, who had increased methylmalonic acid levels in urine, but she died before any further investigations. Mathew and Hamdan[4] reported a newborn girl with transient diabetes mellitus in association with MMA, and she died at the age of 6 months. Another interesting case was described by Abramowicz *et al*.[5] with a $mut^0$ form of MMA with complete absence of pancreatic β cells causing insulin-dependent diabetes mellitus (IDDM). Ciani *et al*.[6] reported a case of late-onset MMA in a 12-year-old female who presented with vomiting, fever, bronchopneumonia and coma associated with hyperglycemia, ketoacidosis, and hyperammonemia. She was misdiagnosed as a case of IDDM and died 3 days later despite receiving insulin. Filippi *et al*.[7] reported a newborn suffering from acute neonatal-onset MMA presented with dehydration, ketoacidosis and hyperammonemia and insulin-resistant hyperglycemia and later on died. A 13-month-old girl was presented with DKA and later on diagnosed as MMA.[8] Imen *et al*.[9] reported a 14-month-old male child who presented with an acute generalized dystonia and lethargy. Investigations revealed hyperglycemia, lactic acidosis, hyperammonemia, and increased urinary methylmalonic acid, tiglylglycine and methylcitrate leading to the diagnosis of MMA. With symptomatic treatment, there was rapid improvement in general condition, consciousness and gradual normalization of glucose after 6 days without using insulin. Sharda *et al*.[10] reported a 13-month-old boy who presented with vomiting, dehydration, coma, hyperglycemia, high anion gap metabolic acidosis (HAGMA) and ketosis. He was

treated in line of DKA with parenteral fluid, electrolytes, and insulin infusion that resulted in an improvement in hyperglycemia, but the persistence of HAGMA and lack of improvement of neurologic status. Urinary organic acid analysis revealed increased methylmalonic acid levels. He also had hyperhomocysteinemia and homocystinuria in the presence of normal Vitamin $B_{12}$ levels. There was some improvement in the neurologic status and metabolic parameters after treatment with low-protein diet, vitamin B12, folic acid, and L-carnitine, but he succumbed to polymicrobial nosocomial sepsis.

Six of these nine (2/3rd) reported cases of MMA presented as DKA died, without any information on long term outcome of those who survived. So, DKA is an exceptional manifestation of MMA and could be a marker of poor prognosis.[9-11] The unusual presentation of MMA as DKA reminds us of the wide clinical spectrum of inborn errors of metabolism. In very young patients, who present with DKA and on being treatment with fluid and insulin show rapid improvement in hyperglycemia and/or poor response in metabolic acidosis or neurological status should be worked up for organic acidemia in particular MMA.

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