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Case report

Double trouble with Maple.

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Abstract

Maple Syrup urine disease (MSUD) is a rare inborn error of metabolism of branched chain amino acids which may present in the newborn period with poor feeding, seizures, altered sensorium and death. We describe rare case of MSUD in a set of monozygotic twins with possible pyruvate E3 complex deficiency.

Keywords: Maple syrup urine disease, Encephalopathy, Metabolic acidosis, Ketonuria, Lactic acidosis, Newborn

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Introduction

Maple Syrup urine disease (MSUD) is an autosomal recessive metabolic disorder characterized by the deficiency of branched chain keto-acid dehydrogenase deficiency which causes accumulation of branched chain aminoacids such as valine, leucine and isoleucine. These aminoacids especially leucine leads to encephalopathy and death [1]. The incidence of MSUD is 1 in 2,00,000 [1].. We describe here a pair of monozygotic twins with MSUD with possible pyruvate E3 complex deficiency.

Case report

A preterm (36 weeks) male baby born by spontaneous vaginal delivery as the first of a twin to a primi mother with normal Apgar score was admitted in NICU at 44 hours of life with poor feeding , reduced activity and convulsions . Within 1 hour, the other male twin was also admitted with similar complaints. The parents were consanguineous, antenatal history was normal and USG had revealed diamniotic monozygotic twins. The first and second twin weighed 2.39 kg and 2.29 kg respectively. There were no problems immediately after delivery and they were breastfed.

On examination the twins were lethargic, hypotonic with reduced spontaneous limb movements. General examination was normal and there was no peculiar odor. Both babies had marked tachypnea. However, auscultation of the chest revealed bilateral equal air entry and no added sounds. The cardiovascular system and abdomen were also normal. Investigations revealed no evidence of sepsis and electrolytes were normal. But hypoglycemia was noted in both the twins. They were administered oxygen by bubble CPAP and dextrose IV. After initial dextrose bolus followed by continuous infusion at 8 mg/kg/minute for 24 hours, euglycemia was achieved. Further seizures even with normal blood sugars were controlled with phenobarbitone and phenytoin. Despite supportive care, there were features of shock and dopamine was added at 10µg/kg/minute in addition to appropriate IV fluids. Around 72 hours of life, both babies started having acidotic breathing. In view of increasing respiratory distress and shock, they were intubated and ventilated in PSIMV mode. As acidosis persisted even after correction of hemodynamic status, bicarbonate correction was given.

Investigations for sepsis including CRP, micro ESR, band cell count were normal. Blood cultures were sterile and CSF analysis was normal. Hemogram, renal and liver function tests did not reveal any abnormality. Chest x-ray and echocardiography were normal while ultrasonography of the cranium revealed evidence of cerebral edema. Shock and encephalopathy in the absence of evidence of sepsis in the twins made us suspect IEM. The initial blood and urine reports are depicted in table 1. Based on these lab reports, a possibility of maple syrup urine disease /organic academia was suspected.

Despite supportive care and mechanical ventilation, the babies remained lethargic. Both were given intravenous high dextrose fluids, vitamin cocktail including thiamine and carnitine with bicarbonate correction for acidosis. Blood samples were taken for tandem mass spectrometry (TMS) and gas chromatography mass spectrometry (GCMS)and the values are depicted in Table 1. With this nutritional management, the arterial blood gas parameters showed mild improvement initially but on day 6 of life

twin 1 had worsening of sensorium and acidosis. Peritoneal dialysis was done but unfortunately sustained cardiac arrest on day 9 of life and could not be revived. The second twin also eventually died on the next day.

Table 1. *Investigational parameters of the twins*

Investigation	Twin 1	Twin 2
Blood group	B+	B+
Blood glucose at admission	26 mg%	30 mg%
pH at 72 hours of life	7.08	7.09
HCO3 at 72 hours of life	2.1	2.9
Pco2 at 72 hours of life	7.3	8.2
Base deficit	27.9	25.1
Urine Ketones	Positive	Positive
Urine organic acids	Positive	Positive
Urine reducing substances	Negative	Negative
Serum ammonia Normal (11-35 mmol/l)	63.5 mmol/l	56.4 mmol/l
Serum Lactate (Normal 3-12mg%)	102 mg %	94 mg %
Leucine	High	High
Isoleucine (Normal <350 nmol/L)	579 nmol/L	520 nmol/L
Valine (Normal <250 nmol/l	357 nmol/L	321 nmol/L
GCMS	Elevated 3-0H butyrate, lactate	Elevated 3-0H butyrate, lactate

Discussion

MSUD is a rare IEM with autosomal recessive inheritance and the reported incidence is 1 per 2,00,000 newborn infants . It was first described by Menkes et al in 1954 [2]. It is caused by a deficiency of the enzyme branched-chain 2-keto dehydrogenase (BCKAD) complex which catalyzes the conversion of each of the 3-ketoacid derivatives of the branched chain amino acids (BCAAs) - leucine, isoleucine, and valine into their decarboxylated coenzyme metabolites within the mitochondria [2,3].The disease most commonly presents in newborn period. The children will be apparently normal till 2-3 days of life and may develop lethargy, poor feeding, poor activity, convulsions, hypotonia alternating with hypertonia after consumption of breast milk or formula. The odour of maple syrup may be detected in saliva, breath, urine, faeces and cerumen from the ear. As the disease progresses, babies become more and more obtunded and eventually lapse into deep coma and these may be due to severe cerebral edema [3,4]. Our twins had similar presentation but there was no specific odour.

The biochemical features include metabolic acidosis ketonuria and normal ammonia values. The levels of the plasma BCAAs leucine, isoleucine, and valine will be elevated [4] . Very Rarely patients may have a defect in the enzyme 2(E2) component or, in the enzyme 3(E3) component which manifests as lactic acidosis. The twins described above had classical biochemical features and at normal hemodynamic status, arterial blood lactate levels were elevated, which implies defect in the enzyme 2(E2) component or, in the enzyme 3(E3).There has been case reports of twins with Tangiers [5] and Wilsons disease [6] and none so far with maple syrup urine disease and especially with possibility of enzyme 2(E2) or, enzyme 3(E3) complex defect.

Recent evidence shows nutritional management is as effective as dialysis. Nutritional therapy with high calorie and protein free alimentary nutrition was found to lower leucine levels. Rare patients with MSUD may respond favourably to high-dose thiamine therapy [7-9]. The main long term management is to provide BCCA free formula, but one should administer adequate amount of valine, isoleucine to maintain their normal plasma levels. Recently chemical chaperone therapy and liver transplantation have been tried [10]. MSUD has become a part of newborn screening and early diagnosis and intervention should improve the outcome of these patients.

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