

CLASSIC MAPLE SYRUP URINE DISEASE IN A 46-DAY- OLD BABY - A CASE REPORT

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Submission date: 10-Nov-2017 09:20PM (UTC+0500)

Submission ID: 877769080

File name: 18005-70985-1-RV_-_Copy.docx (27.67K)

Word count: 1178

Character count: 6648

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**CLASSIC MAPLE SYRUP URINE DISEASE IN A 46-DAY-OLD
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ABSTRACT:

Maple syrup urine disease (MSUD) is an inborn error of amino acid metabolism secondary to enzyme defect that breaks down branched chain acids (BCAA). Accumulation of these amino acids and their corresponding keto-acids in the body progresses to neurodegenerative disorders and encephalopathy in undiagnosed infants. We report a case of 46 day old baby with classical clinical and biochemical findings consistent with MSUD. Baby was investigated for inborn error of metabolism after he developed lethargy and his oral intake reduced on fifth day of life. A diagnosis of MSUD was established after analysis of plasma and csf amino acid profile. Baby was treated accordingly and improvement in his condition was seen afterwards.

Keywords: inborn error of metabolism, neurodegenerative

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INTRODUCTION:

Maple syrup urine disease is an autosomal recessive disorder characterized by malfunctioning of the branched-chain α -ketoacid dehydrogenase (BCKAD) complex, that is involved in the catabolism of branched-chain amino acids (BCAAs) which includes leucine, isoleucine, and valine. Maple urine syrup disease is marked by elevated levels of branch chain ketoacids in the urine along with elevated BCAAs in the plasma.¹

The disease is characterized by feeding difficulty, neurological deficit, encephalopathy and a maple syrup odor of the urine.¹ MSUD is responsive to dietary restriction. Nutritional management comprises of specially formulated BCAA free food which provides 80%–90% of protein and energy needs.² Metabolic acidosis is one of the main causes of neonatal and infant mortality. Survivors inevitably have mental retardation, developmental delay, spastic paralysis, cortical blindness, and other neurologic impairment.³

Worldwide incidence of approximately one in 185,000 cases has been reported.⁴ The incidence of MSUD is 9.1% among other amino acidopathies according to a study conducted in Karachi Pakistan.⁵ Here we are presenting a classic case of MSUD in a 46 days old baby.

CASE REPORT:

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A 46-day-old baby boy presented to our neonatal intensive care unit in December, 2016 with complaints of lethargy and not taking feed since fifth day of life. Baby was born through lower segment caesarian section at a public sector hospital with uneventful antenatal and intra partum history. Baby developed lethargy and decreased oral intake on fifth day of life and was admitted to hospital for 2 days, where he was managed for neonatal sepsis. Baby was

discharged on request and brought to our hospital with the manifestation of reduced oral intake, lethargy and unresponsiveness. On presentation the baby was hypotonic and unresponsiveness with a score of 3/15 on Glasgow Coma Score. His weight was 3.0 Kg, length was 48 cm and Occipito-frontal circumference (OFC) was 35 cm, all of which lie at the 50th centile for age and gender. The baby had diminished reflexes in all four limbs. Pupils were equal bilaterally and reactive to light. The rest of the systemic examination was unremarkable.

Parents of the baby were consanguineously married and he has one normal and healthy male elder sibling. Maternal history of Pelvic Inflammatory Disease, Gestational Diabetes Mellitus, Urinary Tract Infection and drug intake during the pregnancy was absent. During pregnancy mother had her regular antenatal checkups every month during which growth and anomaly scans were done which were normal. Family history was unremarkable. The baby was admitted and empirical treatment for neonatal sepsis, with broad spectrum antibiotics, was started.

Initial laboratory evaluation revealed a normal complete blood count profile, Prothrombin Time /Partial Thromboplastin time, C- reactive protein (CRP) and blood glucose levels. Arterial blood gas revealed metabolic acidosis. CSF examination was normal for cell count, proteins and glucose. Workup for an inborn error of metabolism was initiated and revealed a plasma lactate to be mildly elevated and plasma ammonia level was found to be 240µmol/L . His plasma amino acid analysis by Ion Exchange Chromatography showed elevated plasma Leucine and isoleucine levels. CSF was also analyzed by High Performance Liquid Chromatography which revealed abnormal levels of Leucine and isoleucine levels, however valine was found to be <1.

PLASMA AMINO ACID ANALYSIS BY IEC		
	Plasma levels	Normal levels
Leucine	2303	46-147µmol/L
Isoleucine	373	12-77 µmol/L

CSF AMINO ACID ANALYSIS by HPLC		
	Csf levels	Normal levels
Leucine	1192	12.1-19.3µmol/L
Isoleucine	171	3.9-11.3µmol/L
Valine	<1	7.6-18.0µmol/L

On imaging, CT scan brain revealed hypo-attenuation of white matter in bilateral cerebral hemispheres with effacement of extra cerebral CSF spaces and slit like lateral ventricles suggestive of cerebral edema

On the basis of plasma and CSF amino acid profiles along with the clinical picture a diagnosis of Maple Syrup Urine Disease was established. MSUD special formula treatment was commenced along with oral Thiamine in the form of injection Neurobion in OG feeds. There was marked improvement in the neurological status of the baby with improvement of GCS to 12/15 on day 8th of life. The family was counseled regarding the disease prognosis and recurrence in future pregnancies and baby discharged home on MSUD special formula.

DISCUSSION

MSUD is a rare disorder and thus ³ published reports of diagnosis and treatment usually involve only a few patients and most have focused on management of the acutely ill neonate.⁶ However literature review confirms a case of MSUD in a 2 day old neonate reported in Turkey.⁷ Furthermore a retrospective study¹ confirmed 10 cases of MSUD in China.⁸ MSUD has five discrete clinical phenotype namely classic, intermittent, intermediate, thiamine¹ responsive and di-hydrolypoyl dehydrogenase (E3)-deficient, that are genotypically unrelated.¹

The classic form is manifested in the first week of life with complaints of poor feeding and vomiting that progress to lethargy, convulsions and finally coma. Similarly our case presented on 5th day of life with lethargy, drowsiness, reduced¹ feed intake and altered GCS score. Most cases of MSUD are often misdiagnosed neonatal sepsis or meningitis, and death may occur resultantly if untreated. The intermittent form usually affects older children and symptoms become evident during stress situations. Intermediate form of MSUD has less severe presentation with delayed onset of neurological symptoms.⁹ Parents of our case are consanguineously married and studies have proved that consanguinity increase the chance of occurrence of MSUD as it is an autosomal recessive disorder.⁵

The diagnosis of MSUD can be established on the basis of clinical features, elevated BCAAs⁴ and branched-chain hydroxyacids and ketoacids (BCKAs) in urine. Newborn screening is possible with the help of tandem mass spectrometry which⁴ measures the amount of combined leucine-isoleucine concentration in the whole blood and its ratio to other amino acids such as alanine and phenylalanine. Cranial CT scan is helpful in detecting cerebral edema.¹⁰ MSUD treatment comprises of a restricted consumption of proteins, with the addition of a semi-synthetic formula of essential amino acids that lacks leucine, isoleucine and valine.¹¹ Studies have shown that thiamine supplementation helps in lowering the levels of BCAA in plasma.¹² This treatment

plan targets to bring the plasma levels of BCAA within normal ranges, thus downscaling the effects of neurological damage associated mainly with raised leucine levels.¹¹ Genetic counseling must be done to reduce occurrence of MSUD.¹⁰

MSUD is a rare disease which is difficult to diagnose and even difficult to treat. A high index of suspicion should be kept in mind in order to timely diagnose and manage this otherwise fatal disease.

REFERENCES:

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