Short Chain Acyl Co-A Dehydrogenase Deficiency
A Rare Inborn Error Of Metabolism

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Abstract:**Background & objectives**: Short chain acyl coenzyme A dehydrogenase deficiency (SCADD) is a rare autosomal recessive inborn error of mitochondrial fatty acid β oxidation. The energy producing fatty acid oxidation pathway is affected at the first step due to deficiency of short chain acyl coA dehydrogenase and is manifested as lethargy, metabolic acidosis and hypoglycaemia. We report a case ofeight day old male neonate born to 32 year old female by caesarean delivery diagnosed with SCADD. **Investigations**: Blood investigations of haematology, serum electrolytes, and enzymes levels were done. Metabolic screening for TSH, galactosaemia, blood ammonia was also conducted. **Results**: Serum sample revealed elevated acyl carnitine levels and urine analysis for organic acid showed slightly elevated Methyl malonic acid. The neonate was mechanically ventilated and metabolic acidosis was corrected with 8.4 % sodium bicarbonate andintravenous dextrose. Carnitor syrup 5ml/500mg was started once daily and the neonate improved in general activity along with weight gain. **Conclusion:** Neonatal screening by biochemical method facilitates earlier diagnosis and, along with effective management prevents morbidity and prolongs survival.[Prasad A NJIRM 2014; 5(1): 125-127]

Key Words: SCADD, fatty acid oxidation, inborn errors of metabolism.

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Introduction: Short chain acyl coenzyme A dehydrogenase deficiency (SCADD, MIM # 201470) is a rare, inherited, autosomal recessive inborn error of mitochondrial fatty acid oxidation first reported in california.[1] Mitochondrial fatty acid oxidation results in sequential cleavage of 2 carbon units from fatty acids. It represents an essential source of energy for the body during fasting and metabolic stress. Short chain acyl coenzyme A dehydrogenase (SCAD, MIM # 606885) is in the family of Acyl CoA dehydrogenase (ACAD), catalyses butyrylcoA dehydrogenation during the first step of short chain fatty acid β-oxidation.[2,3] Deficiency of SCAD results in accumulation of its substrate butyryl CoA (C4-CoA) and its corresponding by-products like butyrylcarnitine (C4-C), butyryl glycine, ethylmalonic acid (EMA) and methyl succinic acid in blood, urine and cells.[4] SCADD generally present with developmental delay, hypotonia, epilepsy, behavioural disorders and hypoglycaemia.[5] Though very few cases of SCADD have been reported, early diagnosis along with effective management minimises morbidity and prolongs survival.[6] In this article, we report the case of a neonate diagnosed with SCADD by clinical suspicion and biochemical tests which aided successful management.

Case Presentation: An 8 days old male neonate was referred to us with history of poor sucking and lethargy. He was born to a 32 year old female, three days prior to expected delivery date by caesarean delivery. The birth weight of newborn was 2510 g, with head circumference of 35.5 cm and crown rump length 49.5 cm. On hospitalisation, he had acidotic breathing, firm hepatomegaly and hypoglycaemia.Physical findings showed a heart rate of 144/min, respiratory rate 84/ min and capillary refilling time of less than 3 seconds. Baby was intubated immediately and mechanically ventilated by synchronised intermittent mandatory ventilation (SIMV). To correct metabolic acidosis pH (7.1) and hypoglycaemia (40 mg/dL), he was intravenously administered sodium bicarbonate 8.4 % and Dextrose 12.5%, followed by IV fluids. The possibility of inborn error of metabolism and sepsis was suspected; urine and blood samples were collected for metabolic screening.

Investigations: Blood investigations of haematology, serum electrolytes, and enzymes levels were normal. Metabolic screening for TSH, galactosaemia, blood ammonia was within the normal range.

Urinary analysis showed

- Proteins - ++
- Ketones strongly positive - +++
- Elevated amino acid profiles of glycine, alanine, valine, tyrosine and arginine.
- Organic acid level in the urine showed methyl malonic acid and acetoacetate.

Table 1: Test Performed in Blood sample

Parameters	Observed results:
Arterial blood gas analysis	Metabolic acidosis
Ammonia	216 mcg/dL
Glucose	105 mg/dL
Lactate	95.1 mg/dL
Pyruvate	6.2 mg/dL
Potassium	3.2 mmol/L
TSH	0.602 mIU/mL
Total bilirubin	0.3 mg/dL
Direct bilirubin	0.2 mg/dL
Total Protein	6.0 g/dL
Serum albumin	3.7 g/dL
Globulins	2.3 g/dl
AST	39 U/L
ALT	12 U/L
ALP	151 U/L
Uric Acid	10.8mg/dL
Urea	53 mg/dL
Serum Creatinine	0.7 mg/dL
Creatinine phosphokinase (CPK)	155 U/L
hs-CRP	1 mg/L

Figure 1: Test for Rothera's (Violet ring) &Tyrosine (Positive -Red Colour)

Figure 2: Tyrosine crystals in urine microscopy

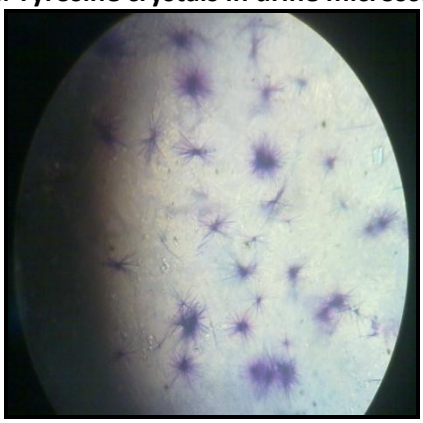

Table 2: Test Performed using HPLC- Urine sample

Amino Acid	Levels in HPLC	Normal Ranges
Serine	292	150-480
Glycine	572	220-403
Glutamine	2466	-
Taurine	538	-
Tyrosine	380	61-159
Tryptophan	425	137-391
Valine	1190	114-265
Leucine	350	65-168
Isoleucine	540	28-74

Table 3: Tests Performed in the Urine sample

Qualitative test	Result
Nitroprusside test (Homocysteinuria)	Negative
DNPH test (MSUD)	Negative
Ferric Chloride test (Phenylketonuria)	Negative
Benedict's test (Reducing Sugars)	Negative
Homogentisic acid (Alkaptonuria)	Negative
Sulfites	Positive
Alpha Nitrosonaphthol test (Tyrosinuria)	Strongly Positive (Figure 1)
Methylmalonic acid test (MMA)	Negative
MPS Spot test	Negative
Rothera's test (ketone bodies)	Reddish violet ring-Strongly Positive (Figure 1)
Urine Creatinine (random)	21.4mg/dL

Outcome and follow up: He was started with 2.5 ml of syrup Levo-carnitine (5ml/500mg) once a day per oral. Organic acid urine analysis repeated after three days showed negative results for P-hydroxyphenylpyruvic acid, homocysteine, homogentisic acid and tyrosine. The baby improved in its general activity, sucking and weight gain was noticed with no acidotic features.

Discussion: SCADD is an error in beta oxidation fatty acid metabolism detected at an early stage by neonatal screening.[2,5] Patient can derive benefit from early detection of fatty acid oxidation defects. Prior to newborn screening, approximately 25% of known MCADD patients died and another 30–40% of cases exhibited variable developmental delay.[7] SCADD patients have a variable clinical presentation and patients diagnosed by neonatal screening are largely asymptomatic and benign. Newborn screening when performed by tandem mass spectrometry and biochemical urine organic acid levels like acyl carnitine levels, ethyl malonic acid have confirmed the diagnosis.[8] However genotype–phenotype correlations of SCADD patients have been inconsistent.[9] Patients identified before the onset of symptoms and managed with appropriate preventive urgent care service have little morbidity and rare mortality with significant cost benefit to the health care system.[10] Therefore, we describe another case of SCADD with typical clinical symptoms like lethargy, poor sucking and hypoglycaemia which was confirmed biochemically by elevated acyl carnitine, and methyl malonic acid levels.

Conclusion: Screening for SCADD should be implemented in neonatal screening to achieve early diagnosis and treatment which could prevent long term complications. It ensures that the rare metabolic disorder can't be missed out.

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