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Case Report

A case of short, medium and very-long-chain fatty acid oxidation disorder in a term infant

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ABSTRACT

A case of a 2nd born baby to healthy parents with second-degree consanguinity. A term female baby, with APGAR 1 minute and 5 minute-8/10 and 9/10 respectively, developed neonatal jaundice on day 2. On day 4, the baby started to refuse breast milk and was lethargic with poor tone and a weak cry. The baby had hypoglycemia, hypertrophic obstructive cardiomyopathy and diagnosed to have fatty acid oxidation disorder by tandem mass spectrometry, which was later confirmed by genetic testing.

Keywords: Fatty acid β-oxidation, Cardiomyopathy, Hypoketotic hypoglycemia, Carnitine, Fatty acid oxidation disorders

INTRODUCTION

Fatty acids are released from adipose tissue storage when there is a requirement of energy demands during prolonged fasting, increased energy demands during stress or illness and periods of reduced intake.[1] Few among the fifteen identified fatty acid disorders are primary carnitine deficiency, long-chain hydroxy acyl-CoA dehydrogenase or mitochondrial trifunctional protein (LCHAD/MTP), glutaric aciduria type 2, deficiencies of carnitine palmitoyltransferase 1A (CPT1A), short-chain acyl-CoA dehydrogenase (SCAD), medium/short-chain hydroxy acyl-CoA dehydrogenase (M/SCHAD), very long-chain acyl-CoA dehydrogenase (VLCAD) and carnitine acylcarnitine translocase (CACT).[2-4] According to reports from Australia, Germany and the United States, the combined incidence of all FAODs is 1 in 9000, but it appears to be much lower in Asian countries.[5] The presentation of fatty acid disorders is varied in people of different ages. The most severe life-threatening manifestations in infants can happen within a few hours of fasting, whereas in adults can take up to 48 hours. The neonatal-onset type is often fatal, with newborns developing profound cardiomyopathy, hypoketotic hypoglycemia and liver dysfunction within days or weeks of birth. Hepatic dysfunction, hypoketotic hypoglycemia, encephalopathy and sudden death can all occur in the infantile-onset type, which begins in infancy or childhood with intermittent episodes of lethargy and vomiting associated with other illnesses. Muscle weakness, myalgias, rhabdomyolysis and the risk of renal damage are all symptoms of the later (or adolescent or adult) onset myopathic type.[6-8]

CASE REPORT

An alive term baby girl with an APGAR of 8/10, 9/10 weighing 2.840 kg was born on 19 December 2019. The baby was active with a good tone and cry and was on breastfeeds. On day 2 of life baby developed neonatal

jaundice and was on phototherapy for 2 days and recovered and was shifted by her mother's side.

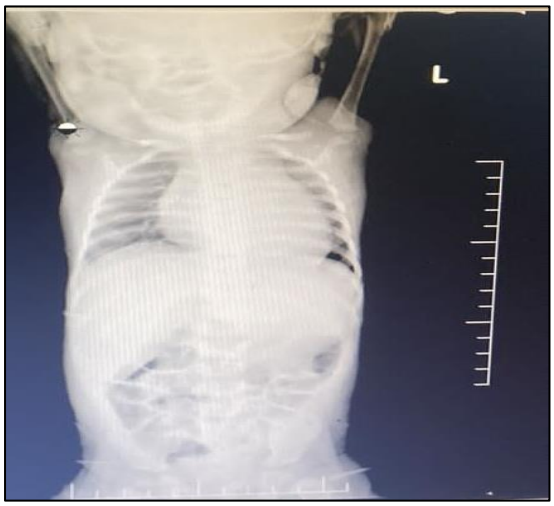

Figure 1: X-ray chest and abdomen of the newborn.

Table 1: Investigations on various days after birth.

Day 1	Day 3	Day 7	Day 10
Hb-16.3gm/dl Total count-17,400 Platelet-3.22 CRP-non reactive	SBR-total 4.65 direct-0.329 SGOT-123 SGPT-192 GGT-265	Hb-14.9gm/dl total count-26,900 platelet-2.54 SBR-total-0.8 direct-0.219 CK-214 CRP-151	Hb-9.6 gm/dl total count-13100 platelet-10,000 SBR-total-0.8 direct-0.219 SGOT-809 SGPT-111 GGT-94 CK-27250 CRP-7200

On day 4 of life baby started refusing breast milk and was lethargic with poor tone and a weak cry. The baby was shifted to NICU and CBG was found to be 28 mg/dl and was started on correction for hypoglycemia with ½ dextrose. Because of high CRP, the baby was started on IV antibiotics and was given expressed breast milk which gave her loose stools and vomiting. She was started on MCT (medium chain triglycerides) and carnitine supplementation by NG tube after diagnosing by tandem mass spectrometry, that she had fatty acid oxidation defect, confirmed by genetic testing as her elder sibling succumbed to cardiomyopathy at 3 months of life. screening 2D ECHO showed hypertrophic cardiomyopathy. The baby was found to have features of sepsis and was given higher antibiotics. Anemia and thrombocytopenia were noted and managed with platelet transfusion. A lumbar puncture was done and was found to be normal. CK values were elevated at -27250. Lactate levels were found to be elevated. The baby was on IV fluids for hypoglycemia correction. The baby showed features of hepatic injury but was tolerating breast milk with an overall improvement in tone, cry and sugar levels and was discharged on day 48 of life. USG abdomen-gall bladder sludge noted.

DISCUSSION

Mitochondrial fatty acid oxidation disorders (FAOD) are inherited errors of metabolism typically present with hypoketotic hypoglycemia, metabolic acidosis, hepatic failure and cardiomyopathy in the neonatal period. Incidence is very rare, that is, 1 in 5000-10000 births.[8]

LC-FAOD can cause hypoglycemia, rhabdomyolysis and cardiomyopathy during times of increased energy demand, such as common infections or moderate exercise. The onset can be sudden and unpredictable and the events can be life-threatening, necessitating emergency medical attention.[9,10]

In a study of 107 cases of inherited fatty acid oxidation defects, symptoms appeared in 84 percent of patients before they were two years old, with about a third of them presenting as newborns.[11] Other symptoms reported in infants included coma triggered by fasting or catabolism, Reye Syndrome-like episodes, cardiomyopathy and symptoms of acute myolysis (46 percent). However, the absence of symptoms in infancy or early childhood does not guarantee that patients will be symptom-free later in life.[12] A 16-year-old girl, for example, developed recurrent exercise-induced rhabdomyolysis that resulted in eight hospitalizations despite being previously healthy. FAOD did not become clinically apparent in a young man with suspected myocarditis until he was 20 years old.[13]

FAOD causes a variety of clinical symptoms, particularly in organs that rely on fatty acid oxidation for energy production, such as the heart, liver and skeletal muscle. FAOD commonly manifests as cardiac dysfunction because fatty acids account for 70% of the heart's energy needs. FAOD-related liver dysfunction usually appears early in life and can range in severity from episodic hypoketotic hypoglycemia to mild liver dysfunction to severe liver disease or Reye-like syndrome. In contrast to the neonatal manifestations of FAOD, the skeletal myopathy symptoms of FAOD usually appear in older people, ranging from toddlers to older children to adults, and usually begin in puberty or adulthood.[14-16]

An acylcarnitine analysis by MS/MS can be performed on newborn screening blood spots to identify and treat patients with a FAOD before they develop symptoms.[17] Pediatricians and other health care providers must be educated about these disorders and how to treat them for such screening programs to have long-term benefits.

CONCLUSION

The FAOD are disorders associated with significant morbidity and mortality. Early diagnosis by TMS and treatment are improving outcomes. The clinical presentations of these disorders range from lethal neonatal cardiomyopathy in the first few days of life to chronic skeletal myopathies. Current treatment strategies include MCT, a low-fat diet and treatment of infections and carnitine supplementation. Even with the significant advances made to date, there remains a significant risk for symptoms including rhabdomyolysis and cardiomyopathy leading to sudden infant death.

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