well.[5] However to best of our knowledge subcutaneous axillary metastasis is being reported for the first time.

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Neonatal intrahepatic cholestatis due to citrin deficiency (NICCD)

Citrin deficiency is an autosomal recessive disorder caused by mutations in the SLC25A13 gene on chromosome7q21.3. It has two major phenotypes: adult-onset type II citrullinemia (CTLN2) and neonatal intrahepatic cholestatic caused by citrin deficiency (NICCD).[1] NICCD is characterized by neonatal/infantile-onset cholestatic hepatitis syndrome associated with multiple aminoacidemia (involving citrulline, threonine, methionine, arginine, and tyrosine), hypergalactosemia, hypoproteinemia, hypoglycemia, cholestasis, and fatty liver.[2] We present a 2 months old with neonatal cholestasis with hepatosplenomegaly and urine organic acids suggestive of NICCD.

Case Report

A 2 months old girl born of non-consanguineous marriage presented with abdominal distension since birth. There was no jaundice. She was born full term and had birth weight of 3.8 kg. She was on breast feeds plus formula feeds. Older brother was asymptomatic. On examination, weight was 5.6 kg, height was 59 cm, she had doll like facies with hepatosplenomegaly. Investigations revealed hemoglobin of 10.9 gm/dl, white cell count of 19,700/cumm, platelets 20,000/cumm, bilirubin 2.8 mg/dl (direct=0.9 mg/dl), SGOT 200 IU/L, SGPT=79 IU/L, total proteins 5.2 gm/dl, albumin 2.4 mg/dl, prothrombin time 16.5 sec., partial thromboplastin time=30.1 sec. Ultrasound abdomen showed hepatomegaly with nephromegaly and 2 nodules in liver 5-9 mm. CT abdomen showed hepatomegaly with bilateral nephromegaly with focal lesion in right lobe of liver. Serum alpha fetoprotein was 1,32,860 IU/L and Beta HCG was normal (1.2). Urine organic acids showed increased excretion of 4 hydroxy phenyl lactate (4 HPL) and 4 hydroxy phenyl pyruvate (4 HPP), phenyl lactic acid, tyrosine, galactose and galactmate with low serine:threonine ratio suggestive of citrin deficiency. Urine succinyl acetoacetate was normal. Plasma aminoacidogram was normal and bone marrow examination was normal. She was started on soya milk

and breast feeds and formula feeds were stopped. She continued to have persistent thrombocytopenia though the liver lesions decreased in subsequent ultrasound. We could not do the genetic testing in the child due to non-availability.

Discussion

NICCD should be suspected in infants with idiopathic cholestasis. At the initial presentation, NICCD patients have higher levels of alkaline phosphatase (ALP) and alpha-fetoprotein (AFP) and lower level of alanine aminotransferase (ALT) than those in non-NICCD patients. NICCD patients show higher citrulline level and threonine/serine ratio than non-NICCD infants.[2,3] Similar features were seen in our patient. In addition, our patient had 2 nodules in the liver which regressed over a period of time. It is thought that citrin deficiency leads to blocking of the malate aspartate shuttle, increasing the ratio of cytosolic nicotinamide adenine dinucleotide to oxidized nicotinamide adenine dinucleotide ($NADH/NAD^+$), which causes an increased lipid synthesis. The high level of fatty acids leads to steatohepatitis that could in turn cause fibrosis and liver cirrhotic nodules.[2,3] Since in our patient the nodules regressed over time, it is unlikely to be nodules of cirrhosis. Another hypothesis is that citrin deficiency behaves like a mitochondrial disorder, and damage caused by increased oxidative stress in the liver might lead to nodule formation.[2,3]

The frequency carriers for the SLC25A13 mutation is one in 65 and one in 48 in the Japanese and Southern Chinese populations, respectively.[4,5] Exact prevalence of NICCD in India has not been documented in literature. Most symptoms in patients with NICCD will resolve within 1 year of age and require no further special treatment. However, several decades later some patients may develop CTLN2. Peculiar fondness for protein and lipid-rich foods but aversion to carbohydrate-rich foods has been recognized in many of them.[2,3] Because clinical manifestations and biochemical findings are nonspecific for NICCD, DNA analysis or Western blot analysis of aspartate-glutamate carrier [AGC2] protein in lymphocytes is the most reliable diagnostic tool.[4,5] We could not do the genetic testing in the child due to non-availability.

This condition is amenable to dietary management, which consists of a high-protein and low carbohydrate diet, and avoidance of risk factors, such as alcohol and certain drugs. It should be noted that lactose may be toxic to NICCD patients and should be avoided while cholestasis persists.[2] The amelioration of NICCD symptoms after infancy suggests hepatocyte maturation and possible compensation by other mitochondrial carriers. However, patients with NICCD should be followed closely as some of them might develop CTLN2, which could be saved by liver transplantation.[6]

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