A rare case of tyrosinemia presenting with abdominal distension with shock

Jenny John Cheriathe1*, Ignatius Edwin D'Souza1, Mahmoud Shamseldeen1
1Department of Pediatrics, Gulf Medical College Hospital and Research Centre, Ajman, UAE

*Presenting Author

ABSTRACT
Tyrosinemia type I is the most severe disease of the tyrosine catabolic pathway resulting from deficiency in fumaryl acetoacetate hydrolase (FAH) leading to elevation of tyrosine in liver, kidney and peripheral nerves. It is characterized by hepatic failure, cirrhosis, renal dysfunction, hepatocarcinoma, and neurologic crisis. The estimated prevalence of type I tyrosinemia worldwide is < 1 in 100,000. We present a rare case of tyrosinemia presenting with abdominal distension and shock. A two-month old male child of 2nd degree consanguineous marriage was born prematurely and was small for gestation (SGA baby). She was noted to have neonatal hyperbilirubinemia in the immediate neonatal period. Weight gain remained poor in spite of adequate feeding and supplementation. Persistent abdominal distension was noted, and anti-flatulence drugs were administered for the same, with no improvement noted. X-ray showed gaseous distension of abdomen. Tests for hypothyroidism and Hirschsprung disease were normal. The baby had persistent vomiting; ultrasonography was normal. After one month she developed cold clammy extremities with thread pulse, poor urine output, persistent vomiting with significantly distended abdomen. Investigations revealed E-coli positive UTI for which appropriate antibiotics were started. However, the condition of the baby deteriorated and baby developed metabolic acidosis which was initially attributed to resistant E-coli sepsis. On investigating further, an elevated level of alpha fetoprotein (AFP) was noted. The other reports revealed significant coagulopathy and the algorithmic work up revealed tyrosinemia. Tyrosinemia type I should be differentiated from other causes of hepatitis and hepatic failure in infants.

Key words: tyrosinemia type 1, fumaryl acetoacetate hydrolase (FAH), abdominal distension

CASE REPORT
A two month old male child was born to 2nd degree consanguineous parents and the mother was elderly primiparous. The baby was noted to have prominent colonic loops on antenatal ultrasound. The baby was born small for gestational age and did not gain adequate weight in spite of adequate feeding and supplementation. Persistent abdominal distension was noted and anti-flatulent drugs were administered. No improvement was observed. Plain X-ray abdomen revealed gaseous distension. Tests for hypothyroidism and for Hirschsprung disease were normal. At two months of life, the baby was noted to have significant abdominal distension, persistent vomiting with poor peripheral pulses, cold clammy extremities and reduced urine output. The initial evaluation showed the presence of E. coli in urine analysis, which was treated with antibiotics. However, in spite of repeat urine culture showing absence of E coli and adequate fluid resuscitation, the baby continued to remain toxic and developed blood stained nasogastric aspirate and severe respiratory distress requiring mechanical ventilation. The blood picture showed significant coagulopathy requiring multiple blood transfusions. In view of poor perfusion and low blood pressure, the baby was put on inotropes. Ultrasonography (USG) of the abdomen showed echogenic kidneys with fullness of pelvi-calyceal system. Blood gas analysis showed metabolic acidosis with urine positive for reducing substance. In view of bleeding diathesis with elevated serum transaminase level and urine positive for reducing substance the possibility of tyrosinemia was considered; serum α-fetoprotein level was markedly elevated. The diagnosis was established by demonstration of elevated level of succinylacetone in the blood.
DISCUSSION

Tyrosinemia type I affects approximately 1 in 100,000 births, the carrier frequency being estimated to be 1:200. Tyrosinemia type I is an autosomal recessive trait. The gene for fumarylacetoacetate hydrolase (FAH) has been mapped on chromosome 15q and numerous mutations have been identified. No correlation is observed between clinical presentation and genotype, and acute and chronic forms have been seen in the same families. One mechanism which explains the clinical variation is gene reversal with spontaneous self-correction. The parents of an affected child are obligate heterozygotes. At conception each sibling of an affected individual has a 25% chance of being affected, 50% chance of being an unaffected carrier and 25% chance of being neither affected nor a carrier.

Untreated tyrosinemia type I presents with severe liver involvement in early infancy or later with liver and renal tubular dysfunction with associated growth failure and rickets. Death in untreated children usually occurs in the first decade, from fulminant hepatic failure, neurologic crisis, or hepatocellular carcinoma. In early infancy an untreated baby may progress to liver failure with ascites, jaundice, and gastrointestinal bleeding. Children may have a characteristic odor of boiled cabbage, and occasionally persistent hypoglycemia or low grade acidosis. In the more chronic disorder proximal renal tubular acidosis with phosphate loss and resultant rickets may develop. Older children present with altered mental status, peripheral neuropathy, and/or respiratory failure requiring mechanical ventilation. Repeated neurological crisis may often be unrecognized, with 10% of deaths among untreated children occurring due to neurologic crisis. Children who are not treated with nitisinone and low tyrosine diet have high risk of developing hepatocellular carcinoma. Among the cases diagnosed before two months of age, the two-year survival is about 29%; those diagnosed between ages of two and six months have a two-year survival rate of 76%, and those diagnosed after six months have a two-year survival rate of 96%.

A diet low in tyrosine and phenylalanine and tyrosine can slow but not halt the disease process. Treatment of choice is nitisinone, which inhibits tyrosine degradation and prevents hepatic and neurologic crisis; but it does not reduce the risk of hepatocellular carcinoma as the pretreatment liver damage is not reversible. In our case the baby presented with significant abdominal distension since birth with poor weight gain. There were no reported cases in the family, so the present case should be considered a sporadic case. The urinary tract infection probably led to sudden deterioration in the general condition of the baby.

CONCLUSION

Tyrosinemia type I should be differentiated from other causes of hepatitis and hepatic failure in infants. Tyrosinemia should be considered in the differential diagnosis of infants presenting with hepatic failure and unexplained clinical deterioration. Early diagnosis and prompt treatment can prevent irreversible neurological damage, although the occurrence of hepatocellular carcinoma cannot be reduced as the liver damage incurred is irreversible. Prenatal diagnosis helps in detecting new cases, and the newborn can be treated since birth thus reducing the likelihood of permanent damage.

REFERENCES

