Case Report

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A Rare Entity in a Common Condition - Congenital Tyrosinemia Type 1

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Abstract

Tyrosenemia type 1 is a rare inherited metabolic disorder attributable to a deficiency of enzyme fumarylacetoacetate hydrolase. It has an autosomal recessive pattern of inheritance. The accumulation of tyrosine and its toxic metabolites succinyl acetone and succinyl acetoacetate in various tissues leads to the charecteristic hepatic failure, renal dysfunction and neurological crisis. Here we report 21 months old child presented with signs and symptoms of hepatic failure. This case report highlights that clinical examination has not lost its significance even in this new era of advanced extensive investigations.

Keywords: Congenital Tyrosinemia; Neurological Crisis; Tyrosin.

Introduction

Hereditary Tyrosinemia type 1 is the most severe disorder of tyrosine metabolism. It is characterized by severe progressive liver disease and renal tubular dysfunction. HT1 is caused by mutations in the fumarylacetoacetate hydrolase gene (FAH). Progression of the liver disease may present as chronic or acute form, with rapid deterioration and early death. Acute form of the disease presents within first month of life with hepatic failure and its complications. However, Chronic form present up to 2 years of life with hepatomegaly and developing cirrhosis. Here we report a case with chronic hereditary tyrosinemia type 1 presented as acute hepatic failure precipitated by drug induced hepatitis.

Case Report

A 21 month old girl referred from outside hospital with history of jaundice for 20 days, generalised anasarca with ascites for 10 days, Vomiting and Altered sensorium for 5 days. She got admitted in private hospital 10 days before with above complaints diagnosed as hepatic encephalopathy stage 3, received symptomatic treatment. After stabilization transferred to our hospital for further management. 5 months back child was started on 3 drugs AKT from outside in view of mantoux positive. On examination there was icterus and bilateral pedal edema with features of vitamin D deficiency. Liver was firm, smooth surface, 3 cm below right costal margin with span of 11 cm. our initial impression was 21 month old female child on AKT with acute hepatic failure with recovering Hepatic encephalopathy along with features of rickets most likely AKT induced Hepatitis or Autoimmune Hepatitis or Wilson's disease or other Metabolic cause. lab investigations showed SGOT/SGPT- 312/216, Total bili/Direct bili- 22/9.2, PT/INR-20/1.7, serum ammonia- 330, vitamin Dlevel 12IU, Ca/PO_4 level- 8.7/4.4, ALP 334. All viral markers were negative. USG abdomen was suggestive of mild hepatomegaly with heterogeneous echo texture of liver. ABG showed Normal Anion gap metabolic acidosis. Urine PH was 6 with high phosphorus level. Meanwhile child started on vitamin A, D, E, K supplements with oral ursodeoxycholic acid. Keeping in mind about hepato-renal involvement in form of firm

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liver with heterogeneous echo texture, rickets and normal anion gap metabolic acidosis; we went ahead with serum alpha protein level which came as high as 11,860. CT abdomen showed micro-nodular cirrhosis. Liver biopsy done also confirmed micronodular cirrhosis with activity and rulled out Wilson's disease as dry copper weight was normal (77 microgm/gm). Urine succinyl acetone level sent, suggested four fold raise in primary tyrosine metabolites indicating congenital tyrosinemia type 1. Child started on tyrosine free diet. FAH gene study sent for confirmation; report awaited.

Discussion

Type1 tyrosinosis is an inborn error of metabolism caused by deficiency of enzyme fumeryl acetoacetate hydrolase. Autosomal recessive disease associated with FAH gene mutation in chromosome 15q 25.1. Patients have peculiar cabbage like odour, with severe liver involvement within 2-6 months of life or later in the first year with liver dysfunction and renal tubular dysfunction (fanconi syndrome) associated with growth failure and rickets. Children may have repeated neurologic crises include change in mental status, abdominal pain, peripheral neuropathy, and/or respiratory failure requiring mechanical ventilation. Death in the untreated child usually occurs before age ten years, typically from liver failure, neurologic crisis, or hepatocellular carcinoma. Typical biochemical findings include: increased succinylacetone concentration in the blood and urine; elevated plasma concentrations of tyrosine, methionine, and phenylalanine; and elevated urinary concentration of tyrosine metabolites and the compound δ-ALA. Genetic testing for FAH gene use for confirmation. Combined treatment with nitisinone and a low-tyrosine diet has resulted in a greater than 90% survival.

Conclusion

This case reports highlights that clinical examination has not lost its significance even in this new era of advanced extensive investigations. All siblings of a child with tyrosinemia type I should screened with urine and blood succinylacetone analyzed as soon as possible to enable the earliest possible diagnosis and initiation of therapy. Early recognition of tyrosinemia type I and adequate treatment should always be followed by intensive follow up for the risk of development of HCC both at the short and the long term.

References

1. Healey PJ, Reyes JD. Liver transplantation for hepatocellular carcinoma in children. Curr Opin Organ Transplant [Internet]. 2006 Oct;11(5):528–31.
2. Sassa S, Kappas A. Hereditary tyrosinemia and the heme biosynthetic pathway. Profound inhibition of delta-aminolevulinic acid dehydratase activity by succinylacetone. 1983 Mar;71(3):625–34. pubmed.
3. Lindstedt S, Holme E, Lock EA, Hjalmarson O, Strandvik B. Treatment of hereditary tyrosinaemia type I by inhibition of 4-hydroxyphenylpyruvate dioxygenase. 1992 Oct:813–7. pubmed.
4. National Organization for Rare Disorders, Physician's Guide to Tyrosinemia Type 1.