University Journal of Surgery and Surgical Specialities

ISSN 2455-2860 2019, Vol. 5(9)

A RARE CASE OF TYROSINEMIA TYPE I

SENTHILNESH A
Department of CHILD HEALTH, MADURAI MEDICAL COLLEGE AND HOSPITAL

Abstract : Tyrosinemia type1 is a rare autosomal recessive metabolic disorder, characterized by the lack of enzyme fumaryl acetoacetate hydrolase which is involved in metabolism of aminoacid tyrosine. This lead to abnormal accumulation of tyrosine and its metabolites in the liver, leading to liver disease. Tyrosinemia has rarely been reported in india due to lack of diagnostic facilities. We present a case of tyrosinemia type1 confirmed with plasma and urinary succinylacetone.

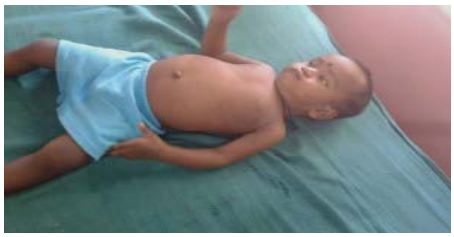
Keyword : Tryosinemia type 1, Fumaryl acetoacetate hydrolase enzyme, Succinylacetone

INTRODUCTION:

Tyrosinemia type1 is common in Quebec and Scandinavia with worldwide incidence of 1per 100,000 population. The first case of typical clinical and biochemical picture of tyrosinemia type 1 was described by sakai et al in 1957.

CASE REPORT:

A 8 month old male child born of consanguineous marriage was brought with complaints of multiple ecchymotic patches over the trunk associated with yellowish discoloration of eyes over a period of 2 weeks. There was no other significant history. On examination the child was icteric and afebrile. The weight was 7kg, head circumference was 42cm and length 70cm. Per abdominal examination revealed a firm liver palpable 3cm below the right costal margin and a firm spleen 3 cms palpable below the left costal margin. The investigations performed were as follows: Hemoglobin- 6.6gm/dL, Total leukocyte count -16800 cells/ cu. mm , Differential count: Neutrophils -30%, Lymphocytes-69%, Eosinophils- 1%, Platelets- 3,42,000 cells/cu.mm, Packed Cell Volume- 24%, Mean Corpuscular Volume -60.9 fL, Mean Corpuscular Hemoglobin- 16.7pg/cell, Mean Corpuscular Hemoglobin Concentration- 27.4g/dL, Red Cell distribution width -40%. Red blood cell count -3.89 million/ cu.mm, Mentzer index -18.2, Reticulocyte count -1.1%. Prothrombin time - 16.5sec (control 12.8), INR -1.28, Peripheral smear study- Hypochromic microcytic anemia . Serum ferritin-183.9ng/mL , Serum iron-152 microgram/dL, Total iron binding capacity- 214 microgram/dL, Transferrin -168mg/dL, iron saturation -71% Random blood sugar was 85mg/dL. Total bilirubin -3.8mg/dL , Direct- 2mg/dL ,Indirect -1.8mg/dL, Total protein- 3.6gm/dL, Albumin -1.5gm/dL, Globulin- 2.1gm/dl, AST- 114 IU/L, ALT -45 IU/L, ALP- 342 IU/L. Urea- 16mg/dL, Creatinine- 0.7mg/dL, HBsAg-negative . Triiodothyronine -143ng/dl, Thyroxine - 12 microgram/dL, Thyroid stimulating hormone -1.27 mIU/L. Ultrasonogram Abdomen showed-mild hepatosplenomegaly and a distended gall bladder. Urine for reducing substance was negative. Suspecting chronic liver disease , liver biopsy was done. It showed cirrhosis with pseudoacinar pattern which suggested a possibility of Tyrosinemia. Plasma and urinary succinylacetone levels were elevated 4.5 and 3 micromoles /L respectively, which confirmed the diagnosis of tyrosinemia.



CHILD AT THE TIME OF ADMISSION

LIVER BIOPSY REPORT

PICTURE OF THE CHILD ON FOLLOW UP (3 MONTHS LATER)

Tyrosine low diet (fruits and vegetables-apple, pear, grapes, watermelon and tyrosine low formula feeds) was adviced. Tyrosine rich diet (milk and milk products, peanuts, cashew, almond, walnut, chicken, eggyolk) was advised to be omitted. The child was kept on regular follow up. The family was provided genetic counseling and explained the inheritance with 25% risk of recurrence in future pregnancy and informed that prenatal diagnosis would be possible.

DISCUSSION:

Hereditary infantile tyrosinemia is caused due to deficiency of the enzyme fumarylacetoacetae hydrolase. Affected infant appears normal at birth and typically presents between 2nd and 6th month of life. The disease manifests in early infancy with acute hepatic crisis and bleeding manifestations precipitated by intercurrent illness that cause catabolic state. Most hepatic crisis resolve spontaneously but may progress to liver failure and death. Between crisis hepatomegaly and coagulation abnormality often persist. The chronic form of tyrosinemia type 1 occurs less frequently than the acute form. Cirrhosis and eventually hepatocellular carcinoma occurs with increasing age. Episodes of peripheral neuropathy mimicking acute porphyria occurs in 40% of affected children.

Renal involvement manifests as fanconi like syndrome with hyperphosphaturia, hypophoshatemia, normal anion gap metabolic acidosis and vitamin D resistant rickets. The diagnosis in this patient was based on hepatosplenomegaly, bleeding diathesis, deranged liver function tests , coagulation profile, and liver biopsy report which suggested a possibility of tyrosinemia. Raised plasma and urinary levels of succinylacetone further confirmed the diagnosis. Molecular diagnosis is possible and it is the preferred technique for prenatal diagnosis. Nitisinone started as soon as possible can prevent liver and renal damage . It can also stop neurologic crisis. It inhibits 4 hydroxyphenylpyruvate dioxygenase there by reducing the formation of toxic metabolites maleylacetoacetic acid and fumaryl acetoacetic acid, which have the potential to be converted to succinylacetone.

Nitisinone increases the blood concentration of tyrosine and tyrosine restricted diet is required. Liver transplant is curative for this disorder and was the mainstay of treatment prior to Nitisinone. Liver transplant may be required in cases where the child develops end stage liver failure, poor response to nitisinone, or evidence of liver cancer. Prenatal diagnosis can be done by three techniques. One method is measuring the level of succinylacetone in amniotic fluid, second method is Enzyme assay in chorionic villi taken at 12 weeks. Third method by molecular technology is the most accurate method, where mutations in fumaryl acetoacetate hydrolase gene can be found. Fumaryl acetoacetate hydrolase gene is located on chromosome 15q and has 14 exons.

CONCLUSION:

It is important to diagnose this rare disorder , where early diagnosis has better outcome. Prompt identification and treatment may prevent liver, kidney and neurological complications.

REFERENCES:

1.Nelson Textbook of paediatrics. First southasia edition. Volume-1 .Kliegman. Stanton.St Geme. Schor. chapter 85.Defects in metabolism of aminoacids.page number640.

2.Essential paediatrics. seventh edition.Op Ghai.Vinod K Paul.Arvind Bagga.chapter 22.Inborn errors of metabolism.page number629.

3. Mitchell GA, Grompe M, Lambert M, et al. Hypertyrosinemia. In: Scriver CR, Beaudet AL, Sly W, Valle D, eds. The Metabolic and Molecular Basis of Inherited Disease, 9th ed. New York: McGraw-Hill, 2001:1777–1805

4. Levine SZ, Marples E, Gordon HH. A defect in the metabolism of aromatic amino acids in premature infants: The role of vitamin C. Science 1939;90:620

5. Kvittingen E. Hereditary tyrosinemia type I—an overview. Scand J Clin Lab Invest 1986;46:27–34 .

6. Mitchell G, Larochelle J, Lambert M, et al. Neurologic crises in hereditary tyrosinemia. N Engl J Med 1990;322:432–437

7. Croffie JM, Gupta SK, Chong SK, et al. Tyrosinemia type 1 should be suspected in infants with severe coagulopathy even in the absence of other signs of liver failure. Pediatrics 1999; 103:675–678

8. De Braekeleer M, Larochelle J. Genetic epidemiology of hereditary tyrosinemia in Quebec and in Saguenay-Lac -St-Jean. Am J Hum Genet 1990;47:302–307

9. Labelle Y, Phaneuf D, Leclerc B, et al. Characterization of the human fumarylacetoacetate hydrolase gene and identification of a missense mutation abolishing enzymatic activity. Hum Mol Genet 1993;2:941–946

10. St-Louis M, Leclerc B, Laine J, et al. Identification of a stop mutation in five Finnish patients suffering from hereditary tyrosinemia type I. Hum Mol Genet 1994;3:69–72

11. Grompe M, St-Louis M, Demers SI, et al. A single mutation of the fumarylacetoacetate hydrolase gene in French Canadians with hereditary tyrosinemia type I. N Engl J Med 1994; 331:353–357

12. Jakobs C, Stellaard F, Kvittingen EA, et al. First-trimester prenatal diagnosis of tyrosinemia type I by amniotic fluid succinylacetone determination. Prenat Diagn 1990;10:133–134

13. Grenier A, Cederbaum S, Laberge C, et al. A case of tyrosinaemia type I with normal level of succinylacetone in the amniotic fluid. Prenat Diagn 1996;16:239–242

14. Kvittingen EA, Steinmann B, Gitzelmann R, et al. Prenatal diagnosis of hereditary tyrosinemia by determination of fumarylacetoacetase in cultured amniotic fluid cells. Pediatr Res 1985;19:334–337

15. Demers SI, Phaneuf D, Tanguay RM. Hereditary tyrosinemia type I: strong association with haplotype 6 in French Canadians permits simple carrier detection and prenatal diagnosis. Am J Hum Genet 1994;55:327–333

An Initiative of The Tamil Nadu Dr. M.G.R. Medical University
University Journal of Surgery and Surgical Specialities

An Initiative of The Tamil Nadu Dr. M.G.R. Medical University
University Journal of Surgery and Surgical Specialities