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Case Report Open Access

Fanconi Bickel Syndrome: A Rare Entity

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Abstract

Fanconi-Bickel syndrome (FBS) is a rare inherited glycogen storage disease (GSD) caused by defects in facilitative Glucose Transporter (GLUT2) gene that codes for the glucose transporter protein 2 expressed in hepatocytes, pancreatic beta cells, enterocytes, and renal tubular cells. The clinical picture is characterized by glycogen accumulation in liver and kidney resulting in hepatomegaly and nephromegaly, impaired utilization of glucose and galactose, proximal renal tubular acidosis, hypophosphatemia rickets, and short stature. This is an autosomal recessive disorder discovered in 1949 and the pathogenic mutation of GLUT 2 gene of hepatocytes, beta cells of pancreas and renal tubules were discovered in 1997.

Keywords: Renal tubular acidosis; GLUT 2; Hepatocytes; Renal tubular cells; Urine

Case Report

An 8 month old male child, product of consanguineous marriage belonging to far flung area presented with progressive abdominal distension from 3 months. Patient was born at term, appropriate for gestational age (birth weight 2.8 kg) by normal vaginal delivery without any perinatal complication, exclusive breast fed till 6 month of age. Supplemental feeds were started 2 months back in the form of cereals and banana. There was no history of seizures, jaundice, pedal edema, cataract, and polyuria. On examination weight and height was between 5th and 10th centile, patient had doll like face with hypotonic and marked rickets (wrist widening, Harrison's sulcus, frontal bossing) [1,2]. Liver span was 12 cm. developmental age was 3 months, patient achieved head control and recognizes mother but not able to sit with support. Rest of the examination was normal. There was history of 2 sib deaths in infantile age, cause of which couldn't be ascertained and no record was available.

In view of rickets hepatomegaly, failure to thrive, doll like face and developmental delay, a possibility of Fanconi-Bickel disease was made and patient was extensively evaluated for the above disorder. Investigations revealed normal serum calcium (9.7 mg/dl) reduced serum phosphorous (2.29 mg/dl), mild transaminitis (ALT 97 U/L, AST 174 U/L) and raised alkaline phosphatase (883 U/L). Serum triglycerides were also mildly elevated (280 mg/dl). But LDL, HDL cholesterol was normal. We documented fasting hypoglycemia (serum Glucose 41 mg/dl a ter 4 hours of sleep). ABG analysis revealed compensated metabolic acidosis (pH 7.4, HCO_3 16.0).Serum sodium and potassium were normal. Urine analysis showed marked glycosuria (4+), proteinuria (1+) and aminoaciduria. Radiological, bone survey revealed diffuse osteopenia with rachitic triad; cupping, fraying and widening of metaphysical ends (Figure 1). Liver biopsy showed accumulation of glycogen in the hepatocytes. So a case of Fanconi-Bickel disorder was confirmed based on above symptoms and laboratory investigations. Patient was started on calcitriol, multivitamins, and Shohl's solution, and the mother was advised to give frequent meals with adequate calories especially before bedtime. The use of corn starch in his diet was also recommended. Child is under follow-up from 3 months, his serum phosphorous and alkaline phosphatase improved however patient still is lagging in development with no improvement in growth failure.

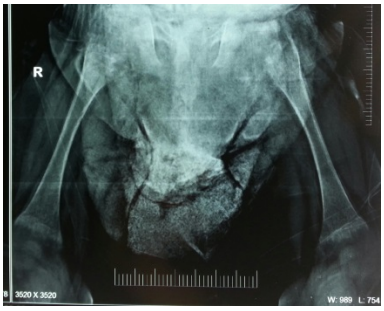

Figure 1: Urine analysis showed marked glycosuria (4+), proteinuria (1+) and aminoaciduria. Radiological, bone survey revealed diffuse osteopenia with rachitic triad; cupping, fraying and widening of metaphysical ends.

Discussion

Fanconi-Bickel syndrome is a rare metabolic disorder of hepatorenal glycogen accumulation, proximal renal tubular dysfunction, and impaired utilization of glucose and galactose [3,4], first described in 1949 by Guido Fanconi and Horst Bickel. It is a single gene disease and is caused by defects in the facilitative glucose transporter 2 (GLUT2) gene or (SLC2A2)1. The gene was localized to human chromosome 3q26.126.3 [5,6]. Patients usually presents early in life with rickets and hepatomegaly. By two years of age enlarged kidneys are noticeable clinically. Fasting hypoglycemia, hyperglycemia and hypergalactosemia in the post absorptive state, and hyperlipidemia may be present [3,4]. Our index case presented at 8 months of age with progressively increasing abdominal distension and rickets. On extensive investigation we documented proximal renal tubular dysfunction in the form of glycosuria, phosphaturia, proteinuria and bicorbonaturia. Liver biopsy also revealed hepatic glycogen

accumulation. Long bone X-ray in our patient showed florid rickets. Fanconi Bickel disease has autosomal recessive inheritance and cases have been reported from all parts of Europe, Turkey, Israel, Arabian countries of the Near East and North Africa, Japan, and North America [3,4]. In India very few cases have been reported till date and in fact none has been reported from north India. Kashmir is a closed society with wide spread consanguinity, as a result autosomal recessive disorders are quite common here. We couldn't ascertain the cause of 2 previous sib deaths in index case as records were not available. Since the overall prognosis of survival of Fanconi Bickel syndrome to adulthood seems to be favorable; in addition to Fanconi and Bickel's original patient at least two more patients have reached adulthood in stable condition. Whether these 2 sibs represented severe form of same disorder the question remains unanswered.

In summary we presented a case of Fanconi Bickel syndrome, an 8 month old male child with previous 2 sib deaths presented to us with progressively increasing abdominal distension and rickets. Patient was found to have proximal RTA and hepatomegaly with liver biopsy confirming hepatic glycogen deposition. This is a first case reported in Kashmir where consanguinity is very common.

References

1. Santer R, Schneppenheim R, Dombrowski A, Götze H, Steinmann B, et al. (1997) Mutations in GLUT2, the gene for the liver-type glucose transporter, in patients with Fanconi-Bickel syndrome. Nat Genet 17: 324-326.
2. Sakamoto O, Ogawa E, Ohura T, Igarashi Y, Matsubara Y, et al. (2000) Mutation analysis of the GLUT2 gene in patients with Fanconi-Bickel syndrome. Pediatr Res 48: 586-589.
3. Santer R, Schneppenheim R, Suter D, Schaub J, Steinmann B (1998) Fanconi-Bickel syndrome: The original patient and his natural history, historical steps leading to the primary defect, and a review of the literature. Eur J Pediatr 157: 783-797.
4. Santer R, Steinmann B, Schaub J (2002) Fanconi-Bickel syndrome: A congenital defect of facilitative glucose transport. Curr Mol Med 2: 213-227.
5. Manz F, Bickel H, Brodehl J, Feist D, Gellissen K, et al. (1987) Fanconi-Bickel syndrome. Pediatr Nephrol 1: 509-518.
6. Fukumoto H, Seino S, Imura H, Seino Y, Eddy RL, et al. (1988) Sequence, tissue distribution, and chromosomal localization of mRNA encoding a human glucose transporter-like protein. Proc Natl Acad Sci USA 85: 5434-5438.