Fanconi-Bickel syndrome due to a Novel SLC2A2 Mutation Presenting with Transient Neonatal Diabetes

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Background: Fanconi-Bickel syndrome (FBS) is a glycogen storage disease caused by the homozygous mutations of SLC2A2 gene which codes GLUT2 protein. It is characterized by growth retardation, hepatomegaly and hypophosphatemic rickets. While most of the cases with FBS have fasting hypoglycemia and postprandial hyperglycemia, only few cases had been shown to have neonatal diabetes (ND).

Case Presentation: A 14 days old girl was admitted to hospital with difficulty in feeding and persistant vomitting since from birth. Her antenatal history was normal except bilateral renal enlargement in intrauterine ultrasonography. She was born 2620 gr at 39 weeks with vaginal delivery. Her parents were first degree cousins and she had two siblings with histories of sudden infant death.

•In physical examination she was pale and had %12 weight loss. Her kidneys were palpable. She had hyperglycemia (bloodsugar: 651 mg/dl) and metabolic acidosis (blood pH:7,1 HCO3: 11); intravenous fluid and insulin treatment were started with diagnosis of ND. Levels of C-peptit was 0,5 ng/ml and fructosamine was 383 mmol/L. She was hypertensive, had renomegaly and increased parenchymal echogenicity in renal ultrasonography but her renal functional tests (RFT), serum electrolytes were normal and she did not have proteinuria. She was discharged with subcutaneus NPH insülin and captopril.

At the age of four months insülin was discontinued and captopril was switched to ramipril because of newly diagnosed proteinuria. Molecular genetic study showed she is **homozygous for a novel missense mutation (p.A127D, c.380C>A) in SLC2A2 gene. Her parents were heterozygous for that mutation.** When she was evaluated for FBS findings in addition to present growth failure, renomegaly and proteinuria at nine months of age; RFT and serum electrolytes were normal but 24 hour urine findings were competible with tubulopathy. After diagnosis of FBS, galactose free diet was started.

Her last visit was made at the age of 15 months. She could not have implemented galactose free diet properly and had serious growth retardation. She was still off insulin, mostly normoglycemic except infection periods. Her AST and ALT levels were normal, serum creatinine level was elevated, proteinuria was persisting but serum phosphorus and calcium levels were normal and there was not any bone deformity as a rickets sign. The progression of clinical and laboratory findings of the case is summarized in Table 1.

Conclusion: Neonatal diabetes can be the initial finding of FBS. After excluding frequent causes, FBS should be kept in mind for differential diagnosis for ND. Cases with homozygous SLC2A2 mutations should be followed for growth retardation, hepatomegaly and hypophosphatemic rickets.

Table 1 The progression of clinical and laboratory findings of the case

Age	15 days	4 months	9 months	15 months
Weight/Height (SD)	-2,98/-2,27	-2,45/-1,96	-2,86/-2,95	-3,27/-3,76
HbA1C (%)	-	5,2	6,0	5,9
Serum Creatinin (mg/dl)	0,7	0,55	0,59	0,8
Serum Ca(mg/dl)/P(mg/dl)/ALP(U/L)	9,8/4,4/1084	10,4/6,7/1861	10,2/4/805	9,8/3,1/587
Serum AST/ALT (IU/L)	45/27	160/68	137/100	47/39
Renal Ultrasound	Renomegaly, Echogenicity↑	Renomegaly, Echogenicity↑	Renomegaly, Echogenicity ↑	Renomegaly, Echogenicity ↑
Liver Ultrasound	Normal	Normal	Normal	Normal
Spot urine findings	Protein:- Glucose:+ Prt electrophorese: Normal	Protein:+ Glucuse:+ Protein/creatinin: 6	Protein:+ Glucose:+	Protein:+ Glucose:+
24 hour urine findings	-		Glomerular filtration rate:39 mL/min/m^2 Tubular phosphate reabsorption:%48 Calciuria: 7 mg/kg/day	
Treatment	0,8 u/kg/day insulin Captopril	İnsulin Ø Ramipril	İnsulin Ø Ramipril Galactose free diet	İnsulin Ø Ramipril Galactose free diet

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