



Case Report

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An Iranian Patient with Fructose 1,6 Bisphosphatase Deficiency: A Case Report

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ABSTRACT

Background: Deficiency of hepatic fructose 1,6 bisphosphatase (FBPase), a key enzyme in gluconeogenesis, impairs the formation of glucose from all gluconeogenic precursors including dietary fructose. Patients present with life threatening metabolic acidosis, fasting hypoglycemia, hepatomegaly, hyperketosis, elevated lactate and uric acid level. Glycerol and glycerol-3 phosphate have been found in the urine. The diagnosis of FBPase deficiency is confirmed via DNA molecular analysis from peripheral leukocytes. The acute life threatening episodes are treated with IV glucose at high rate and bicarbonate to control hypoglycemia and acidosis.

Case Report: Here we report a girl referred with anorexia, lethargy, recurrent vomiting, progressive respiratory distress, and hepatomegaly following respiratory viral infection. She also had a history of twice similar attacks but milder than previous episodes. The test results showed hypoglycemia and severe metabolic acidosis. Despite proper treatment, the patient died of pulmonary edema following a respiratory viral infection.

Conclusion: Once FBPase deficiency has been diagnosed and adequate management introduced, its course is usually benign. Growth both psychomotor and intellectual development are unimpaired and tolerance to fasting improves with age.

Introduction

Fructose 1,6 bisphosphate (FBPs) deficiency is a rare autosomal recessive inborn error of gluconeogenesis that impairs the formation of glucose from all gluconeogenetic precursors, including dietary fructose.^{1,2} Clinical manifestations are characterized by life-threatening episodes of acidosis, hypoglycemia, hyperventilation, convulsion and coma.^{2,3} In about half of the cases, the deficiency presents in the 1st week of life.⁴ In infants and young children, episodes are triggered by febrile infections and gastroenteritis if oral food intake decreases.^{5,6} The frequency of the attacks decreases with age. Physical examination may show tachycardia, tachypnea, muscle weakness and hepatomegaly. During the episodes patients are metabolically stable with mild intermittent or chronic metabolic acidosis.^{6,7} Laboratory findings show hypoglycemia, lactic acidosis, ketosis, and elevated uric acid. Glycerol and glycerol-3-phosphate appears in the urine.^{4,8,9} The diagnosis is established by demonstrating an enzyme deficiency in either liver or intestinal biopsy.⁶ The gene coding for FBP1 is located on chromosome 9q22.¹⁰ The disease is transmitted as an autosomal recessive trait. The true incidence of which is not yet known.⁷ Treatment of acute attacks consists of hypoglycemia and acidosis management with IV glucose infusion and bicarbonate solution.⁴ The response is usually rapid and the avoidance of fasting, aggressive management of infections and restriction of fructose, sucrose and sorbitol from the diet can prevent further episodes.^{6,11} For long term

prevention of hypoglycemia, slowly released carbohydrates such as corn starch is useful. Patients who survive childhood develop normally.¹²

Case Report

A 20-month-old girl was referred to pediatric ward at Shahid Sadoughi hospital due to anorexia, recurrent vomiting, and progressive respiratory distress following a viral respiratory infection. She had previously been hospitalized on the second day of birth due to tachypnea and at 11 months old because of hypoglycemia and metabolic acidosis and elevated liver enzymes following gastroenteritis. She had normal development. She was born out of consanguineous marriage. On examination, she weighed nine kilograms (5%) and had severe respiratory distress and hepatomegaly (Liver span: 9 cm). Her laboratory data is presented in Table 1.

In urine organic acid test: Lactic acid (754 mmol/molcr, NL<60), Glycerol-3-phosphate (186 mmol/molcr, NL<13) were increased while glycerol was normal. This pattern is suggestive of Fructose 1,6 bisphosphate deficiency. Genetic studies confirmed this diagnosis.

Patient with suspected hereditary metabolic disease was treated with serum DW10% (1.5 times preservative fluid), intravenous bicarbonate, and antibiotics after sending in metabolic tests. Given the high blood sugar during treatment, intravenous insulin was prescribed at a dose of 0.05 Iu/Kg/hour.

The patient's acidosis ameliorated after 12 hours (VBG: pH 7.31, HCO₃ 15, PCO₂ 30) but she still had respiratory distress and was dependent on oxygen.

Table 1. Laboratory Data

VBG						
pH	PCO ₂	HCO ₃	Anion gap	BS	Uric acid	Ammonia
6.89	15.8	3	22	25 mg/dL	16 mg/dL	252 µg/dL
Lactate	SGOT	SGPT	ALKP	INR	Albumin	
88 mg/dL	148 U/L	44 U/L	435 U/L	1	3.2mg/dL	
CBC						
WBC	PMN	Hb	PLT	CRP		
25900	79%	12.3	471000	2+		

Increased respiratory distress, cyanosis, decreased arterial oxygen saturation and progressive lung involvement resulted in the intubation of the patient be connected to a ventilator. According to the infectious consultation, the patient was prescribed antibiotics. Echocardiography reported right and left heart failure (EF = 30-35%) and appropriate management was undertaken for heart failure. Pulmonary edema (White lung) was reported on chest x-ray due to respiratory infection and unfortunately the patient expired.

Discussion

The enzyme FB Pase regulates an essential step in the pathway of gluconeogenesis. The enzyme catalyzes the irreversible conversion of fructose 1,6 bisphosphate to fructose 6-phosphate. FB Pase deficiency is a cause of life threatening metabolic acidosis in the neonatal period. Subsequent episodes usually follow fasting and are precipitated by intercurrent infections. Onset may be presented with vomiting and anorexia. Long periods of fasting leads to hypoglycemia and metabolic acidosis. Hepatomegaly develops in infancy, but there is usually no sign of liver disease.¹² Our patient referred at the age of 20 months with severe metabolic acidosis and hypoglycemia following a viral respiratory infection. However, she had milder symptoms during the neonatal period and at 11 months in the absence of follow up. Despite proper treatment, the patient died due to progressive lung involvement after a viral infection.

Conclusion

Due to the wide spectrum of clinical symptoms, life-threatening conditions of FB Pase deficiency and the lack of screening test in the screening panel of inherited metabolic diseases at birth; physicians should be more aware of the clinical signs of the disease. However, early diagnosis and treatment are effective in prognosis. Fasting tolerance improves with age and patients usually develop normally by childhood.

Conflict of Interests

Authors have no conflict of interests.

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The present study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences (IR.SSU.REC.1401.034).

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