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BETA-KETOTHIOLASE DEFICIENCY*
A Case Report

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SUMMARY: Altıntaş B, Teziç T, Coşkun T, Özalp İ, Kükner Ş, Kaya A. (Dr. Sami Ulus Children's Hospital, and the Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Beta-ketothiolase deficiency: a case report. Turk J Pediatr 34:43-46, 1992.

A four-month-old boy with beta-ketothiolase deficiency is described in this report. Presenting symptoms and signs were vomiting, irritability and acidotic respiration. Laboratory investigations revealed hyperglycinemia, metabolic acidosis and ketosis. Subsequent urinary GC-MS analysis of the patient's urine sample showed the typical pattern of beta-ketothiolase deficiency. Our experience with this case indicates that accurate diagnosis and early treatment of inborn errors might be lifesaving.
Key words: ketotic hyperglycinemia, beta-ketothiolase deficiency.

Beta-ketothiolase deficiency is a rare metabolic disorder of branch chain amino acids, which is characterized by an increased plasma glycine level, metabolic acidosis and ketosis. The differential diagnosis of beta-ketothiolase deficiency should include propionic acidemia, methylmalonic acidemia and isovaleric acidemia[1].

This report describes a four-month-old boy with beta-ketothiolase deficiency. To the best of our knowledge, this is the first case of beta-ketothiolase deficiency reported from Turkey.

Case Report

A four-month-old boy was admitted to Dr. Sami Ulus Children's Hospital with the chief complaints of irritability, crying and vomiting of two days' duration. The prenatal period and delivery were uneventful. The parents were unrelated. Past history disclosed normal physical and motor development. The patient had a two-year-old healthy sister.

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Physical examination revealed a feverish child (body temperature 40 °C) with a pulse rate of 180 beats/min and a respiratory rate of 72/min. The patient appeared critically ill, was irritable and had acidotic respiration. The liver was 2 cm palpable below the right costal margin. He weighed 4700 g (above the 5th percentile) and measured 54 cm in length (above the 5th percentile) and 39.5 cm in head circumference (above the 5th percentile).

Laboratory investigations revealed a hemoglobin of 10.6 g/dl, white blood cells 16100/mm^3 with 82% polymorphonuclear leukocytes, 14% lymphocytes and 4% monocytes. The platelet count was normal. Urinalysis yielded 2+ ketonuria. The blood pH was 7.1 and HCO_3– 7.9 mEq/L. Paper chromatography of the blood and urine samples demonstrated increased concentrations of glycine. Urinary organic acid analysis by gas chromatography and mass spectrometry (GC-MS) showed a pattern consistent with the diagnosis of beta-ketothiolase deficiency (Table I).

TABLE I: Urinary and Serum Organic Acid Pattern of the Patient

Organic Acid	Urine (µmol/mol creatinine)	Serum (µmol/L)
Lactic acid	110	3600
2-OH-butyric acid		120
3-OH-butyric acid	980	310
Adipic acid	70	
3-OH-2-methylbutyric acid	300	820
4-OH-phenylacetic acid	90	
4-OH-phenyllactic acid	60	
Hippuric acid	220	

Following intravenous alkali replacement therapy and the initiation of a protein restricted diet, the patient's condition improved. The child was subsequently discharged on a low-protein diet. Within two weeks, he became symptom-free and his psychomotor status became normal.

Discussion

Since the first description of a beta-ketothiolase disease by Daum et al[2,3], Keating et al[4], Hillman et al[5,6] and Gompertz et al[7] attributed the disease to an inherited disorder of isoleucine catabolism. Later, it was discovered that the disease was not simply a defect of isoleucine degradation, but that the deficient enzyme was the K^+ dependent short-chain mitochondrial thiolase which also plays a major role in ketone body metabolism[8]. Deficient activity of mitochondrial acetoacetyl CoA thiolase in fibroblasts of patients with beta-ketothiolase deficiency has been reported[9,10].

Beta-ketothiolase deficiency presents with vomiting, acidosis, lethargy and coma usually triggered by intercurrent infections during infancy and late childhood. Our patient presented with vomiting, irritability and acidotic respiration during a febrile illness[1].

The "ketotic hyperglycinemia syndrome" was first described by Childs et al[11] in 1961. Elevated plasma glycine levels may occur in a number of inborn errors including propionic acidemia, methylmalonic acidemia and isovaleric acidemia[1]. In all these disorders, acidosis and ketosis are in association with increased plasma and urinary concentrations of glycine, as in the case presented. GC-MS analysis of a urine sample is, therefore, needed to make a distinction between these metabolic disorders having similar clinical and biochemical findings. Beta-ketothiolase enzyme converts alpha-methyl acetoacetyl CoA to acetyl CoA and propionyl CoA during the degradation of isoleucine. Patients with this disorder excrete large amounts of 3-OH-2-butyric acid, 2-methylacetoacetate and tiglylglycine[1,12]. We detected increased excretion of 3-OH-2-butyric acid in our patient (Table I). Although neutropenia and thrombocytopenia were not present in our patient, hematologic abnormalities have been reported in some cases[12].

The control of an acute metabolic crisis by intravenous fluid and alkali therapy, and the implementation of a protein restricted diet, as in our case, demonstrated that most of the inborn errors of metabolism can be managed successfully if a correct diagnosis is made and treatment is initiated early in the course of the illness. Establishment of a correct diagnosis not only increases the chance of controlling the disorder but also affords the parents an opportunity of having a healthy child in subsequent pregnancies by making use of prenatal diagnosis.

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