
Case Reports

Propionic Acidemia in the Newborn

Ashutosh Marwah
S. Ramji

Propionic acidemia is a rare, autosomal, recessively inherited inborn error of propionate metabolism. It presents most often as a neonatal life threatening emergency with metabolic acidosis, hyperammonemia, hyperglycinemia and hyper glycinuria. Since its first description in a male infant with episodic metabolic acidosis and hyperglycinemia(1), more than 100 cases have been reported. The present communication reports the course of a neonate with propionic acidemia.

Case Report

A 3200 g male infant was delivered at term gestation with normal Apgar scores to a fourth para mother with non-consanguineous marriage, following an uneventful antenatal period. The infant was exclusively breastfed till 70 h, when he presented with lethargy, refusal to feed, groaning and respiratory distress. The infant's temperature was 39 °C, heart rate 142/ min and respiratory rate 42 per min. The infant was hy-

potonic and had no organomegaly. Initial investigations revealed: Hematorcrit-47%, ESR 1 mm 1st h, TLC 2100/cu mm, DLC-lymphocyte 78%, polymorphs 22% and I/T ratio 0.18. Blood sugar was 90 mg/dl and the chest skiagram was normal. Blood gas evaluation revealed a metabolic acidosis (pH 7.22, base excess-15). Lumbar tap was normal and blood culture was sterile. Antibiotic therapy (cefotaxime and gentamicin) was initiated on an initial diagnosis of septicemia, and acidosis was appropriately and adequately treated with sodium bicarbonate. Acidosis persisted inspite of bicarbonate therapy and over the next 48 h there was progressive sensorial obtundation. Cranial ultrasound was normal and urine examination revealed ketonuria. A possibility of an inherited metabolic problem was considered and urine screened for organic acids by gas chromatography and mass spectroscopy (GC-MS) and blood for aminoacidopathies. The results of GC-MS of urine sample revealed elevated levels of 3- OH propionic acid, methylcitric acid, 2-methyl-3-OH-butylic acid, 3-OH valeric acid, tiglyl-lycine, and absence of methylmalonic acid which confirmed the diagnosis of propionic acidemia. The infant died on day 7 of life.

Discussion

Propionic acidemia has a heterogeneous clinical presentation(1-5). Two-thirds of the patients manifest within the first week of life and almost 80% by two weeks. The neonatal presentation usually has a typical presentation of non-specific symptoms which include feeding difficulties (80-90%), vomiting and dehydration (70%), respiratory problems (60-65%), hypotonia, seizures, coma and severe metabolic acidosis. The

From the Neonatal Division, Department of Pediatrics, Maulana Azad Medical College, New Delhi 110 002.

Reprint requests: Dr. S. Ramji, Professor, Neonatal Division, Department of Pediatrics, Maulana Azad Medical College, New Delhi 110 002.

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present case too presented within the first week with feeding difficulties, respiratory distress, hypotonia, coma and severe metabolic acidosis. It has been suggested that propionic acidemia must be considered in all newborn infants with unexplained neurological deterioration even in the absence of a metabolic acidosis(6). Neutropenia, thrombocytopenia and anemia are frequently encountered during the acute crisis (probably a result of propionate mediated marrow suppression). The late onset form, however, poses a challenge in diagnosis. A typical face has been described in infants with propionic acidemia-hypertelorism, depressed nasal bridge, pseudoepicanthic folds, long philtrum and upward curvature of upper lip. The nipples may be hypoplastic, inverted or supernumerary. The midfacial and nipple anomalies suggest that propionic acid acts as a teratogen in the fetus(5). In the present case the 'typical faces' were absent. The clinical course is variable. Death is reported in 30% during the initial presentation, in 40% during subsequent crisis. The rest have either frequent crisis or a mild course.

The diagnosis is best confirmed by screening urine samples for propionic acid metabolites by GC-MS. The most valuable diagnostic metabolites excreted include 3-OH propionate, 2-methyl citrate, 2-methyl-3-oxyvalerate, 3-OH butyrate and tiglyl-lysine. Prenatal diagnosis of propionic acidemia is possible by determining propionyl CoA carboxylase (PCC) enzyme activity in chorionic villous biopsies, cultured amniotic fluid cells or by measuring methylcitrate concentration in amniotic fluid(7).

Propionic acidemia needs to be differentiated from methylmalonic acidemia, multiple carboxylase deficiency and isovaleric acidemia. The clinical presentation of methylmalonic acidemia is very

similar to propionic acidemia, but can be differentiated from the latter by the presence of methylmalonic acid in the urine. Multiple carboxylase deficiency is differentiated from propionic acidemia by skin manifestations, which include generalized erythematous rash with exfoliation and alopecia totalis. Isovaleric acidemia is differentiated by its sweaty feet odor (characteristic odor is absent in propionic acidemia) and absence of propionic acid in the urine.

Therapy of propionic acidemia has to begin during the acute metabolic crisis when the diagnosis is still uncertain. The main principles of management during this phase include prevention of toxic metabolite accumulation by restricting protein intake, adequate caloric intake - glucose (25-30 g/kg/day) and lipids (2-4 g/kg/day), and metronidazole therapy (10-20mg/kg/day) which has been found to reduce urinary excretion of propionate metabolites by 40%(8); elimination of toxic metabolites by exchange transfusion, peritoneal or hemodialysis; and supportive measures such as assisted ventilation, correction of fluid and pH imbalances, L-carnitine (100mg/kg/day) and therapeutic trial with oral biotin (10 mg/day)(4). Long term management of propionic acidemia is a very challenging risk. High protein or low caloric intake, or catabolic states such as infections, trauma or surgery can lead to serious life threatening crises. A protein intake of 0.7-1.5 g/kg/day with non-propionogenic amino acids(9), adequate caloric intake and L-Carnitine (100 mg/kg/day, orally) form the mainstay of therapy. Special amino acid mixtures are available for patients with propionic acidemia (Milupa's OS1, OS2, Weyth Byla's S14, and Maxamaid)(7). Most survivors have been documented to have poor psychomotor outcome, probably a result of delayed diagnosis and inability to prevent and treat intermittent crisis.

There is a need for early selective screening of patients with non-specific clinical symptoms and laboratory findings and initiate emergency non-specific treatment as outlined above if mortality and long term neurodevelopment morbidity are to be improved.

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Valvular Heart Disease: Rheumatic or Rheumatoid ?

Amita Trehan
Surjit Singh
N. Ambalavanan
Lata Kumar

Juvenile rheumatoid arthritis (JRA) was first described by Still in 1897. Extra-articular involvement in JRA is well known but

cardiac involvement is said to be uncommon. The association of articular rheumatism and rheumatism of the fibrous tissue

From the Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh 160 012.

Reprint requests: Dr. Surjit Singh, Associate Professor, Department of Pediatrics, Post Graduate Institute of Medical Education and Research Chandigarh 160 012.

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