

with functional status of the hand. Cleft hand and cleft foot may be found singly or in association with each other. These may be present unilaterally or bilaterally. Miura(3) in a study of 152 congenital anomalies described associated abnormalities of cleft foot, syndactyly, polydactyly, pectoral muscle anomaly and cleft palate. Suzuki *et al.*(4) described 11 cases of typical cleft hand along with bilateral cleft feet in 3 cases, unilateral cleft foot in 2 and syndactyly of fingers and toes in one case each. Miura(5) noted intermediate cases between cleft hand and syndactyly suggesting similarity in the embryological failure in these two types.

The reported case is a rare combination of bilateral typical cleft and with bilateral cleft foot. It also had syndactyly and the classical radiological features. As the clefts were deep and functionally useful, no treatment was offered.

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## Carbamylphosphate Synthetase-I Deficiency in a Newborn: Survival After Early Diagnosis and Therapy

K. Raghavan  
S. Chabra  
J. Mondkar  
R. Aiyar  
L.M. Ambani  
A. Fernandez

Carbamylphosphate synthetase-I (CPS) deficiency is a rare, autosomal recessive inborn error of metabolism involving the urea cycle. Deficiency of CPS results in accumulation of ammonia, causing vomiting, lethargy, seizures, coma and death if hyperammonemia is not controlled. Review of the approximately 25 cases in world literature reveals 2 variants of CPS-I deficiency—a group with virtually complete deficiency of the enzyme resulting in death within the first week of life and a group, with a partial deficiency and a variable clinical course(1). Of the previously reported cases with the neonatal form, only 4 have survived with treatment(2,3). We report here a case of the neonatal type of CPS-I deficiency with a typically severe presentation in the first few days of life, but which could be successfully managed. To our knowledge, this is the first report of CPS-I deficiency from India.

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*From the Department of Pediatrics, L.T.M.G.H. and L.T.M.M.C., Sion, Bombay 400 022.*

*Reprint requests: Dr. Kalyani Raghavan, 6, Sneh Sadan, Sitaladevi Temple Road, Mahim, Bombay 400 016.*

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## Case Report

The propositus, a female newborn child, was referred to us on the 3rd day of life for refusal of feeds and lethargy since 1 day. The child was the 6th issue of a 1st degree consanguineous marriage between a 35-year-old mother and a 40-year-old father, who were first cousins. Their previous issues consisted of 2 normal children aged 9 years and 4 years, an abortion at 2 months amenorrhea and 2 males who died in the newborn period at 9 days and 3 days, respectively with similar complaints as the propositus.

The child was a full term normal delivery, weighting 2.5 kg who cried immediately after birth. The antenatal period was uneventful. Breast feeds were started 4 hours after birth. She fed well during the first day of life, but by 48 hours she developed refusal of feeds and lethargy. On examination, there was poor cry and activity, absent Moro's reflex, hypotonia and intermittent tachypnea. She was admitted to the Neonatal Intensive Care Unit for investigations and monitoring.

Blood gases were:  $PO_2$  80 mm,  $PCO_2$  28 mm, pH 7.401,  $HCO_3$  22 mEq/L, and anion gap of 15 mEq/L. Blood urea nitrogen was 4 mg/dl. There were no ketones in the urine. Complete blood count was normal. Blood sugar was 45 mg/dl. The CSF was normal. Blood and CSF cultures were performed and a provisional diagnosis of sepsis was made. Ampicillin (200 mg/kg/day) and amikacin (15 mg/kg/day) were started. However, the child continued to deteriorate and became completely comatose by day 5.

Ultrasonographic as well as computerized tomographic examination of the brain revealed no abnormalities. All culture results were negative. On day 7, the child

developed chronic convulsions which responded to phenobarbitone (20 mg/kg) loading dose. A subsequent maintenance dose of 5 mg/kg was continued. However, convulsions recurred on day 9, and phenytoin (10 mg/kg) was added to the regimen.

The plasma ammonia level was found to be 940  $\mu$ m (normal <35  $\mu$ m). Further biochemical studies showed the plasma citrulline level to be zero and the urinary orotic acid to be negative. The presence of hyperammonemia without acidosis in a female neonate with absence of plasma citrulline and absence of urinary orotic acid established the diagnosis of carbamylphosphate synthetase-1 deficiency. Peritoneal dialysis was started and continued for 36 hours when the plasma ammonia level was 100  $\mu$ m. All protein containing feeds were stopped for 48 hours, and sodium benzoate, arginine and citrulline 250 mg each, three times a day were given through the nasogastric tube. Pyridoxine (5 mg/day) and folic acid (0.1 mg/day) were also given orally. The sensorium improved within 48 hours and by 72 hours, the child was feeding well at the breast.

All anticonvulsants were withdrawn and child remained symptom free. Child was discharged on day 20 of life with the same treatment of Sodium Benzoate, arginine and citrulline each 250 mg three times a day, pyridoxine (5 mg/day) and folic acid (0.1 mg/day). At follow up the child had delayed milestones, achieving social smile at 14 weeks, head control at 20 weeks and turning over at 24 weeks.

At 28 weeks of age, the child was readmitted with coma. History revealed that the parents had omitted the treatment on their own, due to a financial crisis in the family. The plasma ammonia was 1080  $\mu$ m. The child died 6 hours following admission

in a hyperammonemic crisis.

## Discussion

Carbamylphosphate synthetase-1 (CPS-I) deficiency is one of the urea cycle enzymopathies (UCE), which lead to hyperammonemia as a result of defective detoxification of ammonia. CPS-I catalyzes the synthesis of carbamylphosphate from ammonia and bicarbonate, and is the first committed step in urea synthesis. Although each of the UCE appears rarely, when all five of the disorders are included, the incidence probably approaches 1/30,000 births(4).

The urea cycle disorders typically present in the neonatal period with acute overwhelming symptoms. Because they are associated with protein intolerance, symptoms typically begin after feeding has been instituted. The initial findings are those of poor feeding and lethargy. Patients then progress to tachypnea, alternating hypotonia and hypertonia, opisthotonus, seizures and loss of consciousness. Pulmonary hemorrhage has been a common post mortem finding in some patients. Infants with a complete absence of enzyme activity, though asymptomatic at birth, may deteriorate rapidly and die of hyperammonemia within a few days following the intake of milk feeds.

The signs and symptoms of CPS-I deficiency are non-specific and could be seen in conditions like septicemia, respiratory distress syndrome, intraventricular hemorrhage and gastroenteritis. The 3 major causes of neonatal hyperammonemia are the other UCE like ornithine transcarbamylase deficiency, citrullinemia, argininosuccinic aciduria and hyperargininemia, organic acidemias and transient hyperammonemia of the newborn (THAN). The

organic acidemias can be differentiated by the presence of acidosis, ketosis, and an increased anion gap. CPS-I deficiency can be differentiated from the other UCE by the absence of citrulline in the plasma and the absence of orotic acid in the urine(5).

Severe hyperammonemia leading to coma is a medical emergency requiring prompt recognition and aggressive therapy. Hemodialysis and peritoneal dialysis are advocated as they have been found to be more successful than exchange transfusion for removal of ammonium from the circulation(5). Ammonium production from endogenous proteolysis is minimized by intravenous administration of 10-15% glucose. Arginine hydrochloride (0.8 mg/kg) and sodium benzoate (0.25 g/kg) should be given intravenously over a period of one hour.

In the long term management, restriction of protein intake below 1.5 g/kg/day must be carefully balanced with an adequate calorie intake to meet the needs for growth. Sudden increase in tissue catabolism following starvation or infection may precipitate severe hyperammonemia(1). Cheese and cough mixtures containing ammonia must also be restricted. The nitrogen load must be spread over the day by giving frequent small feeds.

Long term therapy of urea cycle enzymopathies using dietary manipulation alone has had limited success(6). The mainstay of the treatment consists of exploiting alternative pathways of waste nitrogen synthesis and excretion(5,6). This is accomplished by administering sodium benzoate and phenylacetate which conjugate with glycine and glutamine respectively to yield hippuric acid and phenylacetylglutamine. These amino-acid acylation products are easily cleared by the kidney, thus preventing accumulation of ammo-

nium in the body. Sodium benzoate and sodium phenylacetate are both given orally in the dose of 0.25 g/kg/day.

An absolute requirement for dietary arginine occurs in these patients, because the urea cycle must be intact for the *de novo* biosynthesis of arginine. Hence, arginine must be supplied in the dose of 0.25 g/kg/day because it imposes a lower nitrogen burden than arginine and is readily converted in the body to arginine.

Most surviving patients have significant mental retardation(2). The severity of neurologic sequelae is proportional to the magnitude of hyperammonemia and duration of coma(5). Hence, early diagnosis and institution of therapy is a must, not only for the survival, but also for improving the quality of life for these patients.

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## Transfusion Associated Malaria in Endemic Areas

N. Choudhury  
J.G. Jolly  
N.K. Ganguly  
R.C. Mahajan  
M.L. Dube

Malaria is a common parasitic infection among pediatric patients in endemic areas(1). When transmitted through blood, post transfusion malaria (PTM) may carry special risk to pediatric patients. It usually delays the diagnosis and complicates an already underlying disease(2). Only limited literature is available on PTM in pediatric patients(3,4). The children who received blood transfusion were followed up vigilantly and any patient developing malarial fever was checked alongwith its blood donor for malarial antigen using monoclonal antibody (MAB) to ascertain the diagnosis.

#### Material and Methods

All pediatric patients who received blood transfusion (excluding thalassemia

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*From the Transfusion Medicine Department, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Post Box 375, Lucknow 226 001, and Departments of Experimental Medicine and Pathology, Post Graduate Institute of Medical Education and Research, Chandigarh 160 012.*

*Reprint requests: Professor J.G. Jolly, Transfusion Medicine Department, Sanjay Gandhi Post Graduate Institute of Medical Sciences, P. Box 375, Lucknow 226 001.*

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