Letters to the Editor

Persistant Unconjugated Hyperbilirubinemia in an Infant with Crigler-Najjar Syndrome Type I

Crigler-Najjar syndrome type-1 (CNS-I) is a potentially lethal disorder characterized by severe unconjugated hyperbilirubinemia, resulting from a recessively inherited deficiency of hepatic uridine diphosphate glucoronosyl transferase (UGT) activity, leading to neurological damage due to bilirubin encephalopathy and eventual death(1). The diagnosis of CNS-I can usually be made from a combination of response to phenobarbitone, bile bilirubin pigment analysis, and genetic studies(2). A reasonable diagnosis of CNS-I can be arrived at by classic clinical presentation, by process of exclusion of other persistent unconjugated hyperbilirubinemia conditions in infancy and by non-responsiveness to phenobarbitone therapy. We report our clinical exercise of diagnosis of persistent unconjugated hyperbilirubinemia most probably due to CNS-I, a very rare entity-1 in 1,000,000 population(3).

A 6-month-old baby born to a consanguineously married couple, presented with jaundice since day 3 of life (total biluribin of 22.6 mg/dL with indirect fraction of 21.8 mg/dL) along with abnormal movements in the form of stiffening of limbs and arching of body. Review of medical records showed no features suggestive of hemolysis, liver cell failure, hypothyroid state and breast milk jaundice. Trial of phenobarbitone therapy was also found to be ineffective in bringing down bilirubin levels.

Now at 6 months of age, with regular home phototherapy for the past 5 months, baby weighed 5 kg and was irritable. Developmental history revealed delayed attainment of milestones with social smile at 5 months and partial head control at 6 months. Examination revealed deep icterus with staining of palms and soles and signs of kernicterus. Routine blood and urine tests were normal. Serum bilirubin was 25 mg/dL (indirect fraction of 23.8 mg/dL) and other liver function tests were normal. A screening for TORCH infection was negative. A second trial of phenobarbitone therapy was also ineffective.

The diagnosis of CNS-I was considered in our case based on clinical characters - severe persistent unconjugated hyperbilirubinemia developing early in neonatal period with no response to two trials of phenobarbitone therapy, early development of features of kernicterus and by excluding other conditions like breast milk jaundice, hemolysis and hypothyroid state. CNS type II is the most important differential diagnosis. The major differentiating characteristic between the two types of Crigler-Najjar syndrome is the response to drugs that induce activity of cytochrome P450 enzymes like pheno-barbitone that causes a significant decline in the serum bilirubin of patients with type II diseases(4). However, differentiating Crigler-Najjar syndrome type I from type II solely on the basis of response to phenobarbitone can sometimes be misleading and confirmatory diagnosis rests on demonstration of absence of UGT activity in liver and mutation analysis and these test are complicated and not routinely available(4). In our case, extracted DNA samples of the patient and parents are

stored for future analysis in definitive diagnosis. Crigler-Najjar syndrome type I was considered in our case by its classical clinical presentation, non-response to two trials of phenobarbitone therapy and by a process of exclusion of other conditions causing persistent unconjugated hyperbilirubinermias in infancy. Currently the treatment of CNS-I consists of phototherapy followed by liver transplantation(2), Tin-mesoporphyrin, hepatocyte transplantations(5), ursodeoxy-cholic acid, bilirubin oxidase, antioxidants, calcium supplements, clofibrate, flumecinol, chlorpromazine and urine alkalinization have been tried in CNS-I. The most exiting new therapy discussed is the gene therapy(5).

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Improving Oxygenation in Preterm Neonates with Respiratory Distress

We read with interest the communication by Patole, *et al.*(1). Definitely the adminis-tration of antenatal glucocorticoids and availability of Hudson-Prongs (HP) conti-nuous positive airway pressure(CPAP) are remarkable breakthroughs in management of preterm babies and have played a role in reducing the need for ventilation. Our neonatal set up is very similar to the authors and we would like to share our experience of a similar case. This baby was the second of twins delivered by cesarean section in view of fetal decelerations at 30 week gestation and weighed 1245 grams. He was transferred from operation theater to newborn care with CPAP support by Neopuff resuscitaire and was put on 5 cm CPAP in 28% FiO_2 (fraction of oxygen in inspired air). Chest radiograph at six hours of life was typical of hyaline membrane disease. At about 24 hours of birth, he deteriorated and oxygen requirement rose to CPAP of 6 cm with 40% FiO_2 and upto 55% in next four hours. We were in a dilemma at