



Crigler Najjar syndrome with pregnancy

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Key words : Crigler Najjar syndrome

Case report

Mrs. S, a 25 year old woman was admitted to the labor room on 16th May, 2002. She gave history of amenorrhoea for 9 months and jaundice since birth. She was an unbooked but immunized. Her jaundice was persistent, though the severity fluctuated from time to time, increasing during periods of stress and pregnancy.

During this pregnancy, she had been hospitalized three times in the medicine ward at 8 weeks, 17 weeks and 28 weeks of gestation for exacerbation of her jaundice. Every time, she was managed conservatively. There was no history of fever, pruritis, malena, hematemesis, blood transfusion, or pain in the right hypochondrium.

A year ago, she had a full term normal delivery of a male child, who is also suffering from congenital hyperbilirubinemia. She gave history of exacerbation of jaundice during that pregnancy also.

Family history revealed that she has an unmarried sister who is also suffering from congenital jaundice. Her brother is unaffected, while another brother died in early infancy due to unknown causes. Both parents are unaffected and there is no history of consanguinity.

On admission, her vitals were stable. Icterus was present. There was no pallor or cyanosis. Cardiovascular and respiratory systems were normal.

On abdominal examination, liver and spleen were not palpable. The uterus was term size, with fetus in longitudinal lie with cephalic presentation. The fetal heart was regular.

On vaginal examination, the cervix was 8 cm dilated and 80 % effaced. Membranes were absent, liquor was clear and vertex was at - 3 station. She had a normal vaginal delivery of a male baby weighing 2.9 kg. The baby had normal apgar score and was transferred to the nursery because of jaundice at birth. Post-partum period was uneventful.

Investigations revealed Hb to be 10 g/dL and platelet count of 1,62,000 m³. Total serum bilirubin was 10.8 mg% (unconjugated bilirubin - 6.6 mg % and conjugated bilirubin - 4.2 mg %), SGOT - 67 IU/ L, SGPT - 41 IU/L, and serum alkaline phosphatase - 276 IU/L. Urine was negative for bile salts and bile pigments. Peripheral smear did not show any evidence of hemolysis. Coagulation profile was normal. Ultrasound scan revealed mild splenomegaly with normal liver. HbsAg, hepatitis A, IgM and hepatitis E IgM were found to be negative.

She was managed conservatively and the serum bilirubin levels dropped gradually to 7.6 mg % with persistence of unconjugated hyperbilirubinemia. (unconjugated bilirubin - 4.5 mg%, conjugated bilirubin - 3.1 mg %).

Examination of the newborn in the nursery revealed presence of icterus. Pallor was absent. There was no facial dysmorphism. Eyes and ears were normal, both testes were descended and the spine and the feet were normal. Head was normal with caput formation. Anterior fontanelle was 2 x 2 cm wide, posterior fontanelle was closed. No sutural diastasis /overlapping was noted. Head circumference (HC) was 32 cm. The baby's weight was 2.9 kg and length 50 cm.

Investigations of the baby at birth revealed serum bilirubin 10.2 mg% (unconjugated bilirubin - 0.6 mg%, conjugated

Paper received on 14/04/2003 ; accepted on 18/08/2004

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bilirubin – 9.6 mg%), SGOT, 581 IU/L, SGPT, 198 IU/L and serum alkaline phosphatase 361 IU/L. Urine was negative for bile pigments.

Baby received blood transfusion and phototherapy and was discharged with a advice to take phenobarbitone 5 mg/kg/day he baby came for only one follow up visit when his serum bilirubin level had dropped to 3.4 mg% (conjugated 0.2mg% and uncagugated 3.2mg%. and there was no evidence of kernicterus.

The sibling who is a one year old male child had resulted from a full term normal delivery. He also had congenital jaundice, for which he had received exchange transfusion and phototherapy in infancy. At present he is icteric but has no history of seizures. He does not have abnormal facial features, abnormal head size or delayed milestones. On examination, he has hepatosplenomegaly. Investigations reveal a negative HbsAg test. He has not got a HIDA scan or liver biopsy done.

Discussion

A strong family history of persistent unconjugated hyperbilirubinemia, absence of hemolysis, and normal liver enzyme levels lead us to a diagnosis of Crigler Najjar Syndrome type II. Crigler Najjar Syndrome ¹ is a rare disorder of impaired bilirubin conjugation due to absence or deficiency of the enzyme glucuronyl transferase.

Type I disorder is due to the complete absence of the enzyme glucuronyl transferase. Infants have high unconjugated bilirubin levels in the range of 20 - 45 mg %, and usually die within the first year of life due to kernicterus. The stools are pale. Type I disorder shows an autosomal recessive inheritance pattern. Only 100 cases of type I disorder have been reported so far ¹.

Type II disorder is due to a deficiency of glucuronyl transferase activity and is consequently a less severe entity. Serum unconjugated bilirubin levels range from 6 – 20 mg %. Jaundice appears late and decreases after one week treatment with phenobarbitone (5 mg/kg/24 hrs). Stools are

normal. Type II disorder shows an autosomal dominant inheritance pattern with marked variability of penetrance.

Given that early death is almost inevitable with Crigler – Najjar disease type I, only patients with type II and Gilbert syndrome are seen in the reproductive years. There is only one case report of a patient with Crigler –Najjar disease type I with pregnancy, which resulted in the birth of an icteric infant who later developed signs of kernicterus ². Pregnancy in patients with type I syndrome may present a special risk of neurological manifestations ¹ due to increased serum bilirubin concentrations and altered albumin binding. Therefore, patients with type I Crigler – Najjar syndrome if they attain reproductive age group should be advised not to get pregnant. If they get pregnant, they should be adequately monitored and intercurrent infections, febrile episodes and any other illnesses should be promptly treated as the severity of this disease increases during periods of stress and pregnancy. They may require frequent hospitalization for increased bilirubin levels.

However, Crigler –Najjar disease type II seems to pose no maternal risk during pregnancy ³. Furthermore, hyperbilirubinemia has no significant ill effect on the fetus in utero and baby's outcome is usually good with phenobarbitone, phototherapy and exchange transfusions ³. Therefore, patients with type II disease can lead a normal reproductive life as it poses no threat to the mother or fetus.

The case has been reported because it is an extremely rare disorder. It highlights the existence of a rare differential diagnosis of jaundice in pregnancy and the importance of taking a detailed family history in a case of jaundice in pregnancy.

References

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