Naphthalene induced hemolysis in a glucose 6 phosphate dehydrogenase deficient neonate - A case report

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ABSTRACT
Glucose-6-phosphate dehydrogenase (G6PD), a critical enzyme in the hexose monophosphate pathway, is a key component in the antioxidant mechanism of all cells, particularly erythrocytes. Its deficiency may manifest in the neonatal period in the form of severe hyperbilirubinemia. Hemolysis in neonate may occur de novo or be precipitated by stressors such as oxidant drugs or naphthalene. We report a case of 3 days old, G6PD deficient neonate, with naphthalene induced hemolysis, requiring exchange transfusion.

Key words: Deficiency, Glucose-6-phosphate dehydrogenase, Hemolysis, Hyperbilirubinemia, Naphthalene, Oxidants

CASE REPORT
A male baby was born to a booked and immunized 25-year-old primigravida female with term gestation without any sepsis setting. Baby cried immediately after birth, weighed 2500 g and given Vitamin K 1 mg at birth. Breastfeeding was initiated and the baby was transferred to the mother in postnatal ward. The first 24 h of life were uneventful; the baby passed urine and stool and was accepting breastfeeds well. At 42 h of life, the baby was icteric till abdomen with transcutaneous bilirubin 13 mg/dl. There was no pallor, bruising, cephalhematoma, or hepatosplenomegaly.
Phototherapy was started and the baby was investigated. The maternal blood group was O−ve, baby’s blood group was O−ve, direct Coombs test: Negative, total serum bilirubin: 13.8 mg/dl (direct: 1.9 mg/dl and indirect: 11.9 mg/dl) and hemoglobin (Hb): 14.1 g/dl. Despite effective phototherapy (light emitting diodes), at 54 h of life, the baby presented with features of acute hemolysis: Deep icterus till soles, pallor and hepatosplenomegaly. The baby underwent double volume exchange transfusion uneventfully, and phototherapy was continued.

The pre-exchange serum bilirubin was 28 mg/dl (direct: 2.6 mg/dl and indirect: 25.4 mg/dl), Hb: 7 g/dl, hematocrit: 19.9%, and reticulocyte count: 12%. The peripheral smear was suggestive of anisopoikilocytosis, polychromatic, few nucleated cells without any sphere, or elliptocytes. The renal function tests including serum electrolytes were within normal range; sepsis screen and blood culture were negative. The post-exchange serum bilirubin was 10.9 mg/dl, Hb: 14.3 g/dl, and hematocrit 42%. All other investigations were within normal limits. The serum bilirubin declined to below phototherapy levels in 2 days, and the baby was accepting well orally.

The baby’s pre-exchange G6PD level was 9.1 U/g Hb (normal value for neonate: >14 U/g Hb); although, G6PD level of maternal uncle was normal.

DISCUSSION
G6PD is an X-linked recessive enzymopathy, critical in the redox metabolism in all aerobic cells as it maintains glutathione in the...
reduced form which helps to combat oxidant stress. Its deficiency has predominantly hematological manifestations as it is the only source of NADPH in erythrocytes. The disease is expressed in heterozygous males and homozygous females, while heterozygous females may have an intermediate expression. Its geographical distribution coincides with endemic malaria worldwide. In India, Punjab, Orissa, parts of West Bengal, Andhra Pradesh, and Kerala contribute to majority of the cases.

Hyperbilirubinemia in G6PD deficient neonates is a well-documented entity [6]. In addition to defective glucurondiation and hemolysis, coinheritance of uridine diphosphate-glucournyltransferase-1 deficiency of Gilbert’s syndrome and pregnant women ingesting oxidant drugs are implicated in the pathogenesis of jaundice [1]. The damage starts in utero but clinically manifests at day 2 or 3 of life. In a recent study conducted in India in 2015, 13.3% of the all jaundiced neonates are G6PD deficient, of which 12% were females [7]. Prematurity, sepsis, asphyxia, and major and minor blood group incompatibilities are compounding factors leading to severe hyperbilirubinemia [5]. However, none of these factors were present in our case. Certain G6PD mutation variants, seen in some racial groups increase the susceptibility to severe hemolysis and have higher rates of bilirubin encephalopathy and death [8,9].

Apart from exposure to oxidant drugs or maternal intake of such drugs during pregnancy, ingestion of fava beans and exposure to naphthalene balls are well documented to trigger hemolysis in such cases [10]. On reviewing the history with the parents, we found exposure to naphthalene in this case, starting from day 1. Hyperbilirubinemia may also appear in the absence of hemolysis triggering factors, especially in neonates [11]. A similar case was reported from Panama, where a 4 days old term neonate, who presented with jaundice, generalized tonic clonic seizures, required management with anticonvulsants, phototherapy, and exchange transfusion. A history of using naphthalene impregnated garments was recorded [12]. Valaes et al. also reported 21 neonates who developed hemolysis after exposure to naphthalene, 12 of whom were found be to G6PD deficient [13]. Newborns are unable to conjugate naphthalene metabolites, have thinner skin; oil massage also enhances absorption as naphthalene is lipophilic [14]. Phototherapy and exchange transfusion are the mainstay of management in jaundiced neonates.

Affecting about 5% of the world population, G6PD deficiency is not a rare entity and is easily preventable by avoidance of few triggers. In addition, avoidance of exposure to oxidant drugs if any, blood transfusion for severe anemia and folic acid supplementation play an important role. Repeat G6PD assay should be performed 3 months later in case of doubtful results. WHO recommends routine screening in populations in which 3-5% or more males are G6PD deficient [15]. G6PD deficiency should be considered with a high index of suspicion in cases who develop jaundice in the first 24 h of life, history of jaundice in a sibling, bilirubin levels >95th percentile, and in Asian males [16].

CONCLUSION

G6PD deficiency may manifest in the neonatal period in the form of severe hyperbilirubinemia. Hemolysis in neonate may be precipitated by stressors like naphthalene; therefore, careful history is very important to reach the diagnosis and to manage such cases.

REFERENCES


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