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Case Report

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, G lucose-6-phosphate dehydrogenase, Hemolysis, Hyperbilirubinemia, Naphthalene, Oxidants*

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common red cell enzyme defect, affecting about 400 million people worldwide [1]. The prevalence of G6PD deficiency in India ranges from 2% to 27%, the most common variant being G6PD Mediterranean [2]. G6PD is a house keeping enzyme and critical in redox metabolism of all aerobic cells, more importantly erythrocytes as they do not have an alternate pathway of nicotinamide adenine dinucleotide phosphate hydrogen (NADPH) generation. Neonatal hyperbilirubinemia is one of its most common presentations of G6PD deficiency [3]. About 10-50% of the deficient neonates are affected, requiring phototherapy, and often exchange transfusion [4]. In the neonatal period, hemolysis may be precipitated in the absence of an obvious trigger [5]. Despite extensive literature review, sparse reports exist on the naphthalene triggered hemolysis in neonates. We present a case of a G6PD deficient male neonate with exposure to naphthalene, presenting with severe hemolysis requiring exchange transfusion.

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 by enzymatic flour immunoassay). There was no history of intake of oxidant drugs by either mother or baby.

On retrospectively reviewing the history, we found that after birth, the baby was wrapped in sheets and made to wear clothes kept in the cupboard with naphthalene balls. Later, samples for G6PD levels were sent to the mother, and found be 14 U/g Hb (normal value for adult: >20 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 glucuronidation and hemolysis, coinheritance of uridine diphosphate-glucornyltransferase-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

1. Frank JE. Diagnosis and management of G6PD deficiency. Am Fam Physician. 2005;72(7):1277-82.
2. Mohanty D, Mukherjee MB, Colah RB. Glucose-6-phosphate dehydrogenase deficiency in India. Indian J Pediatr. 2004;71(6):525-9.
3. Valaes T. Severe neonatal jaundice associated with glucose-6-phosphate dehydrogenase deficiency: Pathogenesis and global epidemiology. Acta Paediatr Suppl. 1994;394:58-76.
4. Cappellini MD, Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. Lancet. 2008;371(9606):64-74.
5. Carvalho CG, Castro SM, Santin AP, Zaleski C, Carvalho FG, Giugliani R. Glucose-6-phosphate-dehydrogenase deficiency and its correlation with other risk factors in jaundiced newborns in Southern Brazil. Asian Pac J Trop Biomed. 2011;1(2):110-3.
6. Kaplan M, Hammerman C. Severe neonatal hyperbilirubinemia. A potential complication of glucose-6-phosphate dehydrogenase deficiency. Clin Perinatol. 1998;25(3):575-90, viii.
7. Goyal M, Garg A, Goyal MB, Kumar S, Ramji S, Kapoor S. Newborn screening for G6PD deficiency: A 2-year data from North India. Indian J Public Health. 2015;59(2):145-8.
8. Slusher TM, Vreman HJ, McLaren DW, Lewison LJ, Brown AK, Stevenson DK. Glucose-6-phosphate dehydrogenase deficiency and carboxyhemoglobin concentrations associated with bilirubin-related morbidity and death in Nigerian infants. J Pediatr. 1995;126(1):102-8.
9. Nair PA, Al Khusaiby SM. Kernicterus and G6PD deficiency-a case series from Oman. J Trop Pediatr. 2003;49(2):74-7.
10. Dhillon AS, Darbyshire PJ, Williams MD, Bissenden JG. Massive acute haemolysis in neonates with glucose-6-phosphate dehydrogenase deficiency. Arch Dis Child Fetal Neonatal Ed. 2003;88(6):F534-6.
11. Kaplan M, Muraca M, Hammerman C, Vilei MT, Leiter C, Rudensky B, et al. Bilirubin conjugation, reflected by conjugated bilirubin fractions, in glucose-6-phosphate dehydrogenase-deficient neonates: A determining factor in the pathogenesis of hyperbilirubinemia. Pediatrics. 1998;102(3):E37.
12. de Gurrola GC, Arauz JJ, Duran E, Aguilar-Medina M, Ramos-Payan R, Garcia-Magallanes N, et al. Kernicterus by glucose-6-phosphate dehydrogenase deficiency. J Med Case Rep. 2008;2:146.
13. Valaes T, Doxiadis SA, Fessas P. Acute hemolysis due to naphthalene inhalation. J Pediatr. 1963;63:904-15.
14. Ostlere L, Amos R, Wass JA. Haemolytic anaemia associated with ingestion of naphthalene-containing anointing oil. Postgrad Med J. 1988;64(752):444-6.
15. American Academy of Pediatrics Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004;114(1):297-316.
16. Bhutani VK, Johnson LH, Keren R. Diagnosis and management of hyperbilirubinemia in the term neonate: For a safer first week. Pediatr Clin North Am. 2004;51(4):843-61, vii.

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