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Case Report: Infant With Glucose 6 Phosphate Dehydrogenase Deficiency

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ABSTRACT:

CASE:A 7-week-old came with complaints of not gaining weight yellowish discoloration of body and lethargic, no h/o fever, vomiting , loose stools. no h/o previous hospitalization. birth history: 2.8kg normal vaginal delivery cried immediately after birth no h/o nicu admission. h/o bottle fed with formula feeds.

On physical examination, his weight is 3.7 kg (<5th percentile), length is 55 cm (25th percentile), and head circumference is 39 cm (25th-50th percentile). Vital signs are: temperature 98.2°F (36.8°C), heart rate 159 beats/min, blood pressure 75/51 mm Hg, and respiratory rate 36 breaths/min. The baby is thin, jaundiced, and pale but is alert and cooing. He appears severely dehydrated, with delayed capillary refill of 3 seconds. There is no rash, petechiae, or organomegaly.

Laboratory evaluation shows total bilirubin of 15.2 mg/dL (259.98 mmol/L) and conjugated bilirubin of 0.5 mg/dL (8.55 mmol/L). Complete blood cell count reveals a white blood cell count of 7,600/mL (7.6 x 10^9/L), hemoglobin of 7.6 g/dL (76 g/L), hematocrit of 22.6% (0.226), platelet count of 251 10^3/mL (251 x 10^9/L), mean corpuscular volume of 84.7 mm^3 (84.7 fL), and red cell distribution width of 18.3%. Urinalysis is negative for blood, leukocyte esterase, nitrites, and reduc-ing substances. Urine and blood cultures are obtained. The newborn screening result is checked and is negative for congenital hypothyroidism but reveals homozygous sickle hemoglobin (Hgb SS) consistent with sickle cell disease (SCD). Additional evaluation leads to the cause of his pallor and jaundice.

DISCUSSION:

The infant was hospitalized for failure to thrive and evalu-ation of jaundice and pallor. The initial consideration was life-threatening causes of unconjugated hyperbilirubinemia, including infection, hemolysis, and visceral bleeding from nonaccidental trauma. Peripheral blood smear showed poly-chromasia and nucleated red blood cells (RBCs), suggest-ing increased RBC destruction and reticulocytosis. Direct and indirect Coombs tests were

negative. His blood and urine cultures did not show any growth of organisms. Abdominal ultrasonography did not show any abnormalities

Because glucose-6-phosphate dehydrogenase (G6PD) de-ficiency is the most common RBC enzyme defect, we mea-sured G6PD activity, which was low at 2 U/g hemoglobin (0.03 nkat/g hemoglobin) (normal range 4.6–13.5 U/g hemoglobin [0.08–0.23 nkat/g hemoglobin]) and established the diagno-sis of G6PD deficiency. Thus, his unconjugated hyperbiliru-binemia was due to G6PD deficiency, dehydration, impaired conjugation due to immature hepatic glucuronyl transferase (GT), and increased enterohepatic circulation from decreased oral intake. We attributed his anemia to physiologic nadir exacerbated by hemolysis due to G6PD deficiency.

Understanding the causes of unconjugated hyperbiliru-binemia requires a review of bilirubin metabolism. Bilirubin is formed from the breakdown of heme in a 2-step process. First, heme is catabolized to biliverdin and carbon monoxide by heme oxygenase in the reticuloendothelial system. Second, biliverdin is converted to bilirubin by biliverdin reductase. This unconjugated bilirubin is lipid-soluble and binds to albumin in the bloodstream. Uncon-jugated bilirubin is then conjugated in the liver by GT and excreted by the biliary system into the gastrointestinal tract. Conjugated bilirubin is water-soluble and, thus, cannot cross the small intestinal epithelium. Some of the conju-gated bilirubin is converted back to unconjugated bilirubin by glucuronidase and reabsorbed in the small intestine where it travels through the portal vein in a process known as enterohepatic circulation. The remainder of the conju-gated bilirubin is reduced by bacterial proteases in the colon to urobilinogen and eventually eliminated in the stool as stercobilinogen and in the urine as urobilinogen.

Unconjugated hyperbilirubinemia can be due to increa-sed production of bilirubin, decreased clearance of bilirubin, or both (Table). Increased bilirubin production can be due to increased RBC mass or increased RBC breakdown. Increased RBC breakdown can have nonimmune-mediated or immune-mediated causes. Nonimmune causes of hemolysis in-clude RBC membrane defects, defective or deficient cytosolic enzymes, or qualitative or quantitative defects in globin syn-thesis. Folate or vitamin B_{12} deficiency leading to impaired DNA synthesis and ineffective erythropoiesis can also cause unconjugated hyperbilirubinemia.

G6PD deficiency is the most common RBC enzyme defect and should be suspected in all patients with nonimmune-mediated hemolysis. Because this disorder has an X-linked inheritance, the diagnosis should be considered in males. Rarely, females with lyonization (inactivation of one X chro-mosome) may also develop symptomatic hemolysis. G6PD deficiency can present with neonatal jaundice, acute hemo-lysis due to triggers (fava beans, drugs, infections), or chronic hemolysis without a clear trigger. Diagnosis is made by assaying the activity level of G6PD. False-negative results can occur because young RBCs have increased G6PD activity levels. Therefore, the assay should be repeated 3 months after an acute hemolytic episode if the diagnosis is suspected. Management is supportive and

involves iden-tifying and avoiding the trigger. Prevention is key, and patients should be provided a list of foods and drugs that could exacerbate the condition, Impaired conjugation because of immature hepato-cyte GT activity likely contributed to this infant's jaun-dice as well. Children younger than age 2 years have impaired conjugation compared to older children and adults.SCD can cause a hemolytic anemia and unconjugated hyperbilirubinemia. However, this 7-week-old infant's hyperbilirubinemia cannot be attributed to SCD. At birth, 55% to 65% of hemoglobin is fetal hemoglo-bin (HgbF). Although the ratio of HgbF-to-Hgb S di-minishes throughout the first postnatal year, anemia from increased hemolysis does not become apparent until age 3 months. This is because approximately 50% of the hemoglobin in infants younger than age 3 months is still HgbF and, thus, not subject to sickling and hemolysis.

Although this patient had both SCD and G6PD de-ficiency, the 2 conditions are not causally linked; the genes responsible for them are on different chromo-somes. SCD and G6PD deficiency cause hemolysis by different means. Therefore, a hypothesis that their effects might be additive is reasonable. Historically, data on this topic have been conflicting. Steinberg et al found that the presence of G6PD deficiency does not increase the frequency or severity of hemolysis in patients with SCD. However, Benkerrou et al found that G6PD deficiency along with SCD conferred a more severe anemia and an increased transfusion requirement in children younger than age 42 months. This discrepancy may have an age-related explanation. G6PD concentrations natu-rally diminish in RBCs as they age. In older children and adults, the decreased HgbF concentrations and con-comitant rise in Hgb S results in a younger population of RBCs with relatively higher G6PD levels. This may be the reason why older children and adults with SCD have a similar degree of hemolysis and anemia regard-less of the presence or absence of concurrent G6PD deficiency.

Patient Course

With intravenous fluid hydration and feeding, this patient's total bilirubin decreased from 15.2 mg/dL (259.98 mmol/L) to 7.7 mg/dL (131.70 mmol/L) over 3 days. He was dis-charged home with foster parents and prophylactic peni-cillin VK 125 mg twice daily for SCD. The foster parents were instructed that the baby should avoid fava beans, legumes, soy, peanuts, antimalarials, and sulfonamides that could trigger hemolysis in the setting of G6PD defi-ciency. He is currently gaining weight, achieving develop-mental milestones, and being followed in primary care and hematology clinics.

Lessons for the Clinician Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common red blood cell (RBC) enzyme defect and should be suspected in all patients with nonimmune-mediated hemolysis.

- In infants with sickle cell disease, anemia and jaundice do not become apparent until after age 3 months due to the presence of fetal hemoglobin.

- False-negative results can occur with the G6PD activity assay because young RBCs have increased G6PD activity. Therefore, the assay should be repeated 3 months after an acute hemolytic episode.

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