Maternal Cautopyreiophagia as a Rare Cause of Neonatal Hemolysis: A Case Report
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Hyperbilirubinemia in the first 24 hours of life in a newborn is pathologic, necessitating additional evaluation. We report the first case of hemolysis and subsequent hyperbilirubinemia in an otherwise normal term neonate resulting from oxidative stress in the form of maternal cautopyreiophagia: the ingestion of burnt matchstick heads. During the third trimester of pregnancy, the infant’s mother consumed more than 300 burnt matchstick heads weekly for 4 weeks. Matches contain potassium chlorate, a powerful oxidant that when ingested can ultimately lead to the destruction of erythrocytes, disseminated intravascular coagulation, kidney injury, or death. The infant’s bilirubin rose as high as 17 mg/dL at 22 hours of life; however, the infant did well with a brief course of phototherapy. This case highlights the importance of prenatal questioning about maternal ingestion of potentially oxidative substances and assessing the possible risk for the infant.

Hyperbilirubinemia presenting in the first 24 hours of life is considered pathologic and necessitates additional investigation. Common causes include infection, blood type incompatibility, and hemolysis. Hemolysis in the newborn can be caused by hereditary spherocytosis, unstable hemoglobinopathies, pyruvate kinase deficiency, and glucose-6-phosphate dehydrogenase (G6PD) deficiency. With G6PD deficiency, the erythrocyte becomes susceptible tooxidant damage because of its decreased ability to regenerate reduced glutathione (GSH) in the hexose monophosphate shunt. Cases in the literature describe infants with G6PD deficiency showing signs of significant hemolysis shortly after birth, caused by maternal ingestion of known oxidants, but there are no cases reported showing similar hemolysis and oxidative injury in an otherwise normal infant.1,2 We describe the first case of pathologic neonatal hyperbilirubinemia in a normal infant associated with maternal cautopyreiophagia: the ingestion of burnt matchstick heads.

CASE
We cared for a full-term African American girl delivered via cesarean delivery at 39 weeks’ gestation to a 29-year-old mother. The pregnancy was complicated by the development of pica during the third trimester. The mother reported she was ingesting >300 burnt matchsticks per week, a behavior known as cautopyreiophagia. Because she was unable to modify her behavior and because of the potential for toxicity, the obstetricians proceeded with an elective induction at term. Routine prenatal laboratories were reassuring; her blood was type A− and negative for the presence of red cell antibodies. The infant was vigorous at delivery, with Apgar scores of 8 and 9. She was appropriate for gestational age and her physical examination was normal. At 22 hours of life the infant was found to have jaundice.

abstract

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Dr Bernardo cared for the patient presented, conceptualized the mechanism of hemolysis, reviewed the literature, and drafted the initial manuscript. Dr Matos initiated the investigation of the mechanism of hemolysis, reviewed the literature, and critically reviewed and revised the manuscript. Dr Dawood cared for the patient presented and reviewed and revised the manuscript. Dr Whiteway reviewed the literature, provided vital intellectual hematology content, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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have an elevated screening transcutaneous bilirubin level of 17 mg/dL, high risk according to the Bhutani chart. Serum unconjugated bilirubin was confirmed at 16.7 mg/dL. Additional laboratory evaluation showed an elevated conjugated bilirubin of 1.65 mg/dL (normal, 0.1–0.3 mg/dL), aspartate transaminase of 170 U/L (normal, 5–32 U/L), and alanine transaminase of 37 U/L (normal, 4–33 U/L). Reticulocyte count and lactate dehydrogenase were also elevated at 19% (normal, 0.5%–2.2%) and 1381 U/L (normal, 135–225 U/L), respectively. The infant’s complete blood cell count was significant for an elevation in the number of white blood cells at 62.1 × 10⁹/L (normal, 9–30 × 10⁹/L), normal hematocrit of 48% (normal, 43%–65%), and anisocytosis, macrocytes, and polychromasia on peripheral blood smear. Her blood type was AB+, and direct antiglobulin testing was negative.

The infant was treated with phototherapy for 72 hours until her bilirubin level was 8.1 mg/dL, and she did not experience a rebound in bilirubin levels. She completed a 7-day course of empirical gentamicin and ampicillin; blood cultures were negative for growth. She was discharged from the hospital on day of life 8. Follow-up at 2 months of life showed 2 normal newborn screens and a normal G6PD level of 15.1 U/g hemoglobin (normal, 7–20.5 U/g). At her 9-month well child visit the infant was growing along the fourth percentile for weight, 15th percentile for height, and 13th percentile for head circumference. She was meeting age-appropriate developmental milestones and her physical examination was reassuring. Laboratory evaluation revealed a normal hematocrit of 34.3%, reticulocyte count 1.6%, total bilirubin 0.1 mg/dL, conjugated bilirubin <0.2 mg/dL, and lactate dehydrogenase 243 U/L. The patient’s transaminitis was also improving: aspartate transaminase 62 U/L and alanine transaminase 54 U/L. Hemoglobin electrophoresis showed hemoglobin A 96.8%, hemoglobin A2 2.7%, and hemoglobin F 0.5%, with a negative result for variant hemoglobins. Osmotic fragility was not elevated.

**DISCUSSION**

Jaundice is one of the most common problems encountered in term newborns. Hyperbilirubinemia presenting in the first 24 hours of life is considered pathologic, with causes including infection, liver dysfunction, metabolic disease, hemolytic disease secondary to blood type incompatibility, erythrocyte membranopathies, and erythrocyte enzyme deficiency such as pyruvate kinase or G6PD. The erythrocyte is reliant on the enzymes present in the hexose monophosphate shunt, such as G6PD, to prevent oxidant injury via the production of reduced nicotinamide adenine dinucleotide phosphate (NADPH). Oxidants such as the superoxide anion and hydrogen peroxide are formed in the erythrocyte via reaction of hemoglobin with oxygen and can also be produced by exogenous factors such as drugs, infection, and oxidant exposure. Within the erythrocyte, GSH is generated via a reaction between oxidized glutathione (GSSG) and NADPH, catalyzed by the enzyme glutathione reductase. The enzyme glutathione peroxidase then drives the reaction between the produced GSH and oxidant to form water and GSSG (Fig 1). Without NADPH and the glutathione pathways, oxidant exposure leads to membrane injury, methemoglobin formation, osmotic fragility, and destruction of erythrocytes. Ingestion of matches during pregnancy dates back decades, but literature thoroughly describing cautopyreioaphagia is scarce. In the United States, commercially available matchsticks contain sulfur, potassium...
chlorate (KClO₃), and many other toxins. KClO₃ is the powerful and slow oxidizing agent that sustains the flame once the match is ignited. In evaluating potential toxicity, animal studies have shown that chronic KClO₃ ingestion over 3 to 9 months results in decreased GSH levels and subsequent hemolysis. Additional studies using the same rat and chicken model demonstrated alterations in red cell morphology, with electron microscopy showing echinocytes and dacrocytes. In vitro studies using human erythrocytes have found a dose-dependent decrease in the activity of G6PD and glutathione peroxidase that results in a decrease in GSH levels by 50% within the first 60 minutes of exposure. Human erythrocytes also exhibit increased membrane rigidity when exposed to various concentrations of KClO₃. As seen in both human and animal data, the combined effect of a decrease in GSH and increased membrane rigidity leaves the erythrocyte susceptible to oxidant injury, altered membrane kinetics, and ultimately hemolysis. Clinically this mechanism is evident in several case reports describing the toxic effects of chlorate exposure with patients exhibiting hemolysis, disseminated intravascular coagulation, liver failure, renal injury, and death. Safety assessments have found the toxic dose of KClO₃ in humans to be 5 g and the lethal dose is estimated at 15 to 35 g. To reach the toxic dose of 5 g of KClO₃, ~400 unburned matches must be consumed. Toxicity data for children are scarce, with only 1 case report describing an infant death after the ingestion of 1 g of KClO₃.

Within 24 hours of delivery our patient showed evidence of hemolysis, hepatic injury, and hyperbilirubinemia. Potential causes including infection, blood type incompatibility, spherocytosis, and hemoglobinopathies were ruled out. At subsequent follow-up visits she showed no additional evidence of hepatic injury or ongoing hemolytic disease. The infant was also monitored for methemoglobinemia and renal injury, which she did not develop.

KClO₃ found in matchsticks, is a powerful oxidant that animal and in vitro human studies have shown to cause oxidative injury by reducing levels of GSH and inducing erythrocyte membrane rigidity, with subsequent lysis of erythrocytes. The human adult toxic dose of KClO₃ can be reached with the ingestion of ~400 unburned matches. Data on ingestion of burnt matchstick heads are not robust because their composition varies depending on how long the match was allowed to burn. However, reports in the forensic sciences reveal the presence of KClO₃ in both unburned and burnt matches, although no quantification is provided. In this case, the mother lit the matches and quickly extinguished them, leaving some KClO₃ intact. We hypothesize that our patient developed hemolysis, acute hepatic injury, and hyperbilirubinemia secondary to toxic levels of KClO₃ remaining in the burnt matchsticks her mother ingested. Thus, this is the first reported case of neonatal hemolysis with subsequent hyperbilirubinemia associated with maternal cautopyreiaphagia. Although the infant did well clinically after the initial in utero exposure period, the long-term effects of these oxidants are not yet known. In addition, many household disinfectants, cosmetics, mouthwashes, toothpastes, and medications contain oxidative agents such as chlorates. This case highlights the importance of prenatal questioning about maternal ingestion of nonfood substances, specifically oxidants, because of the potential risk for the infant.

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