Maternal Cautopyreiophagia as a Rare Cause of Neonatal Hemolysis: A Case Report

Erika O. Bernardo, MD, Renée I. Matos, MD, MPH, Taslim Dawood, MD, Susan L. Whiteway, MD

abstract

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.

San Antonio Uniformed Services Health Education Consortium, Fort Sam Houston, Texas

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.

www.pediatrics.org/cgi/doi/10.1542/peds.2014-2498

DOI: 10.1542/peds.2014-2498

Accepted for publication Dec 8, 2014

Address correspondence to Erika O. Bernardo, MD, Department of Pediatrics, San Antonio Military Medical Center, 3551 Roger Brooke Dr, Fort Sam Houston, TX 78234. E-mail: erika.o.bernardo@gmail.com

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275); published in the public domain by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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 to oxidant 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 an elevated screening transcutaneous bilirubin level of 17 mg/dL, high risk according to the Bhutani chart.[3] 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 $\times$ 10^9/L (normal, 9–30 $\times$ 10^9/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.[4]

Ingestion of matches during pregnancy dates back decades, but literature thoroughly describing cautopyreiophagia is scarce.[5–7] In the United States, commercially available matchsticks contain sulfur, potassium

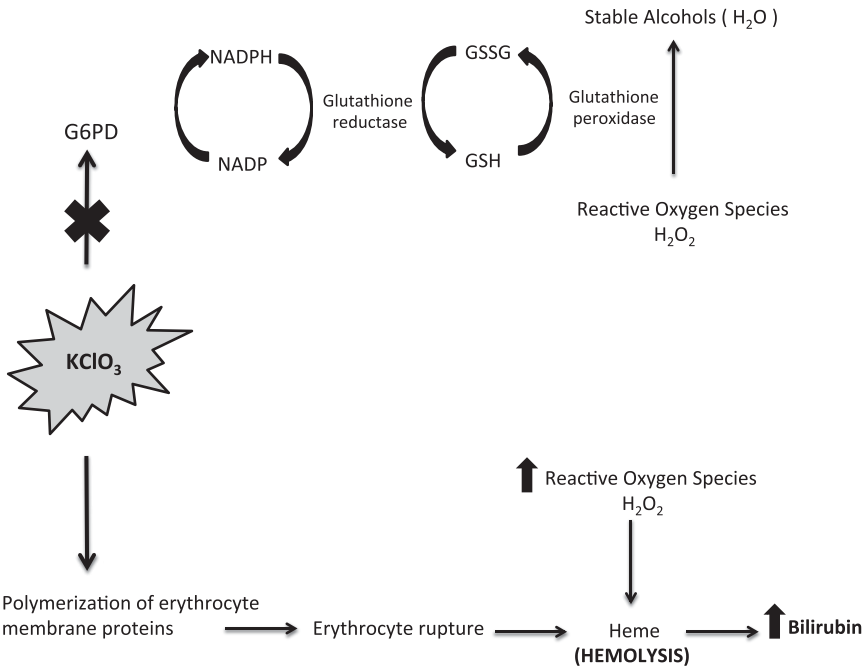

FIGURE 1

Proposed mechanism of hemolysis and hyperbilirubinemia. $KClO_3$ leads to hemolysis and hyperbilirubinemia via 2 pathways. In the first pathway, $KClO_3$ inhibits G6PD, decreasing GSH, and leaves erythrocytes susceptible to reactive oxygen species. $KClO_3$ also induces polymerization of erythrocyte membrane proteins, causing rupture of erythrocytes and thus hemolysis.

chlorate ($KClO_3$), and many other toxins.[8,9] $KClO_3$ is the powerful and slow oxidizing agent that sustains the flame once the match is ignited.[10,11] In evaluating potential toxicity, animal studies have shown that chronic $KClO_3$ ingestion over 3 to 9 months results in decreased GSH levels and subsequent hemolysis.[12,13] Additional studies using the same rat and chicken model demonstrated alterations in red cell morphology, with electron microscopy showing echinocytes and dacrocytes.[14] 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.[15,16] Human erythrocytes also exhibit increased membrane rigidity when exposed to various concentrations of $KClO_3$.[15,17] 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.[18–21] Safety assessments have found the toxic dose of $KClO_3$ in humans to be 5 g and the lethal dose is estimated at 15 to 35 g.[22] To reach the toxic dose of 5 g of $KClO_3$, ~400 unburned matches must be consumed.[9,23] Toxicity data for children are scarce, with only 1 case report describing an infant death after the ingestion of 1 g of $KClO_3$.[24]

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.

$KClO_3$, 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 $KClO_3$ 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 $KClO_3$ in both unburned and burnt matches, although no quantification is provided.[25] In this case, the mother lit the matches and quickly extinguished them, leaving some $KClO_3$ intact. We hypothesize that our patient developed hemolysis, acute hepatic injury, and hyperbilirubinemia secondary to toxic levels of $KClO_3$ remaining in the burnt matchsticks her mother ingested. Thus, this is the first reported case of neonatal hemolysis with subsequent hyperbilirubinemia associated with maternal cautopyreiophagia. 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.[22] This case highlights the importance of prenatal questioning about maternal ingestion of nonfood substances, specifically oxidants, because of the potential risk for the infant.

ACKNOWLEDGMENT

We thank Dr David Hsieh for his comments and revision of the manuscript.

REFERENCES

1. Harley JD, Robin H, Robertson SE. Thiazide-induced neonatal haemolysis? *BMJ*. 1964;1(5384):696–697
2. Kaplan M, Vreman HJ, Hammerman C, Schimmel MS, Abrahamov A, Stevenson DK. Favism by proxy in nursing glucose-6-phosphate dehydrogenase-deficient neonates. *J Perinatol*. 1998;18(6 pt 1):477–479
3. 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
4. Coetzer T, Zail S. Membrane protein complexes in GSH-depleted red cells. *Blood*. 1980;56(2):159–167
5. Abu-Hamdan DK, Sondheimer JH, Mahajan SK. Cautopyreiophagia. Cause of life-threatening hyperkalemia in a patient undergoing hemodialysis. *Am J Med*. 1985;79(4):517–519
6. Perry MC. Cautopyreiophagia. *N Engl J Med*. 1977;296(14):824
7. Smulian JC, Motiwala S, Sigman RK. Pica in a rural obstetric population. *South Med J*. 1995;88(12):1236–1240
8. Wisniak J. Matches: the manufacture of fire. *Indian J Chem Techn*. 2005;12(3):369–380
9. Jarden Corporation. Wooden stick, strike on box matches (SOB) (AKA: safety matches) [material safety data sheet]. 2013. Available at: http://media.lifeandhome.com/media/downloads/5064/42925025_MSDS.pdf. Accessed October 21, 2014
10. Siegel R. Ignition of the safety match. *J Chem Educ*. 1940;17(11):515
11. Murty CR, Rao GG. Studies on potassium chlorate as a primary oxidimetric reagent. *Talanta*. 1972;19(1):37–43
12. Couri D, Abdel-Rahman MS, Bull RJ. Toxicological effects of chlorine dioxide, chlorite and chlorate. *Environ Health Perspect*. 1982;46:13–17
13. Couri D, Abdel-Rahman MS. Effect of chlorine dioxide and metabolites on glutathione dependent system in rat, mouse and chicken blood. *J Environ Pathol Toxicol*. 1979;3(1–2):451–460
14. Abdel-Rahman MS, Couri D, Bull RJ. Kinetics of ClO_2 and effects of ClO_2,

ClO_2^-, and ClO_3^- in drinking water on blood glutathione and hemolysis in rat and chicken. *J Environ Pathol Toxicol*. 1979;3(1–2):431–449

15. Singelmann E, Wetzel E, Adler G, Steffen C. Erythrocyte membrane alterations as the basis of chlorate toxicity. *Toxicology*. 1984; 30(2):135–147
16. Steffen C, Wetzel E. Chlorate poisoning: mechanism of toxicity. *Toxicology*. 1993; 84(1–3):217–231
17. Singelmann E, Steffen C. Increased erythrocyte rigidity in chlorate poisoning. *J Clin Pathol*. 1983;36(6):719
18. Steffen C, Seitz R. Severe chlorate poisoning: report of a case. *Arch Toxicol*. 1981;48(4):281–288
19. Gebhardtova A, Vavrinec P, Vavrincova-Yaghi D, et al. A case of severe chlorite poisoning successfully treated with early administration of methylene blue, renal replacement therapy, and red blood cell transfusion: case report. *Medicine (Baltimore)*. 2014;93(9):e60
20. Picaud JC, Cochat P, Parchoux B, et al. Acute renal failure in a child after chewing of match heads. *Nephron*. 1991; 57(2):225–226
21. Sein Anand J, Barwina M, Zajac M, Kaletha K. Suicidal intoxication with potassium chlorate successfully treated with renal replacement therapy and extracorporeal liver support. *Przegl Lek*. 2012;69(8):585–586
22. Flume M. Final report on the safety assessment of potassium chlorate. *Int J Toxicol*. 1995;14(3):221–230
23. Bright PD. *Military Dog Training Aids: Toxicity and Treatment*. Report no. 89-130EH0100LOC. Washington, DC: US Government Printing Office; 1989
24. Witthaus RA, Becker TC. *Medical Jurisprudence Forensic Medicine and Toxicology*. 2nd ed. York, PA: The Maple Press; 1911
25. Stam M. The forensic analysis of wooden stick matches in a southern California arson case and subsequent examinations in two other arson cases. Presented at: The Great Scientific Exchange; October 2013; Milwaukee, WI

Maternal Cautopyreiophagia as a Rare Cause of Neonatal Hemolysis: A Case Report

Erika O. Bernardo, Renée I. Matos, Taslim Dawood and Susan L. Whiteway

Pediatrics 2015;135;e726
DOI: 10.1542/peds.2014-2498 originally published online February 23, 2015;

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Maternal Cautopyreiophagia as a Rare Cause of Neonatal Hemolysis: A Case Report

Erika O. Bernardo, Renée I. Matos, Taslim Dawood and Susan L. Whiteway

Pediatrics 2015;135;e726
DOI: 10.1542/peds.2014-2498 originally published online February 23, 2015;