Case Report

A case of Hyperthermia Induced Acute Haemolysis in a Preterm

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Chettinad Health City Medical Journal 2015; 4(2): 97 - 100

Abstract

There are many causes for hemolysis in a preterm neonate. To our knowledge there are no reports of high environmental temperature associated haemolysis in preterm neonates. Investigators have reported on the effects of heat on blood. We report hemolysis associated with high environmental temperature in a preterm neonate after discharge from the hospital.

Key Words: Environmental Hyperthermia, Preterm Neonate, Hemolysis.

Introduction

Haemolysis refers to the rupture of erythrocytes and release of their contents into the surrounding fluid and defined as premature destruction of red blood cells[1]. Common causes of in vivo haemolysis include ABO or Rh incompatibility, toxins released by gram positive bacteria or parasites (e.g. haemolytic streptococci, plasmodium), Sickle cell disease, G6PD deficiency, and burns which cause erythrocyte cell membrane destruction. To our knowledge there are no reports of high environmental temperature associated haemolysis in preterm neonates. Investigators have reported on the effects of heat on preterm blood. We report haemolysis associated with high environmental temperature in a preterm neonate after discharge from the hospital.

Case history

A preterm female infant weighing 1.185 kg was born to a 27 year old primipara, O-group Rh positive mother, at 30 weeks of gestation by emergency cesarean due to premature rupture of membranes. Apgar scores were 5 and 8 at 1 and 5 minutes respectively. Early onset respiratory distress necessitated treatment with one dose of surfactant, and ventilation till day five, followed by continuous positive airway pressure support till day eight. Hyperbilirubinemia (highest total serum bilirubin of 10.4mg/dl on day four) was treated with phototherapy for 12 days. Blood group was A-group Rh positive and Direct Coombs was negative. Peripheral smears were normal (table 1). The blood culture sent on day one did not grow pathogens and was negative. On third day of life preterm infant deteriorated due to collapse of upper right lobe and sepsis screen revealed Acinetobacter sepsis and recovered after appropriate antibiotics. Started tube feeding the infant on day 1 which reached 150 ml/kg/day on 20th day of life. Oral iron and multivitamins were started on day twenty one and tolerated well. The infant was discharged home on day thirty with infant weight of 1505grams, against medical advice as insisted by the parents. The pre-discharge Hb was 11.8 mg%.

The infant was readmitted within 20 hours after discharge with complaints of excessive crying and fever for four hours. The history revealed that the family had moved to their temporary home in a first floor terrace with galvanized steel sheet roofed room. There was no

Table 1 - Peripheral Smear

16/ April	21/April	17/ May	21/ May	24/ May
RBC: macrocytic norchromic few occasional spherocytes seen WBC- lymphocytic preponderance platelets - adequate	RBC- polychromic macrocytes nucleated rbcs	RBC : shows moderate anisopoikilocytosis , normocyctic normochromic to microcytic hypochormic with many schistocytes, polychromatic cells , few bite cells and irregularly contracted cells WBC: lymphocytosis band forms 2%. platelets: thrombocytosis	Blast form -02% macrocytic norchromic to normocytic normochromia anaemia with thrombocytosis and mild eosinophilia	RBC: erythropenia few with macrocytes occasional spherocytes and a population of normocytic nomrochromic cells. WBC; within normal limits, platelet-high normal

history of chemicals used to clean the room or of bathing or cleaning the infant. There were no signs of sepsis on physical examination, except for vigorous incessant crying, and axillary temp was 40.5˚C/105˚F. The infant was sponged with water, administered a dose of acetaminophen in the emergency room, and shifted to the neonatal intensive care unit (NICU) where axillary temperature of 39.6˚C/103˚F was recorded. The temperature further reduced to axillary 101˚F/rectal 100˚F. After another half an hour of sponging, temperature recorded was axillary 100˚F/rectal 99˚F. The capillary glucose level was 109mg%. Weight was 1505 grams, which was same as discharge weight but showed weight gain of 25 grams per day next day onwards. Antibiotics were commenced for possibility of sepsis. She was breast feeding and also given supplemental expressed breast milk. Pallor was noticed when her temperature was normalised. Antibiotics were stopped after 48 hours when the blood counts and cultures did not indicate sepsis. Infant was well and routine oral multivitamins, iron were restarted. Laboratory data (Table: 2) on first day [and day five] of readmission revealed anemia (RBC count: 2.66 million [2.62], Hemoglobin: 9.3 g/dl [8.8], platelet Count: 5.69 lakh /cmm [6.16]) thrombocytosis. The leukocyte count (14000cells /cmm [15200]), urine results, and chest x-ray were normal. Peripheral smear revealed 2% blasts, anisopoikilocytosis, microcytic hypochromic with several schistocytes, polychromatic cells, few bite cells and irregularly contracted cells, consistent with haemolysis. Reticulocyte count was 2.8%. No Heinz bodies were seen. Other investigations towards possible cause of haemolysis were normal (Table:3). cranial ultra Sonography on day three of life and before first discharge were normal. Subsequent cranial USG before discharge after second admission was also normal. Following an uneventful stay in the NICU the infant was discharged home on day thirteen after the readmission. No retinopathy of prematurity was noted. At the age of 13 months the infant was thriving well, weighed 10.0 kg, height-74cms with Hb of 13.0gm%. Child has normal growth and development at 3 years of life and attending preschool.

Table 2. Complete blood count on different days

DATE 2012	16- April	18- April	21-April	07-May	17-May	21- May
HB- g/dl	18%	16.2	15.9	11.9	9.3	8.8
PCV %	53.3	48.3	46.6	35.5	27.9	27.1
RBC million/cmm	4.66	4.27	4.21	3.28	2.66	2.62
MCV FL	114	113	111	108	105	103
MCH pg	38.8	38	37.7	36.2	34.8	33.6
MCHC g/dl	34.1	33.6	34	33.4	33.2	32.6
RDW %	11.2	11.5	11.7	11.6	12.5	12.5
TC cells/cmm	8400	6800	10000	19200	14000	15200
PLATELET lac/cmm	2.58	1.63	2.88	3.13	5.6	1.26
POLY %	30.8		27.1		21.2	
EOS %	1.9		1.5		7.4	
BASO %	3.3		3.9	1.5	1.5	
LYMPH %	55.6		49.6	44	58.9	
MONO %	8.4		17.6	6.6	11.9	

Table 3. Special investigations

Hemoglobin Variant Analysis	
Hemoglobin A	16.3 (37.1-70.6%)
Hemoglobin A2	0.0 (0.4 -1.9%)
Hemoglobin F	85.1 (29.0-61.0%)
Hemoglobin S	0.0 (0.0%)
Hemoglobin D	0.0 (0.0%)
Hemoglobin C	0.0 (0.0%)
Osmotic Fragility test	
Hemolysis Start	0.51% (0.45-0.45)
Hemolysis End	0.30% (0.25-0.35)
Reticulocyte Count	
Reticulocyte Count	2.8% (2.00-6.00)
G6PD	
G6PD	16.98u/g Hb (6.4 to 18.7)

Discussion

We have reported possibly the first documented case of hyperthermia and haemolysis in an otherwise well infant due to exposure to high environmental temperature. In early neonatal period, overheating is a common cause of hyperthermia which is defined as temperature more than 40˚C[1]. An increased set point for temperature control has been reported in certain central nervous system anomalies, birth asphyxias and indicates poor prognosis. Equipment failures, incubators exposed to direct sunlight, over-wrapping, especially in summer are important causes for neonatal overheating and hyperpyrexia with complications such as apnoea, shock, cerebral hemorrhage and sudden death[2, 3, 4].

Rapid heating of blood to temperatures above 47°C has been reported to produce visible damage to erythrocytes without haemolysins or agglutinins in the blood in humans and dogs. Heat damaged cells show morphologic changes and increases in osmotic and mechanical fragility. Apart from spherocytosis and increased osmotic fragility, the blood films may show fragmentation, budding, spherocytosis, and severe microspherocytosis. These changes were documented in patients with burns, and are particularly evident if blood smears are prepared promptly after the burn[5]. The damaged erythrocytes are removed from circulation through the spleen whereas the haemolysed erythrocytes are removed through liver[6]. Alterations of red cell phospholipids and cholesteryl esters have been documented[7].

Heat can cause lytic damage and shorten the erythrocyte's normal survival time. When heated, the spectrin comprising the erythrocyte skeleton melts and spectrin's molecular architecture becomes randomized. Upon cooling, the randomized architecture becomes rigid[8]. Red cells have shape memory to a level of shear stress[9]. A normal erythrocyte in a flowing fluid behaves physically as a drop of fluid because the flexible membrane allows the surface of the cell to rotate around the intracellular content[10]. Because of the normal erythrocyte's fluid-like properties, collisional kinetic energy is coupled to the viscous haemoglobin solution within the cell allowing large amounts of collisional energy to be dissipated through the entire cell. This protects the membrane from the damage that would ensue from undissipated energy localized only to the membrane. The rigidity of a previously heated red cell membrane prevents this coupling of kinetic energy to the intracellular contents, forcing the membrane to absorb it in total. Repeated assault by such concentrated kinetic energy results in serious membrane damage, shortening the red cell life span. Another study has shown that an isotonic suspension of human erythrocytes, when subjected to a rapid temperature jump of approximately 0.5°C induced cell haemolysis[11]. It is important to note that the above studies were mainly in adults. Preterm infants have poorly deformable RBC, and the increased number of rigid RBC which may contribute to the shortened life span of fetal RBC[12]. Temperature rise in vehicles is significant on clear, sunny days even when ambient temperature is low and puts infants at risk for hyperthermia when left unattended in parked car[13]. Hyperthermia easily sets in infants as they have more surface areas for the weight and poor sweating to keep the body cooler[14]. Similar heat up of the preterm neonate in this case report resulted in hyperthermia and in turn lead to haemolysis which stopped after temperature control. The routine iron was started early and was continued for a year to consider its oxidative stress in this case.

Considering the circumstantial evidence, negative results of all investigations, and the infant's recovery after normalising the temperature, we believe that the most probable diagnosis in this case was haemolysis due to hyperthermia caused by high environmental temperature. Our diagnosis is supported by the studies showing effects of high temperature on human adult erythrocytes. Considering their high hemoglobulin with a different profile, the large surface area and poor temperature control, neonates especially if they are preterm, are at a higher risk of this complication when the rise in environmental temperature is quick that is often seen in children. We wish to emphasise that hyperthermia induced haemolysis is a diagnosis of exclusion. Awareness of such a diagnosis will assist those involved in neonatal care in the hospital setting and also in the community, especially in the peak heat period of summer in resource poor set ups.

Acknowledgement

We thank Professor Sanjay Patole, for his valuable inputs and critical reviews which encouraged us to send this article for publication. Professor Sanjay Patole MD, DCH, FRACP, MSc, PH is Clinical Professor and Head of Department of Neonatal Paediatrics, KEM Hospital for Women, University of Western Australia.

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