

## LETTER TO EDITOR (VIEWERS CHOICE)

**METHEMOGLOBINEMIA IN A NEONATE WITH DIARRHEA***Madhuradhar Chegondi\*, Oranit Shaked\*\**

A previously healthy 4 week old male child presented to our hospital with a 1 week history of diarrhea, poor feeding and lethargy. The newborn had previously presented to a neighboring hospital for fever and diarrhea. He had a full sepsis work up along with stool cultures and was treated as an inpatient with cefotaxime for 3 days. During his hospital stay, the loose stools partially improved and all cultures were negative. He was subsequently discharged home. The following day, he was brought to our emergency room with worsening diarrhea, poor feeding, and lethargy. There was no report of fever, vomiting or upper respiratory infection. There was no contact with any sick patient and he was not receiving any medications. He was born by full term normal spontaneous vaginal delivery. The mother had a urinary tract infection and gestational diabetes, both of which were adequately controlled during pregnancy. During the newborn's first week of life, he had feeding intolerance and had his formula changed from simlilac sensitive to a soy-based formula. Upon arrival to the emergency room, he appeared dehydrated with perioral cyanosis while crying and an ashen grey color to his skin. The remainder of his physical exam was unremarkable. While on oxygen via nasal cannula, his oxygen saturation was 99% by pulse oximetry. He received a single normal saline bolus of 20ml/kg. On laboratory work up his serum sodium 132meq/l, potassium 4.1 meq/l, chloride 109 meq/l, bicarbonate 12meq/l, blood urea nitrogen (BUN) 5mg/dl, creatinine 0.24mg/dl and blood glucose were 89mg/dl. Blood ammonia level, liver function tests and lactate levels were normal, and a urine toxicology screen was negative. An electrocardiogram, chest x-ray, and echocardiogram were all normal. A co-oximetry reading revealed an abnormally elevated methemoglobin level of 14.5%. Upon admission to the neonatal intensive care unit (NICU), repeat co-oximetry revealed a methemoglobin level of 15%. He was treated with one dose of 1mg/kg of methylene blue intravenously and started on 2mg/kg of oral ascorbic acid every 6 hours. One hour following methylene blue infusion, a repeat co-oximetry revealed a decline in the methemoglobin level to 2.2% and arterial blood gas findings were as follows: pH 7.35, pCO<sub>2</sub> 27.5, paO<sub>2</sub> 99, bicarbonate 18.6 mmol/L, oxygen saturation 99%. Blood, urine and stool cultures including stool rotavirus antigen were all negative. Over next twelve hours the neonate's lethargy and acidosis improved, along with his oral intake. The diarrhea persisted at which point gastroenterology was consulted and considered a diagnosis of milk protein intolerance. The formula was changed to neocate, after which the diarrhea improved. During his second week of hospital stay ascorbic acid was discontinued. Periodic co-oximetry readings revealed methemoglobin levels between 1.3-2.5%. Genetics and hematology work up revealed

an NADH cytochrome B5 reductase level of 4.5 IU/g hemoglobin (normal value 10-20IU/g), work up for unstable hemoglobin was unremarkable. The neonate remained in the neonatal ICU for a total of 3 weeks for failure to thrive, during which the neonate showed improvement in feeding and weight gain.

Methemoglobinemia is an uncommon medical condition that presents with cyanosis and is caused by both inherited and acquired causes. In methemoglobinemia, hemoglobin is oxidized from the ferrous state to the ferric state causing the oxygen dissociation curve to shift to the left, resulting in decreased oxygen delivery to the tissues and leads to hypoxemia and lactic acidosis. The body's primary means of reducing methemoglobin is by the NADH methemoglobin reductase enzyme system. (1) Congenital methemoglobinemia occurs in individuals who are homozygous for NADH methemoglobin reductase deficiency. Infants younger than 4 months of age with congenital methemoglobinemia are more susceptible to develop methemoglobinemia due to absence of full activity of NADH methemoglobin reductase. (1) Acquired causes of methemoglobinemia may be due to exogenous or endogenous factors including dietary nitrates, and several drugs like dapsone, sulfonamides, topical benzocaine spray. (2) Known endogenous causes in infants less than 3 months of age include, infectious diarrhea, urinary tract infections, sepsis, milk protein intolerance and organic acidemias. (3)

The definitive diagnostic test for methemoglobinemia is co-oximetry. The presence of an oxygen saturation gap is consistent with methemoglobinemia and other dyshemoglobinemias. (4) Treatment of methemoglobinemia includes removal of any oxidative stress, supportive care, and administration of methylene blue. In cases of mild methemoglobinemia, withdrawal of the offending agent is the only indicated treatment modality. Persistent methemoglobinemia requires exchange transfusion or hyperbaric oxygen therapy. (5)

We conclude that in our young infant, presence of physiologically lower NADH cytochrome B5 reductase level associated with diarrhea and metabolic acidosis increased the risk of methemoglobinemia. Diarrhea associated methemoglobinemia in infants less than 3 months of age is becoming increasingly more common than previously reported. Methemoglobinemia is a potentially fatal condition in young infants and should be considered in the differential diagnosis of infants presenting with cyanosis, since early intervention with methylene blue can prevent complications resulting from tissue hypoxia.

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