Case Report

Neonatal Atypical Hemolytic Uremic Syndrome may cause Prenatal Asphyxia

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Abstract

Microthrombi formation and hemolytic anemia are signs of hemoly tic-uremic syndrome (HUS) that result from platelet consumption and red blood cell (RBC) destruction due to vascular damage. HUS ma nifests as a triad of signs: micro-angiopathic hemolytic anemia , thrombocytopenia, and uremia. Prenatal asphyxia (PA) also leads to renal insufficiency and vascular damage. There is an overlap betw een the clinical presentation of PA and neonatal atypical HUS. We have reported the case of a neonate with a primary diagnosis of PA and clinical presentation of acute renal failure (ARF), anemia (Hb = 10 g/dl) and thrombocytopenia (Plt = 80000). His APGAR scores were 1 (1 minute), 3 (5 minutes), and 7 (10 minutes). A peripheral blood smear (PB S) was performed, which contained schistocytes (32%) with helme t and burr cells. The neonate's cord blood gas values were: pH of 7.0 7, HCO_3 = 11mmol/L, and CO_2 = 57mmHg. The first two days of life, he was anuric with elevated BUN and Cr (2.1mg/dL) levels. Complement (C3) was within normal limits at 0.65 g/L (0.89 – 1.87 g/L), however C4 was below the lower limit of normal at 0.14 g/L (0.16 – 0.38 g/L). We ruled out other causes of PA such as maternal illness , placenta abnormalities and infections (TORCH). We hypothesized that atypical neonatal HUS can progress to PA because of the presence of severe anemia and microthrombi formation.

Keywords: Acute renal failure, hemolytic uremic syndrome, micro-angiopathic hemolytic anemia, prenatal asphyxia

Cite this article as: Fallahpour M, Hafizi A, Fouladgar A, Rajabian B. Neonatal atypical hemolytic uremic syndrome may cause prenatal asphyxia. *Arch Iran Med*. 2012; **15(11):** 729 – 730.

Introduction

Hemolytic-uremic syndrome (HUS) is the most common cause of acute renal failure (ARF) in young children. Its classical presentation includes micro-angiopathic hemolytic anemia, thrombocytopenia and uremia. In developed countries more than 80% of cases diagnosed with HUS have a history of acute enteritis caused by a shiga-like toxin produced by *Escherichia coli* 0157:H7.[1,2] Non-diarrheal and sporadic recurrent familial causes of HUS are associated with low complement (C3) levels due to complement dysregulation.[3] Asphyxia is resulted from compromised gas exchange in the fetus or neonate and leads to progressive hypoxemia, hypercapnia, and metabolic acidosis. If untreated, asphyxia further progresses to multi-organ damage such as renal, hepatic, and cardiac failure, in addition to encephalopathy and vascular damage.[4,5] The underlying mechanisms of prenatal asphyxia (PA) may begin in the antepartum, intrapartum or postpartum periods.[5] In this article we discuss the case of a neonate born with PA and biological features compatible with HUS.

Case Report

A 39-year-old female presented to our hospital with complaints of decreased fetal movement from three days prior, at 37 weeks of gestational age (GA). The fetus had bradycardia, with a fetal heart rate (FHR) of 50 and ascites as visualized on sonography. Before 37 GA, she had suitable prenatal care (PNC); all prenatal examinations and sonographies were normal. At birth, the boy was cyanotic with a heart rate < 60 beats per minute and generalized edema (scalp, limbs, ascites, scrotom). His birth weight (2900 g), length (50 cm), and head circumference (35 cm) were all normal for GA. His APGAR scores were 1 (1 minute), 3 (5 minutes), and 7 (10 minutes). The infant was resuscitated at birth. Cord blood gas values were: pH (7.07), HCO_3 (11mmol/L), and CO_2 (57mmHg). His blood analysis was remarkable for anemia and thrombocytopenia with the following results: WBC (23500/m3), red blood cells (RBC; 3.25×10^6), Hb (10g/L), Plt (80000/m3), with schistocytes (32%) and fragmented RBCs. Peripheral blood smear (PBS) showed schistocytes, helmet and burr cells, as reported by the pathologist. Thrombocytopenia continued over the next two weeks, however the anemia was corrected following blood exchange and packed cell transfusion. One-hour post-partum laboratory values were: BUN (10mg/dL), Cr (1mg/dL), Na^+ (132meq/L), K^+ (3.1meq/L), Alb (3.2g/dL), Bil (4.5mg/dL), and LDH (5700IU/L). Urinalysis was remarkable for 2+ blood, RBC (70 – 80), and 2+ protein. At 34 hours post-partum, he was anuric, with increased serum Cr (2.1mg/dL), BUN (14.2mg/dL), Na^+ (112meq/L), K^+ (6.3meq/L), Bil (8.4mg/dL), indirect Bil (7.8mg/dL), Hb (11g/L), and Plt (44000/m3).

Exchange transfusion is the removal of a person`s whole blood, RBC or Plt with the intent to replace them with transfused blood products. It is used in the treatment of severe neonatal jaundice, newborn hemolytic disorders, neonatal polycythemia, severe chronic anemia in the uteru , severe sepsis, metabolic derangements, and intoxication. An exchange transfusion with fresh

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Accepted for publication: 14 March 2012

whole blood was performed in this patient, with the transfusion of fresh frozen plasma (10 ml/kg) over four successive days. After the blood exchange, at 38 hours post-partum the patient's urine output was 0.6 ml/kg, which normalized at day four. By day seven, serum Cr and BUN levels returned to normal. Following the exchange transfusion, his anemia was corrected, however Plts normalized on day 16. His C3 level was lower than normal at day 16, when he was discharged. As previously mentioned, the mother had good PNC and normal exams prior to 37 weeks of GA. She did not have hypertension or diabetes mellitus. The TORCH study in both the mother and baby was negative. We ruled out any abnormal pathology or infection in the placenta. According to clinical and para-clinical findings, HUS was the most compatible diagnosis.

Discussion

We report the case of a neonate who presented with PA, low APGAR scores, and umbilical cord acidosis (pH = 7.07). During the first two days of life, he was anuric with an elevated Cr (2.1mg/dL), anemic (Hb = 10g/L), and had thrombocytopenia (Plt = 80000/m3). His LDH level was 5700IU/L and there were schistocytes (32%) and fragmented RBC in his PBS, which favored a diagnosis of hemolytic anemia.[6]

PA can be defined as impaired respiratory gas exchange accompanied by the development of acidosis.[7] Multiple parameters can be used to define PA, however the hallmarks of the disease are low APGAR scores, metabolic acidosis and/or multiple organ failure.[8,9] The underlying etiology of PA must be determined, as PA is secondary to other conditions that are of either maternal, placental or fetal etiologies.[4,10]

According to the mother's normal history and PNC, we eliminated any maternal etiology. The placenta was sent for pathology which was normal and microbial cultures were negative. According to biological features, the most compatible diagnosis was HUS because of the patient's symptoms of micro-angiopathic hemolytic anemia, thrombocytopenia, and uremia.[2,11] HUS as seen in this patient with low complement (C3) levels occurs during the first two weeks of life, has no associated diarrhea, a high recurrence, and positive familial history.[12]

Biran et al. have reported the cases of three neonates with PA and neonatal atypical HUS.[13] Their cases were born with PA and then became anuric with presentations compatible with our case. Severe anemia and microthrombi formation that result from HUS are two pathways that lead to brain damage and asphyxia.[2,14] From our experience, we have noticed that neonatal atypical HUS can involve the brain, especially when it occurs during the prenatal period and manifests similar PA.

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