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COVID-19 DILEMMA: EARLY SEVERE HEMOLYTIC JAUNDICE IN NEWBORN BORN TO MOTHER WITH SARS-COV-2 INFECTION IN PREGNANCY

Neonatology

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ABSTRACT

COVID-19 has been associated with hemolytic anemia in pediatric as well as adult age group. However, very little is known about the clinical course and immune responses in newborn born to a mother who contracted SARS-CoV-2 infection during pregnancy. Previously, few cases of autoimmune hemolytic anemia with SARS-CoV-2 infection due to the cytokine storm or through molecular mimicry has been found. Through this report, we would discuss about the SARS-COV-2 reactive antibodies as a potential etiology of severe early hemolysis leading to severe neonatal hyperbilirubinemia in a neonate born to a mother with SARS-CoV-2 infection.

KEYWORDS

SARS-CoV-19 antibody, neonatal hyperbilirubinemia, immune hemolysis, exchange transfusion

CASE REPORT

A single live male baby was born by lower segment caesarean section (LSCS) at 38 weeks of gestation weighing 2.5 kg. Mother had a relatively uneventful antenatal period until she had an infection with SARS-CoV-2 detected by RTPCR test in the last trimester of pregnancy. Mother had anhydramnios with transverse lie. Emergency LSCS was done at the time when 10 days had passed after a positive RTPCR test. Baby had primary apnea with APGAR score of 6 and 7 at 1 min and 5 minutes of life respectively. Baby developed respiratory distress in the form of tachypnoea and grunting after birth. Non-invasive ventilation in the form of heated humidified high flow nasal cannula (HHHFNC) was initiated. SARS-CoV-19 RT-PCR test on nasopharyngeal swab from the baby was negative. Cord blood investigations were done which showed TSH 7.65 µU/mL, free T4 1.04 ng/dL. Ultrasound KUB evaluation showed no abnormality. Serum creatinine (0.6 mg/dL) and blood urea (12 mg/dL) were within normal reference values.

Within 12 hours after birth, baby developed jaundice. Intensive phototherapy was started while we waited for the serum bilirubin report. Total serum bilirubin (TSB) was 13.7 mg/dl, serum direct bilirubin (DSB) 0.6 mg/dL. Direct coomb's test (DCT) with IgG + CD3 agglutination method was strongly positive. Reticulocyte count was 9% with nucleated red blood cells (67/ 100 WBC). Quantitative G6PD levels were normal (22.9 U/gHb). Investigations are also shown in Table I. TSB rose to 14.8 mg/dL after 4 hours of phototherapy and thus, double volume exchange transfusion was performed. At 24 hours of life, TSB was 6.7 mg/dl but level continued to rise albeit slowly and at 36 hours of life, it was 9.4 mg/dL. Intravenous Immunoglobulin (IVIG) was infused at 36 hours followed which at 48 hours, TSB reduced to 4.9 mg/dL. Figure 1 shows the trend of total serum bilirubin over the hospital stay.

Baby's blood group was B positive and mother's blood group was O positive with high anti-B antibody titre (1:64) against fetal red blood cell antigen in the mother. Baby also harboured anti-SARS-CoV-2 IgG antibodies. Pre-exchange transfusion and post-exchange blood sample reproduced positivity for SARS-CoV-19 IgG antibodies (1368.6 AU/ml and 412.8 AU/ml respectively). SARS-CoV-19 IgG antibody level markedly reduced after the exchange transfusion. SARS-CoV-19 IgG antibody test in mother at the time of delivery shows a positive test but with levels less than that in the baby (782.5 AU/ml in mother versus 1368.2 AU/ml) with a transfer ratio of 1.75. Baby had no neurological deficit or signs of kernicterus and rest clinical examination was normal. Baby was discharged on breast feeds and had no complications seen on follow-up visits.

DISCUSSION:

We present a case of neonatal hyperbilirubinemia in a neonate born to a SARS-CoV-2 positive mother.

ABO incompatibility is a known cause of neonatal hyperbilirubinemia. One-fourth of the babies have ABO incompatibility with their mothers but only very few have significant haemolytic disease of newborn. Fetal erythrocytes express low levels of ABH antigen; thus, severe hemolysis is rare. (1) In majority of babies, it leads to hyperbilirubinemia in first 3-5 days of life and rarely presents within 24 hours of life (2) requiring exchange transfusion. It has been also previously found that it is insignificantly associated with increased reticulocyte count and direct antibody test (DAT) positivity. (3)

In SARS-CoV-2 infection, it has been studied that molecular mimicry might play a role in hemolysis. It is found that anti-SARS-CoV-2 antibodies may cross-react with red blood cell membrane protein like ankyrin-1 leading to haemolytic anemia. Spike protein of SARS-CoV-2 shares immunogenic epitope with ankyrin-1. (4) There are previous reports of autoimmune hemolytic anemia with SARS-CoV-2 infection due to the cytokine storm or through molecular mimicry. (5)

In our case, although baby had non-reactive SARS-CoV-2 antigen test, infection cannot be exactly ruled out in the baby. In past literature, positive correlation between SARS-CoV-2 antibody level in infant and maternal sera was found. (6) Anti-SARS-CoV-2 antibodies in our case were found with transfer ratio of 1.75 which shows highly efficient antibodies transfer or there might be a possibility that baby's immune system developed reactive antibodies in response to SARS-CoV-2 antigen.

Vertical transmission of SARS-CoV-2 virus has been reported in literature previously, although it's rare (7). In view of our case, we thought DAT positivity may be due to the anti-SARS-CoV-2 antibodies on RBC's surface but plasma eluate in our case shows anti-B IgG agglutinins (++) and negative for anti-SARS-CoV-19 antibody. Nevertheless, SARS-CoV-2 is also associated in some cases with DAT negative results demonstrating hemolysis due to other phenomenon like inflammation pathway activation leading to enhancement of complement C3 deposition and the binding of IgG autoantibodies to RBC membrane causing damage. (8)

Hemolytic anemia in a newborn born to mother with COVID-19 during pregnancy has been seldom reported. One of the previous case series demonstrated a newborn born to SARS-CoV-2 positive mother who had haemolytic anemia, with an underlying predisposing condition causing hemolysis similar to the neonate in our case report (9).

The limitation of our case is that we could not measure markers of intravascular hemolysis like lactate dehydrogenase (LDH), haptoglobin and free plasma haemoglobin as we already had done double volume exchange transfusion.

Though, we could not prove vertical exposure of SARS-CoV-2 infection or placental transfer of antibodies as the definite cause of hemolysis, we speculate that it can amplify the severity of hemolysis caused by predisposing conditions such as ABO incompatibility leading to severe hyperbilirubinemia. Future studies are required to consolidate the relationship of hemolysis and jaundice in neonates born to mother with COVID-19 disease. Neonates born to mother with COVID-19 should be investigated for intravascular hemolysis and jaundice for an early intervention.

Table 1: Investigations

S. No	Investigation	Values							
		Birth	12 hours	16 hours	24 hours	36 hours	48 hours	72 hours	Day 5 of life
1.	Hemoglobin (g/dL)	15.6			12.8	11.3			13.8
2.	Leucocyte count (TLC) (cells/mm3)	19910			13130				10960
3.	Platelet	4.63 lacs			1.12 lacs				4.59 lacs
4.	Reticulocyte count		9.8 %						
5.	G6PD (Quantitative) (U/gHb)		22.9						
6.	Total serum bilirubin (mg/dL)		13.7	14.8	6.7	9.4	4.9	3.9	
7.	Direct serum bilirubin (mg/dL)		0.6		0.9				
8.	SGOT(AST) (U/L)		88						
9.	SGPT (ALT) (U/L)		44						
10.	Serum Albumin (mg/dL)		3.6						
11.	Alkaline Phosphatase		141						
12.	Free T4 (ng/dL)	1.04							
13.	TSH (uU/mL)	7.64							
14.	DCT (IgG + CD3)		++						
15.	CRP (Quantitative)		<0.5						
16.	Serum creatinine (mg/dL)		0.6			0.4			
17.	Serum sodium (mEq/L)				140		138		
18.	Serum potassium (mEq/L)				2.9		3.6		
19.	Serum calcium (mg/dL)				7.3				
20.	Serum ionized calcium(mmol/L)				1.01				

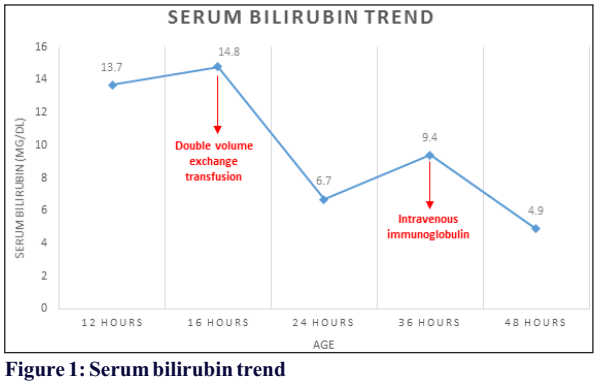

Figure 1: Serum bilirubin trend

REFERENCES:

1. Simmons DP, Savage WJ. Hemolysis from ABO Incompatibility. Hematol Oncol Clin North Am. 2015 Jun;29(3):429-43.
2. Apexa S. Patel, Deepak A. Desai, Aneri R. Patel. Association of ABO and Rh incompatibility with neonatal hyperbilirubinaemia. Int J Reprod Contracept Obstet Gynecol. 2017 Apr;6(4):1368-1375.
3. Bhat YR, Kumar CG. Morbidity of ABO haemolytic disease in the newborn. Paediatr Int Child Health. 2012 May;32(2):93-6.
4. Angileri F, L´egar´e S, Marino Gammazza A, Conway de Macario E, Macario AJL, Cappello F. Is molecular mimicry the culprit in the autoimmune haemolytic anaemia affecting patients with COVID-19? Br J Haematol. 2020;190(2):e92-e93.
5. Lazarian G, Quinquenel A, Bellal M, et al. Autoimmune haemolytic anaemia associated with COVID-19 infection. Br J Haematol. 2020;190(1):29-31.
6. Flannery DD, Gouma S, Dhudasia MB, et al. Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios. JAMA Pediatr. 2021;175(6):594–600.
7. Kotlyar AM, Grechukhina O, Chen A, et al. Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis. Am J Obstet Gynecol. 2021;224(1):35-53.
8. Straat M, van Bruggen R, de Korte D, Juffermans NP. Red blood cell clearance in inflammation. Transfus Med Hemother. 2012 Oct; 39(5): 353–361.
9. Elena Itriago, Krithika Lingappan, Jun Teruya, et al. Case Series of Hemolysis in Neonate Born to Mothers with History of SARS-CoV-2 Infection During Pregnancy. Authorea. October 26, 2020.