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Corpus Journal of Case Reports (CJCR)

Case Report

Neonatal Intravenous Immunoglobulin (IVIG) Treatment for Chronic Anemia Due to Congenital Parvovirus Infection: A Case Report

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Volume 1 Issue 1, 2020

Article Information
Received date: June 05, 2020
Published date: June 14, 2020

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Keywords
Parvovirus B_{19}, Hydrops fetalis, Pure red blood cell aplasia, Intravenous immunoglobulin

Abstract

Congenital Parvovirus B_{19} infection is a rare but serious condition that can result in hydrops fetalis and fetal death. Due to the virus' cytotoxic effect on fetal red blood cell precursors, postnatal infection can cause a neonatal viremia and secondary pure red cell aplasia. Here, we describe a case of congenital parvovirus infection in a preterm infant complicated by hydrops fetalis and chronic anemia that responded to postnatal treatment with intravenous immunoglobulin (IVIG) administered on day of life 44. After treatment, the anemia resolved as the neonate exhibited interval increases in hemoglobin, hematocrit, and reticulocyte count with no subsequent need for red blood cell transfusions.

Introduction

Parvovirus B_{19} is a small non-enveloped DNA virus that frequently infects humans. Parvovirus B_{19} can cause erythema infectiosum, also known as fifth disease, characterized by self-limited fever, rash, and arthropathy. The incidence of parvovirus B_{19} infection in pregnancy is 3.3-3.8% [1]. Parvovirus B_{19} is cytotoxic to fetal red blood cell precursors. Most intrauterine parvovirus infections do not have adverse outcomes; however, in rare cases, transplacental transmission of B_{19} in the setting of maternal viremia can result in fetal hydrops or death due to severe anemia [2]. During pregnancy, a positive parvovirus B_{19} specific immunoglobnulin antibody can be used to diagnose acute or chronic maternal infection. Polymerase chain reaction (PCR) detection of B_{19} in the amniotic fluid is the method of choice for diagnosis of congenital parvovirus infection [3,4]. Fetal anemia is suspected on ultrasound examination when middle cerebral artery peak systolic velocity (MCA PSV) Doppler is >1.5 MoM [5]. Percutaneous umbilical cord blood sampling (PUBS) examines blood from the fetal umbilical cord and confirms the diagnosis. In severe cases of fetal anemia, intrauterine red blood cell transfusions may be indicated to prevent fetal death. After delivery, congenital infection may result in persistent neonatal viremia with secondary pure red cell aplasia (PRCA) and chronic anemia. The mainstay of treatment for PRCA in neonates is red cell transfusion(s). In certain patients with persistently high viral loads, intravenous immunoglobulin (IVIG) has been used successfully for treatment of persistent parvovirus induced anemia, but data remains limited in neonates. Here, we describe a case of congenital parvovirus infection in a preterm infant complicated by hydrops fetalis that responded to a postnatal treatment of IVIG.

Case Report

A preterm male neonate was born at 29 weeks and 2 days gestation to a 27 year old gravida 5, para 1 mother. Maternal blood type was A positive and serologies were negative (rapid plasma regain non-reactive, HIV antibody screen negative, Hepatitis B surface antigen negative, Group B streptococcal status negative). The prenatal course was complicated by ultrasound findings of polyhydramnios, with an amniotic fluid index (AFI) up to 28.5 cm. Fetal ultrasound findings showed scalp edema, ascites, pleural and pericardial effusions, skin edema, and elevated middle cerebral arterial Doppler's consistent with fetal hydrops. Fetal echocardiogram revealed a structurally normal heart. Maternal serologic testing at that time was significant for a positive Parovirus B_{19} immunoglobulin M(IgM) with a previously documented negative Parvovirus B_{19} immunoglobulin G (IgG). Maternal Parvovirus polymerase chain reaction (PCR) was confirmed positive. The mother had no known sick contacts and no history of febrile illness, rashes, joint pain or other infectious symptoms during pregnancy. In the setting of the persistent fetal anemia and severe hydrops, the decision was made to perform a PUBs procedure with intrauterine transfusion of packed red blood cells total three times, at 27 weeks 3 days, 28 weeks 1 day, and 28 weeks 3 days gestation. Red blood cell transfusion consisted of leukocyte reduced, irradiated, CMV negative, type O negative blood. Pre-procedure MCA PSV Dopplers for the three procedures were 106cm/sec, 73.8cm/sec, and 72cm/sec with MCA PSV multiples of the median (MoM) averaging 3.0, 1.99 and 1.92, respectively. Pre-transfusion fetal hematocrit levels were 6.8, 15, and 20%. Post-procedure hematocrits increased to >25% with normalization of MCA dopplers in each case. Last Doppler prior to delivery at 29 weeks and 0 days had an MCA PSV of 60 cm/sec (1.58 MoM). Fetal reticulocyte count 2.2%. The mother also received intrauterine transfusions of platelets for thrombocytopenia, with lowest fetal platelet count 48x106/L.

The mother presented at 29 weeks and 2 days with preterm premature rupture of membranes in preterm labor and delivered via precipitous vaginal delivery. The first course of Betamethasone was given at 29 weeks gestation and a rescue dose was administered immediately prior to delivery. The neonate was intubated in the delivery room for respiratory depression and low heartrate. Apgars were 4 at 1 minute and 7 at 5 minutes of life. Initial postnatal blood work showed white blood cell count of 10,200/mm^3, hemoglobin of 10g/dL, hematocrit of 29.2%, and platelet count of 65x106/L. The neonate received both pack red blood cells and platelet transfusions on day of life 0. Hematocrit level initially improved to 45.3%, but then continued to trend down over the following weeks. Reticulocyte count ranged from 0.9 to 1.7% during first six weeks of life. Subsequent red blood cell transfusions were administered on days of life 18, 32 and 46 for persistent anemia with hematocrit </= to 24.0%. Phototherapy was initiated on day of life 1 for bilirubin level 11.7. Liver function was monitored and showed an evolving direct hyper bilirubinemia, with maximum indirect bilirubin 11.3 mg/dL, and maximum direct bilirubin 4.0 mg/dL. The neonate was started on Actigall and ADEK vitamins, which were discontinued on day of life 40.

Serum Parvovirus B_{19} PCR obtained on day of life 41 showed a viral load of >10,000,000 copies/mL, which exceeded level of count. Due to persistent anemia, low reticulocyte count, and high Parvovirus B_{19} viral load, the decision was made to treat the neonate with one dose of IVIG (dose: 1gm/kg) on day of life 44 for pure red cell aplasia. Blood work within 24 hours after administration showed hemoglobin 8.0g/dL, hematocrit 23.8%, and reticulocyte count 1.3%. Within one week after administration, hemoglobin and hematocrit increased to 11.1g/dL and 33.1%, and reticulocyte count increased for the first time to 3.7%. On day of life 67, hemoglobin and hematocrit remained stable at 10.1g/dL and 31.3%, while the reticulocyte count continued to increase to 4.3%. On day of life 77, lab studies showed hemoglobin 10.6g/dL, hematocrit 31.8%, and reticulocyte count 3.9% with no subsequent need for transfusions. Serum Parvovirus B_{19} PCR obtained on day of life 92 showed a significant decrease in viral load to 582,550 negative copies/mL. The neonate clinically improved and remained hemodynamically stable throughout hospital course. Extubation was performed on day of life 2 with full wean off respiratory support to room air on day of life 47. Postnatal ECHO on day of life 2 showed normal segmental anatomy with qualitatively normal biventricular size and systolic function and estimated pulmonary artery pressures approximately half systemic to systemic; no pericardial effusion. Hospital course was complicated by issues including apnea of prematurity, oral feeding, and weight gain; however, the neonate was safely discharged home on day of life 74 (at corrected age 39 weeks and 5 days gestation).

Discussion

Data about perinatal administration of IVIG for treatment of persistent parvovirus induced anemia are very limited other than a few case reports. IVIG administration to a mother with parvovirus B_{19} infection between 24 and 25 weeks gestations was associated with favorable maternal and fetal outcome [6]. When given at age 5 months in an infant with continued high B_{19} viral load, IVIG administration resulted in marked reduction in viral load and stabilization of hemoglobin level [7]. More recently, IVIG has been shown to decrease viral load in an ex-26 week gestation premature neonate with fetal hydrops and chronic post-natal anemia when given at age 3 months [8]. Due to the presence of persistent anemia in our patient, we elected to give IVIG at 1-2 months of age in an attempt to reduce viral load and decrease need for red blood cell transfusions. Following treatment, we noted a significant decrease in viral burden and stabilization of the hemoglobin level over the following 4-6 weeks. This successfully decreased the need for frequent red blood cell transfusions in our patient. This finding suggests that IVIG may be useful in the treatment of neonatal parvovirus B_{19} induced anemia and red cell aplasia. While a few reports of favorable neonatal responses to IVIG in the setting of congenital B_{19} viremia have been presented, this form of treatment is still experimental. Future studies will be needed to determine long term effects as well as possible mechanisms of action

Acknowledgements

No

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