Case Report

Maternal isoimmunization associated fetal anemia: A case report

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Abstract

Maternal isoimmunization occurs when a pregnant woman develops an immune reaction due to the inheritance of a red-cell antigen, which is paternally derived and can result in fetal anemia, hemolysis, fetal death, and hydrops fetalis as the antibodies might travel through the placenta and get adhered to the antigens present in the erythrocytes of the fetus. This report highlights a rare case of Rh isoimmunization leading to fetal anemia in a 26-year-old female and evaluates the impact of intrauterine transfusion (IUT) in terms of the gestational age at delivery along with the mode of delivery, procedural complications, and overall survival rate of the fetus. In conclusion, the most frequent cause of fetal anemia is Rh alloimmunization, which should be taken into consideration while making a differential diagnosis throughout the assessment. Improvements in IUT procedures and earlier detection of the MCA-PSV by Doppler ultrasonographic examination have also contributed to better results.

Keywords: Fetal anemia, hydrops fetalis, intrauterine transfusion, maternal isoimmunization, Rh alloimmunization

Introduction

Maternal isoimmunization takes place when a pregnant woman develops an immune reaction due to the inheritance of a red-cell antigen, which is paternally derived. It can result in fetal anemia, hemolysis, fetal death, and hydrops fetalis as the antibodies might travel through the placenta and get adhered to the antigens present in the erythrocytes of the fetus.[1] Because fetal hemoglobin (Hb) levels gradually rise during pregnancy, two criteria are used to classify anemia: the degree of Hb divergence from the multiples of the median (MoM) for gestational age (GA) or mean for GA.[2,3] A hematocrit of less than 30% can also be used to diagnose fetal anemia; it is frequently applied in clinical settings and appears to be equally reliable in measuring Hb levels.[4] Regardless of the cause, Doppler ultrasonography can be used to detect fetal anemia based on the rise of peak velocity of systolic blood flow in the middle cerebral artery (MCA-PSV). This is due to the increased velocity of the blood that occurs secondary to decreased viscosity and greater cardiac output in fetal anemia.[2,5] Additionally, there is no substantial association between the concentration of fetal Hb and MCA-PSV when the fetus has mild anemia or no anemia at all. However, the MCA-PSV rises when the Hb value declines; therefore, a good level of approximation can be used to determine the value of Hb.[5] An MoM of more than 1.5 is performed to determine critical anemia in fetus.[3] To perform intrauterine transfusions (IUT) before the onset of hydrops, anemia in fetuses can be detected by MCA-PSV testing before they develop fetal ascites.[3]

Since the early 1980s, IUT has been the basis of treatment for fetal isoimmunization.[1] It currently constitutes the most

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popular and well-known method for treating anemia in fetuses[6] and can be practically applied to all related etiologies.[7] IUT is only recommended in cases of moderate or severe anemia and is carried out under ultrasonography (USG) supervision.[1,2,8] A final transfusion of not more than 34–35 weeks is preferred by most of the clinicians, with the goal of having the baby delivered at 37–38 weeks in a maternal alloimmunization-complicated pregnancy who has received IUTs consecutively with a stable fetus.[2,5,8] Previously, the main factor contributing to perinatal mortality was alloimmune hemolytic disorder. If identification and treatment of anemia is performed in its earlier stages in specialized facilities, the current perinatal survival rates can surpass 90%.[4,8,9] Hence, this case report presents a unique case of fetal anemia caused by maternal alloimmunization, associated procedural complications, and determining the impact of IUT in terms of the overall survival rate of fetus and GA at delivery along with the mode of delivery.

Case presentation

A 26-year-old female, married since 6 years presented to the Department of Obstetrics and Gynaecology with obstetric history of gravida three, parity two from which 1 was living, and 1 death was reported (G3P2L1D1). The corrected GA of 27+1 weeks was conceived spontaneously with a history of amenorrhea since the patient mentioned seven months. The patient perceived the fetal movements well. The menstrual history reported by the patient described that last menstrual period was on 25/09/22 from which estimated due date calculated was 2/7/23.

On examination, the patient had pallor and blood pressure of 100/60 mm of Hg. Per abdomen examination, reported uterus (UT) of 28 weeks, positive external ballotment (EB), and fetal heart sounds (FHS). Per speculum examination, it showed a positive result for mild vaginitis. Laboratory investigations revealed "B" Rh-negative blood group with a positive indirect Coombs test, Hb of 9.8 g/dl, total leukocyte count (TLC) of 8320/cumm, and platelet count (PTL) of 1.56 lac/cumm. Diagnostic assessment consisting of ultrasonography (USG) revealed a small GA of 27+6 weeks with a lie of breech presentation, as illustrated in Figure 1, placenta toward the anterior side, amniotic fluid index (AFI) demonstrating polyhydramnios, and Estimated fetal weight (EFW) of 1111 gms. The USG MCA interpretation resulted in MCA-PSV of 64.5 cm/sec and appears raised, and MoM of 1.84 reported severe anemia.

Based on the above examination and diagnostic assessment, the diagnosis of G3P2L1D1 with corrected GA (CGA) of 27+1 weeks with Rh-negative pregnancy was confirmed, and the patient was advised and counseled for IUT. Before commencing the transfusion, written informed consent was obtained, and the procedure was performed. Under all aseptic precautions, the patient was positioned supine lying. Betadine painting and draping were performed under local anesthesia, and a USG guidance

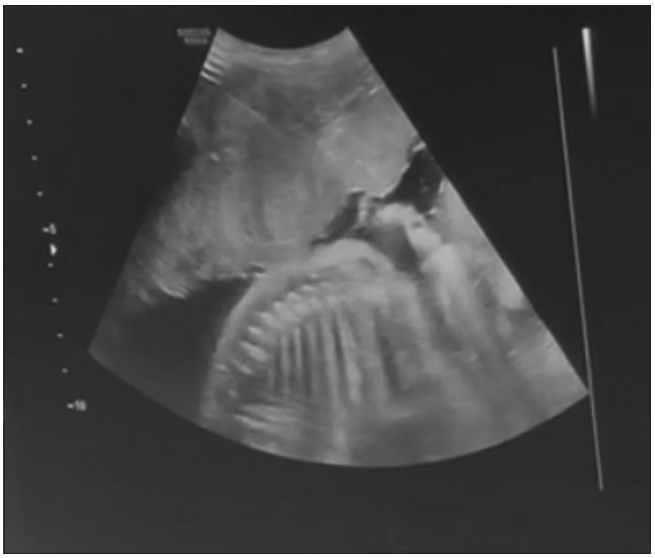

Figure 1: Diagnostic assessment consisting of ultrasonography

20 G needle was inserted abdominally into the umbilical vein at placental insertion, 0.5 ml of fetal blood sample was collected and sent for examination; pre-procedure hematocrit was 18% and calculated desired hematocrit was 45%. 160 cc of blood was transfused into the umbilical vein under continuous USG guidance. Post-procedure fetal movements were audible, along with normal cardiac activities. Following the transfusion, the review on USG reported MCA-PSV – 38.1 cm/sec, MoM-1.09, and fetal heart rate (FHR) of 145 beats/min.

Medical treatment received by the patient consisted of Tab. FES 200 mg, Tab. CALCIUM 300 mg, and Protein powder two times a day for 11 days and was also continued post-discharge for 3 months, injection (inj) STAFCURE 1.5 mg twice a day for 2 days, Tab. SUSTEN 200 mg for 9 days, Tab. DUPHASTON 10 mg twice a day for 9 days, inj PAN 40 mg once a day for 2 days, CANSOFT VAGINAL PESSARY HS for 6 days, and inj PROLUTON given twice weekly. The patient was discharged and advised to have an iron-rich diet, adequate hydration, rest in left lateral position, perineal hygiene, and strict daily fetal movement count. The follow-up was recommended after 15 days.

During follow-up per abdomen examination revealed UT of 30 weeks, EB and FHS positive, USG reported CGA of 30+4 weeks, small for GA (SGA) of 29+6 weeks, lie of cephalic presentation, placenta toward anterior, AF1 of 16, and EFW of 1506. Obstetric Doppler ultrasound reported an MCA-PSV of 55.6 cm/sec and a pulsatility index of 2.14, demonstrating mild anemia. Based on follow-up investigations, the patient was advised for IUT through the same procedure as described above. The pre-procedure hematocrit was 35.5%, and the calculated desired hematocrit was 45%. 100 cc of blood was transfused into the umbilical vein under continuous USG guidance. Post-transfusion mean corpuscular volume (MCV) was 43.88 cm, and fetal movements were audible, along with normal cardiac activities. Following the transfusion, the review on USG reported

MCA-PSV of 42.59 cm/sec and FHR of 145 beats/min. The patient was recommended with the same medical treatment as described above except CANSOFT VAGINAL PESSARY HS. Additionally, inj PAN 40 MG OD was given for only 1 day, and inj dexamethasone 6 mg consisting of four doses was given intramuscularly 12 hours apart. The patient was discharged and was advised to have an iron-rich diet, adequate hydration, rest in the left lateral position, perineal hygiene, and a strict daily fetal movement count. Hb on discharge was 10.8 gm/dl. The next follow-up was recommended after 15 days, which covered a total of 9 months of pregnancy.

During the next follow-up, the provisional diagnosis made was G3P2L1D1 with CGA 37 weeks for safe confinement with Rh-negative pregnancy along with a clinical history of IUT. Per abdomen examination, they revealed a uterus of full-term with cephalic presentation, FHS positive with 146 beats/min. Laboratory investigations revealed Hb of 10.2 gm/dl, TLC of 8530/cumm, and PTL of 1.57 lacs/cumm. USG findings reported CGA of 36+5 weeks, SGA of 35+6 weeks, with a cephalic presentation, placenta toward the anterior wall in the upper uterine segment, AFI of 15 cm, and EFW of 2865 gms. Based on the above findings, the diagnosis of emergency lower segment cesarean section (EMLSCS) in the vision of fetal anemia with Rh-negative pregnancy was confirmed. After 3 days, the patient was headed for EMLSCS delivery.

Following all aseptic precautions and under spinal anesthesia, the patient was positioned in a supine. Betadine painting and drapping were performed. Skin and abdomen were opened by pfannensteil incision and were opened in layers until the peritoneum was observed. The loose ureterovesical fold was separated, and the bladder was pushed down. The lower uterine segment was opened by a transverse curvilinear incision. An amniotomy was performed, and the liquor was clear and adequate. The baby was delivered by vertex and cried immediately after the birth. The cord was clamped and cut, and the baby was handed over to the pediatrician. Placenta and membrane were delivered out completely, but uterus tone was not achieved, for which inj Tranexa 1 gm was given intravenously, and inj methergine 0.2 mg was given intramuscularly. The uterus tone was achieved and was closed in a double layer. Hemostasis was achieved, following which the abdomen and skin were closed in layers.

A male baby of weight 2.9 kg was delivered and was admitted to the neonatal intensive care unit (NICU) for post-resuscitation care and received 1 packed red cell on Hb <10, and post-transfusion packed red cell was 13.2 mg/dl. After 3 days, the baby was shifted from NICU to the ward.

Complete suture removal was performed, and the incision site demonstrated no discharge, induration, or mis-approximation. Medical treatment received by the patient involved inj Stafcure intravenously (IV) twice a day for 2 days, inj Metro 100 cc IV thrice a day for 2 days, inj perinorm 10 mg IV thrice a day, inj PAN 40 mg IV once a day for 2 days, and zonac suppository per rectally thrice a day for 2 days. The patient adhered well to the treatment, and both the mother and the baby were healthy.

Discussion

Rh iso-immunization, in which antibodies are developed on red blood cells (RBCs) of the fetus by the mother who is Rh-negative against paternal Rh antigen. These antibodies are produced as a result of fetal blood entering the mother's bloodstream, which is a result of fetomaternal hemorrhage that occurs following a prior pregnancy, trauma, invasive operation, or an abortion. Sensitization, also known as iso/alloimmunization, is a condition that is more common in the first pregnancy of a Rh-negative woman but less common in subsequent pregnancies.[10] The firstborn infant normally is not affected by sensitization, but future births can develop hemolytic illness. To prevent isoimmunization, anti-D immunoglobulin in the form of a prophylactic dose can be given to Rh-negative pregnant women to counteract the effects of these iso-antibodies. Additionally, hemolytic disease of the newborn (HDN) occurs, which can destroy fetal RBCs due to delay or failure in prophylaxis and is typically treated with exchange transfusion and phototherapy. For many years, the primary cause of perinatal and newborn morbidity and mortality was Rh isoimmunization; however, with the introduction of anti-D immunoglobulin prophylaxis, the rate has decreased significantly.[11,12] Rh isoimmunization leading to anemia in neonates varies from fetal hydrops in utero to mild-to-severe anemia. Fetal RBCs may continue to be destroyed by these iso-antibodies, for which lack of exchange transfusion may be the cause.[12]

Before the development of fetal ascites, MCA-PSV testing can detect anemia in fetuses, leading to the application of IUTs to be performed before the development of hydrops.[2] In non-hydropic fetuses at risk for anemia, the sensitivity of a single MCA-PSV measurement is reported to be 75.5%-95%, with a 10%–12% false-positive rate for moderate or severe anemia.[3,13] After 35 weeks of gestation, there is a noticeable increase in the rate of false positives.[3] With the application of MCA-PSV trends, the false-positive rate might be reduced to approximately 5%.[3] In a study of alloimmunized fetuses at 34–37 weeks, for fetal anemia, the MCA-PSV sensitivity was 69% and ascended to 94% along associated with hydrops.[14] MCA-PSV testing replaced serial invasive testing when it was found that Doppler measurement of the MCA-PSV showed greater sensitivity and accuracy for the prediction of severe anemia in fetuses.[3]

The false-positive rates for the detection of 95% of very anemic fetuses were 14%, 37%, and 90% after the first, second, and third IUT, respectively. This makes it less accurate to utilize MCA-PSV to predict anemia in fetuses.[3] In a previous study, 95 adults with severe anemia from rhesus disease treated with IUT in utero were compared to their siblings who did not have the condition. At rest, the exposed subjects exhibited decreased myocardial perfusion, thicker left ventricular walls and lower left

ventricular volumes, and the study came to the conclusion that severe anemia in utero may raise an adult's risk of cardiovascular disease.[15] The mother never received anti-D prophylaxis, and none of her neonates had HDN, even though the previous children were Rh-positive and the mother was Rh-negative. HDN was not observed in previous pregnancies because of intact placental barrier, which would have prevented sensitization by preventing the combining of maternal and fetal RBCs.[3,12]

Conclusion

This case report highlights a rare case of maternal alloimmunization (Rh-negative pregnancy) that led to severe anemia, for which IUT was performed twice to treat anemia. The most frequent cause of fetal anemia is Rh alloimmunization, which should be taken into consideration while making a differential diagnosis throughout the assessment. Improvements in IUT procedures and earlier detection of the MCA-PSV by Doppler ultrasonographic examination have also contributed to better results. Additionally, it is vital to have follow-up at regular intervals, including repeated assessments of Hb levels. Furthermore, parents should be advised regarding the necessity of prophylactic anti-D immunoglobulin and the significance of prompt medical attention for anemia-related symptoms.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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