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Case Report

A preterm neonate with fetal anemia and immune hydrops fetalis requiring intrauterine transfusion and postnatal exchange transfusion: a case report

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ABSTRACT

Hydrops fetalis is a presenting illness with various immune and non-immune etiologies. It involves fluid accumulation in body cavities, and symptoms specific to its underlying cause. In this case, we report on a preterm neonate with a history of bad obstetrics who presented with hydrops fetalis due to fetal anemia related to RH incompatibility. The patient received an intrauterine transfusion for severe fetal anemia and subsequently required NICU admission. Routine preterm care was provided, along with specific management for jaundice resulting from isoimmune hemolytic anemia.

Keywords: Immune hydrops fetalis, Rhesus incompatibility, Intrauterine transfusion, Exchange transfusion

INTRODUCTION

Hydrops fetalis is a condition in the fetus characterized by abnormal interstitial fluid collection in two or more compartments of the fetal body (peritoneal cavity, pleura, and pericardium).[1] Hydrops fetalis can occur due to various pathophysiologies, each with the potential to severely affect the fetus. It is divided into two categories: immune and non-immune. When found in association with red cell alloimmunization, it is termed immune hydrops fetalis; otherwise, it is called non-immune hydrops fetalis. Diagnosis is based on radiographic findings such as placentomegaly, pleural effusion, pericardial effusion, or ascites.[2] The direct coombs test can grossly separate immune and non-immune etiologies. Management of immune hydrops fetalis is classified antenatally, with interventions such as intrauterine transfusion, and postnatally, with exchange transfusion and IVIG (intravenous immunoglobulin). In this case, we report on a 28-week preterm neonate with antenatally diagnosed hydrops, fetal anemia, and bad obstetric history. The patient was managed with antenatal intrauterine transfusion and postnatal NICU care, including double volume exchange transfusion and routine preterm care.

CASE REPORT

A preterm male neonate, born out of a nonconsanguineous marriage, fifth in birth order, with the first one being a live birth via vaginal delivery, and the second being a spontaneous abortion at 6 weeks of gestation. The third had a history of fetal anemia and hydrops fetalis, requiring intrauterine blood transfusion. Unfortunately, fetal demise occurred intra-procedurally. The fourth was a 29-week LSCS delivery with an antenatal diagnosis of fetal anemia, necessitating a NICU stay and a double volume exchange transfusion, and was later discharged. Our patient, born at 28 weeks preterm, was delivered via emergency LSCS due

to antenatal fetal anemia with maternal ICT (indirect Coombs test) positivity. An antenatal scan at 27 weeks suggested findings of ascites, pleural effusion, and pericardial effusion (Figure 1). Doppler findings suggested MCA PSV >1.5 MOM, indicating severe fetal anemia. With an obstetrician, neonatologist, and interventional radiologist present, intrauterine transfusion was performed. Pre-transfusion fetal HB was 6.6 g/dl, which improved to 12 g/dl post-transfusion. After 48 hours of intrauterine transfusion, emergency LSCS was performed due to leaking foul-smelling liquor vaginally. The baby's birth weight was 1.4 kg, and he required intubation in the delivery room for respiratory distress. The baby was then shifted to the NICU, where surfactant therapy was initiated and ventilatory support was provided. Examination revealed generalized edema of the neonate. An umbilical line was accessed, and total parenteral nutrition was initiated. Chest X-ray showed pleural effusion, and bedside sonography showed ascites and pericardial effusion. Investigations upon admission revealed a positive direct coombs test, CBC showed hemoglobin: 13.8 g/dl, total counts: 7900/mm^3, with differential counts showing neutrophils: 65%, lymphocytes: 21%, and platelet counts: 97,000/mm^3. Total Bilirubin was 10.2 mg/dl, direct was 0.5 mg/dl, and indirect was 9.7 mg/dl. Given these findings, urgent double-volume exchange transfusion under strict aseptic precautions was performed in the NICU for iso-immune hemolytic jaundice. Double surface phototherapy was initiated, and IVIG was administered post-exchange transfusion. Repeat bilirubin after 6 hours of exchange transfusion was 9.1 (total), 0.4 (direct), and 8.7 (indirect), still within the exchange transfusion range. Therefore, a repeat double-volume exchange transfusion was performed, phototherapy continued, and a second dose of IVIG was given. Repeat bilirubin after 6 hours of the second exchange transfusion decreased to total (5.4), direct (0.5), and indirect (4.9). The baby's bilirubin gradually decreased thereafter, so phototherapy was discontinued on the 3rd day of life. The patient was extubated to non-invasive support on the 7th day of life. Feeding was gradually increased, and parenteral nutrition was discontinued on the 14th day of life.

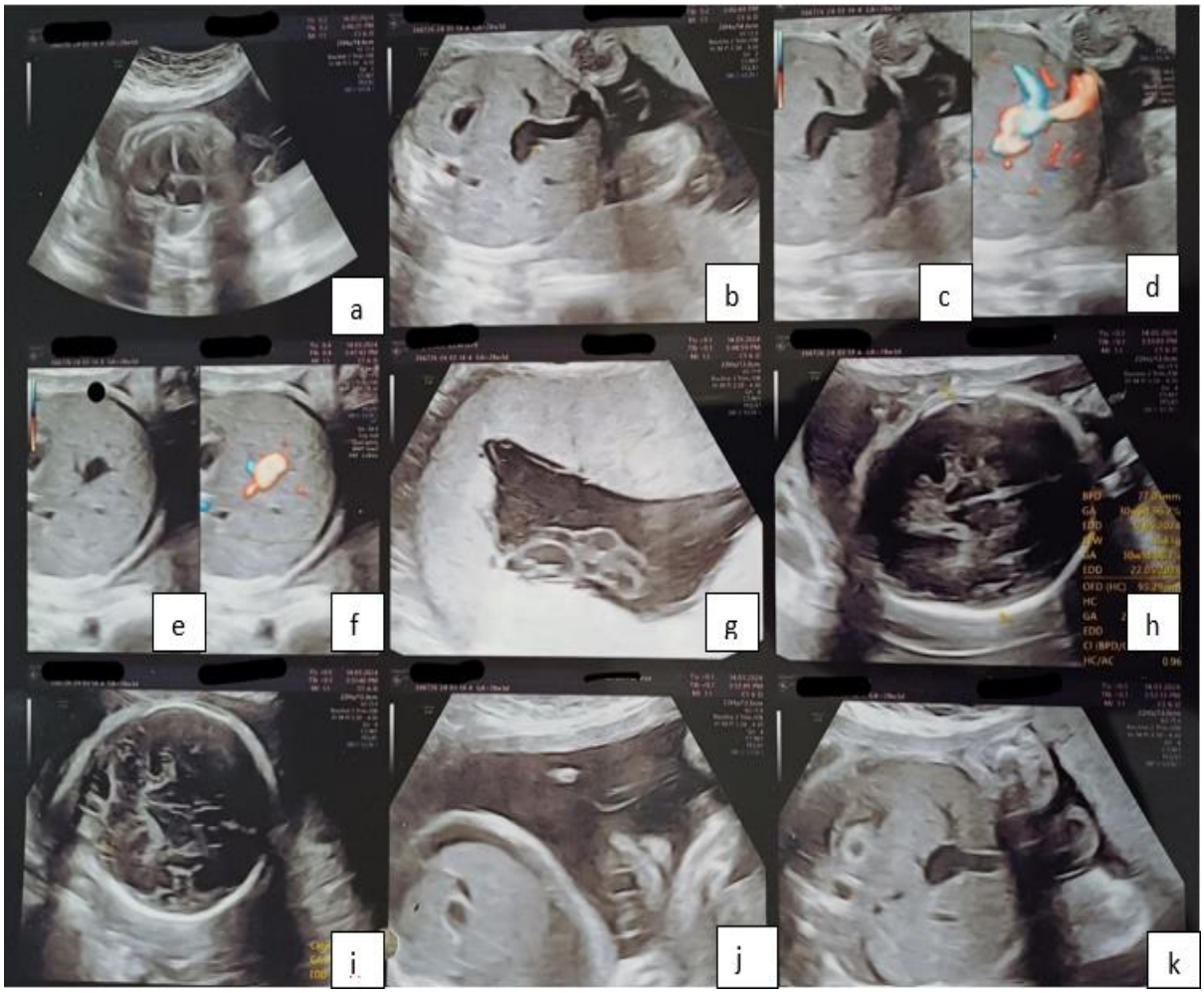

Figure 1 (a-k): Antenatal sonography revealed changes of ascites, pericardial effusion, pleural effusion, and placentomegaly consistent with hydrops fetalis.

Management and outcome

The patient's management involved both antenatal and postnatal care. Due to antenatal fetal anemia (pre-transfusion HB was 6.6 g/dl) at 27 weeks of gestational age, intrauterine transfusion was performed in the operating theater by an interventional radiologist, with the assistance of an obstetrician and neonatologist. Due to persistent leaking, emergency LSCS was performed, and the baby was transferred to the NICU for preterm and very low birth weight care. Upon admission, bilirubin levels were in the exchange transfusion range, prompting two double volume exchange transfusions. Two doses of intravenous immunoglobulin at 1 gm/kg were administered. Standard preterm care protocols were followed, initially initiating parenteral nutrition and gradually transitioning to full feeds. The baby was discharged on oral feeds.

DISCUSSION

Hydrops fetalis, a condition characterized by abnormal fluid accumulation in the fetus, can be classified into two main types: immune and nonimmune. Immune hydrops occurs due to hemolytic anemia pertaining to RH incompatibility. Non-immune hydrops result from fetal disorders affecting the fluid balance between vascular and interstitial spaces. Multiple anatomic and functional fetal abnormalities contribute to non-immune hydrops. The prevalence of NIHF varies, ranging from 1 in 1500 to 1 in 4000 births.[1]

These disorders can be lethal and lead to the presence of at least two abnormal fluid collections in the fetus, including Ascites, Pleural effusions, Pericardial effusions, and Generalized skin edema.

Pathophysiology of non-immune hydrops includes dysregulation of fluid movement between vascular and interstitial spaces. Fetal disorders with Increased interstitial fluid production, Obstruction of lymphatic return, and Decreased plasma osmotic pressure lead to non-immune hydrops fetalis.[2]

Pathophysiology of immune hydrops fetalis includes hemolytic anemia that occurs due to Rh incompatibility leading to heart failure which complicates generalized and compartmental fluid collection.

The etiology of hydrops fetalis divides into immune-mediated and nonimmune-mediated mechanisms. The most common immune-mediated mechanism is Rh hemolytic disease of the fetus and newborn. As in our case, there is a bad obstetric history with previous sibling deaths and NICU admission for isoimmune hemolytic jaundice due to Rh incompatibility. There was a higher degree of clinical suspicion that this preterm neonate could also be a case of immune hydrops. Mechanisms not involving immune-mediated hemolysis of red blood cells include decreased production of normal Hb $\alpha^2\beta^2$ tetramers, and intrinsic red blood cell or Hb abnormalities. Other hydrops causes include parvovirus, cytomegalovirus, herpes simplex virus, varicella, coxsackie virus, and toxoplasma infections. Genetic causes include trisomy 13, trisomy 18, trisomy 21, turner syndrome, triploidy, and tetraploidy. Causes of cardiac etiologies are arrhythmias, cardiomyopathy, twin-twin transfusion syndrome, and myocarditis. Other rare cases include congenital nephrotic syndrome, hypoproteinemia, pulmonary hypoplasia, and renal dysplasia.[3]

In the case of hydrops fetalis, the number of fluid collection sites are directly correlated to the neonatal prognosis. The diagnosis is mainly based on prenatal ultrasound or the postnatal evaluation of the fetus. As in our case, an antenatal scan at 27 weeks showed ascites, pleural effusion, and pericardial effusion. Other features include anemia, placentomegaly, polyhydramnios, or hepatosplenomegaly. Pleural effusion can be unilateral or bilateral. Mild effusions can cause respiratory distress, and severe effusions result in lung hypoplasia and respiratory or circulatory diseases associated with poor prognosis after birth. Ascites can be an early manifestation of hydrops fetalis and are seen as early as 20 weeks of gestation. As isolated fetal ascites is seen in many other systemic diseases, it is essential to differentiate hydrops fetalis from the other causes edema is defined as the subcutaneous tissue thickness on the scalp greater than 5mm. Sometimes, fluid accumulation behind the neck, known as nuchal translucency, and fat under the scalp is mistaken for skin edema. Anemia in hydrops fetalis is caused mainly by red cell alloimmunization and parvovirus-B19 infection. Other causes include alpha thalassemia, Bart hemoglobin, and a mutation in the alpha-globin chain. Polyhydramnios is the vertically measured amniotic fluid volume in the single deepest pocket of more than 8 centimeters or amniotic fluid index of more than 24 centimeters. It is caused mainly due to impaired fetal swallowing, impaired renal function, and intestinal obstruction. Placentomegaly is an abnormally enlarged placenta that occurs due to disruption in the oncotic gradient. It is mainly seen in high cardiac output diseases like anemia and sacrococcygeal teratoma. Placentomegaly and polyhydramnios are considered predictors of survival. Dermatitis, along with or without hepatosplenomegaly, suggests the presence of TORCH (toxoplasmosis, other infections such as rubella, cytomegalovirus, and herpes simplex) infections. Hydrops fetalis is mostly an incidental finding on routine prenatal workup. The underlying cause has a direct influence on the development of symptoms and its prognosis. Hydrops due to chromosomal abnormalities are usually detected during early pregnancy, whereas cardiac causes are detected in the second or third trimester. Hence, a detailed prenatal workup should be done in suspected cases. The following are the various diagnostic modalities for the evaluation of hydrops fetalis. The first detailed ultrasound is done between 18 to 22 weeks of gestation. The most common findings detected during early pregnancy are ascites and skin edema (>5 mm thickness) in the fetal head, back of the neck, thorax, and abdomen. The cause of generalized

skin edema is most probably due to aneuploidy or associated anatomical defects. Polyhydramnios and placental edema are most commonly seen before 20 weeks, whereas pleural effusion and pericardial effusion in the fetus are rarely seen before 15 weeks of gestation.[4] It is mandatory to look for the possibility of maternal toxoplasma, rubella, cytomegalovirus, herpes (TORCH), and parvovirus B19. Parvovirus B19 infection is most commonly associated with fetal anemia and ascites; however, cytomegalovirus and toxoplasmosis present with congenital malformations like ventriculomegaly, microcephaly, and hyperechogenic bowel. Hence, the antibody screen for TORCH infections should always be considered. Fetal heart rate, umbilical artery pulsatility index, end-diastolic flow, and middle cerebral artery peak systolic velocity (MCA-PSV) are also helpful in detecting the underlying causes of hydrops. The measurement of MCA-PSV is very sensitive in determining fetal anemia. An MSA-PSV ratio of more than 1.5 is considered to be fetal anemia. Cordocentesis helps find the cause of fetal anemia.[5] Chorionic villous sampling (CVS) is most frequently done for karyotyping if hydrops fetalis is diagnosed before 15 weeks of gestation. Direct and indirect Coomb test is used for detecting immune hydrops fetalis, but they do not correlate with the disease severity.[1,6]

Prenatal management

Prenatal therapies are available depending on the etiology of hydrops fetalis. When severe anemia is the mechanism, fetal transfusions may be indicated. The umbilical vein is the most desired site for transfusion, free loop of the cord, intrahepatic portion of the hepatic vein, or umbilical artery can be alternatives but are associated with greater complications. As in our case at 27 weeks of intrauterine gestation intrauterine transfusion was given, which improved fetal anemia and ultimately improved the survival of a patient.[7]

Fetal interventions for various causes of hydrops fetalis include fluid diversions such as thoracoamniotic shunt placement, thoracentesis, or paracentesis, which are available but not widely studied.

In cases of cardiac etiology, monitoring cardiac status can assist with management, such as administration of maternal antiarrhythmics, and timing of delivery in the case of non-reassuring fetal testing due to worsening heart failure. Sustained tachycardia can progress to hydrops fetalis and maternal administration of antiarrhythmics with consideration of direct fetal administration of antiarrhythmic therapy can be considered to help establish sufficient sinus rhythm to allow resolution of hydrops fetalis. Maternal digoxin, flecainide, or sotalol are common first-line therapies for tachyarrhythmias, with the latter having decreased absorption in the setting of hydrops fetalis.[6]

Postnatal management

Management of a neonate with hydrops fetalis consists of supportive care while investigating for and treating the underlying etiology. When possible, delivery should occur at a center with a skilled neonatal resuscitation team. The delivery team should be prepared to intubate, if necessary, as neonates with hydrops fetalis can develop cardiorespiratory failure related to multiple underlying causes including cardiac dysfunction and poor perfusion, pulmonary hypoplasia, pleural effusions, or ascites.

As in our case, the patient was antenatally managed with intrauterine transfusion, and a postnatally double volume exchange transfusion with intravenous immunoglobulin transfusion was given. Routine pre-term care was given with total parenteral nutrition, feeding started, and gradually feeds increased to full feeds. Initially, invasive mechanical ventilation and surfactant therapy were given to the patient.[8]

CONCLUSION

Immune hydrops fetalis is characterized by fluid collection in newborn babies. It can result from Rh incompatibility. This leads to fetal anemia, heart failure, and fluid accumulation in tissues and organs. Fortunately, advances in medical management including intrauterine transfusion and exchange transfusion have improved outcomes for affected infants.

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