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Ballantyne Syndrome-The Uncommon in Common Rh Isommunization

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Dear Editor,

Ballantyne or Mirror syndrome is a rare condition characterized by maternal disease that mimics fetal hydrops. This report presents a case that initially manifested as birth asphyxia, severe thrombocytopenia, hydrops, direct hyperbilirubinemia, hypoglycemia, and late-onset hemolysis presenting as anemia.

A 27-year-old gravida 3, para 1, abortion 2 patient, with a history of adverse obstetric outcomes, was admitted to our hospital for labor induction. The pregnancy was considered precious, as the couple had been attempting conception for 10 years. The gestational age was 40 weeks. The patient was a registered case having conceived spontaneously with AB negative blood group. Both previous abortions were spontaneous. Anti-D immunoglobulin was administered during pregnancy. The indirect Coombs test was negative. The patient reported decreased fetal movements during pregnancy. Additionally, she experienced a 4 kg weight gain over a two-week period prior to presentation, with significant pedal edema. Her blood pressure levels remained within normal parameters. An emergency lower segment cesarean section was performed due to non-progression of labor. A female infant weighing 2.3 kg was delivered. Fetal hydrops, placentomegaly, and polyhydramnios were observed. The neonate did not exhibit spontaneous respiration at birth and was managed as a case of birth asphyxia. Following initial resuscitation, the infant was transferred to the neonatal intensive care unit, intubated, placed on mechanical ventilation, and administered broad-spectrum antibiotics. The infant was extubated on day 7.

Initial investigations on day 1 of life revealed hemoglobin 13.2 g/dL; the direct Coombs test was negative. The neonate presented with severe thrombocytopenia (platelet: 35.000/mm^3), which was managed with intravenous immunoglobulin (IVIG) and repeated platelet transfusions.

By the tenth day, the hydrops gradually subsided. On the third day, the infant experienced hypoglycemia (35 mg/dL), necessitating a high glucose infusion rate (exceeding 20 mg/kg/min). This rate was progressively decreased, and oral feeding was initiated on day 12.

On the fourth day, the infant exhibited direct hyperbilirubinemia, with total bilirubin at 11.2 mg/dL and direct bilirubin at 4.7 mg/dL, accompanied by transaminitis. The levels progressively increased, reaching a peak of 22 mg/dL total, and 12.5 mg/dL direct bilirubin by day 12. The condition resolved, returning to normal levels by the conclusion of the second month.

One month after birth, significant anemia was observed (hemoglobin: 5.3 g/dL). A repeated direct Coombs test yielded positive results, indicating ongoing hemolysis. The anemia was treated with a combination of blood transfusion and additional IVIG administration.

Various diagnostic tests were conducted to investigate potential metabolic disorders, including tandem mass spectrometry, gas chromatography mass spectrometry,

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fundus examination, and thyroid-stimulating hormone analysis. Clinical exome studies were performed to exclude genetic causes. Toxoplasmosis, other agents, rubella, cytomegalovirus, herpes and syphilis titers, urine culture, and cytomegalovirus polymerase chain reaction were carried out as part of the assessment for direct hyperbilirubinemia. A critical sample was obtained and examined for serum insulin and cortisol levels to evaluate resistant hypoglycemia. However, all test results were inconclusive. The infant is currently under regular monitoring, showing weight gain, successfully breastfeeding, and progressing well.

Ballantyne syndrome, also known as mirror syndrome, is an uncommon pregnancy complication characterized by a triad of symptoms: fetal hydrops, placental edema, and maternal edema. The underlying mechanisms of this condition remain unclear, but it is believed that placental dysfunction, similar to that observed in pre-eclampsia, may play a role.[1] This syndrome can occur in various circumstances, including rhesus incompatibility, pregnancies with multiple fetuses, viral infections, fetal abnormalities, and tumors affecting the placenta or fetus.

Rh incompatibility typically occurs when a woman with Rh-negative blood is exposed to Rh-positive red blood cells, triggering the production of Rh antibodies. Common manifestations include jaundice, anemia, and, in severe instances, hydrops fetalis. Despite anti-D immunoglobulin prophylaxis, it may manifest as a pseudosyndrome characterized by temporary congenital hyperinsulinism, anemia, and inspissated bile syndrome with conjugated hyperbilirubinemia. This presentation is likely due to late-occurring fetomaternal hemorrhage.[2]

In some instances, infants who initially show minimal or no symptoms at birth may later develop severe hemolytic anemia.[3] There are also reports of early-onset anemia without hyperbilirubinemia as the sole manifestation of Rh isoimmunization.[4] Hydrops fetalis in Rh isoimmunization is frequently accompanied by thrombocytopenia.[5]

Initially, this case was treated as birth asphyxia due to a negative direct Coombs test, and the mother received anti-Rh D. However, as symptoms progressed and other conditions were excluded, mirror syndrome became a likely explanation. After ruling out congenital hyperinsulinism, severe hypoglycemia was attributed to perinatal hypoxia. The failure of anti-D Ig prophylaxis was also considered in this case.

When managing cases that present as hydrops fetalis, birth asphyxia, severe thrombocytopenia, direct hyperbilirubinemia, hypoglycemia, and hemolytic anemia, it is crucial to consider mirror syndrome. Given that mothers with mirror syndrome exhibit symptoms similar to pre-eclampsia, it is essential to rule out mirror syndrome in pregnant women showing signs of pre-eclampsia. Additionally, our case demonstrates that Rh isoimmunization can manifest as hydrops without significant anemia and with an initially negative direct Coombs test.

Footnotes

Author Contributions: Kumar DV: Surgical and Medical Practices, Concept, Design, Data Collection or Processing, Literature Search, Analysis or Interpretation, Writing.; Kumar A: Surgical and Medical Practices, Concept, Design, Data Collection or Processing, Literature Search, Analysis or Interpretation, Writing.; Tiwari S: Surgical and Medical Practices, Concept, Design, Data Collection or Processing, Literature Search, Analysis or Interpretation, Writing.

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