More than Meets the Eye
Hemolytic Disease of The Newborn with DAT Negative Anemia

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Case Presentation

- 17 day old male born to a G₂P₁ female who presents to the Children’s Hospital with pallor, respiratory distress, and jaundice.

- PMHx: Born at 37 weeks NSVD

- Transfusion History: 3 intrauterine red cell transfusions
Laboratory and Blood Bank Studies

- Hemoglobin: 5.4 gm/dl
- Total bilirubin: 15 mg/dl
- Indirect bilirubin: 14.6 mg/dl
- Reticulocyte count: < 0.5%

- Patient typing as 0 negative
- Patient’s antibody screen positive
- Anti-C identified in patient
Questions to Consider

- What historical information would we want from mother of child?
- What is the differential diagnosis for DAT negative anemia in a 2 week old?
- What role does the blood bank have in this case and how can they help?
Questions to Consider

What type of red cells should the patient receive for transfusion now?

Should the transfusion be a simple one or an exchange transfusion?

When are intrauterine red cell transfusions indicated and what type of red cell products should be transfused?
What is Hemolytic Disease of the Fetus/Newborn?

- Fetal RBCs become coated with maternal IgG (alloantibodies) directed against paternal antigens

**NATURAL HISTORY**

- RBCs↑ production in liver
- ↑ nucleated RBC in circulation
- ↓ albumin synthesis
- Anemia – Cardiovascular failure---Tissue Hypoxia---(+)
- ↓ oncotic pressure – edema, ascites, effusions = HYDROPS
Fetal hydrops

- Ascites
- Pleural Effusion
- Scalp Edema
Hemolytic Disease of the Fetus and Newborn

- Usually positive DAT
- Post-natal hyperbilirubinemia
- In utero hemolysis
- In utero death (hydrops fetalis)
## Comparison of Rh and ABO HDN

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Rh</th>
<th>ABO</th>
</tr>
</thead>
<tbody>
<tr>
<td>First born</td>
<td>5%</td>
<td>40 – 50%</td>
</tr>
<tr>
<td>Predictable severity</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>subsequent preg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stillbirth/hydrops</td>
<td>Frequent</td>
<td>Rare</td>
</tr>
<tr>
<td>Jaundice</td>
<td>+++ to ++++</td>
<td>+</td>
</tr>
<tr>
<td>HSM</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Response to bililights</td>
<td>Limited</td>
<td>Excellent</td>
</tr>
<tr>
<td>Infant DAT</td>
<td>+</td>
<td>+ or 0</td>
</tr>
<tr>
<td>Maternal antibody ID</td>
<td>Usually</td>
<td>Not clear</td>
</tr>
<tr>
<td>Spherocytes</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Late Anemia</td>
<td>Common</td>
<td>Rare</td>
</tr>
</tbody>
</table>
Algorithm for the management of RhD sensitized pregnancy

Figure 6-1. A suggested algorithm for the management of RhD sensitized pregnancy. (Used with permission from Moise.)

Intrauterine, Neonatal, and Pediatric Transfusion: Wong, Luban In:Transfusion Therapy: Clinical Principles and Practice
Middle Cerebral Artery (MCA) Doppler

- > 1.50 multiples of the mean (MoM) MCA peak velocity for the detection of moderate/severe anemia
- Sensitivity 100%
- False positive 12%
- Positive predictive value rate 65%
- Perform prior to 35 weeks
- Measure must be > 1.5 MoM before fetal blood sampling is performed
- Percutaneous umbilical blood sampling (PUBS) has a 1-2% risk of fetal loss

Mari et al. N Eng J Med 2000; 342;9-14
Percutaneous umbilical blood sampling (PUBS)
Queenan and MCA Charts

Invasive Amniotic fluid monitoring

Non-invasive MCA velocity monitoring

Figure 6-2. Queenan chart to monitor amniotic fluid AOD450 nm for management of D-immunized pregnancies. (Modified from Queenan et al.19)

Figure 6-3. Comparison of middle cerebral artery peak velocity and gestational age in relation to fetal anemia. (Used with permission from Moise.23) MCA = middle cerebral artery; MOM = multiples of the median.

Intrauterine, Neonatal, and Pediatric Transfusion: Wong, Luban In:Transfusion Therapy: Clinical Principles and Practice
Red Cell Alloimmunization
Antibodies Necessitating Intrauterine Transfusion

- Anti-D
- Anti-Kell (K1)
- Anti- c, C
Thresholds and Transfusion Rates in Intrauterine Transfusions

- Hemoglobin < 10 g/dL or two standard deviations below the mean for gestational age

- Transfusion volumes between 20 – 50% of fetoplacental blood volume

- Non-hydrops fetus infusion rates 5 – 7 mL/minute

- Hydropic fetus 1 – 2 ml/minute (can be 3 transfusion of red cells 1 -2 weeks apart

Am J Obstet Gynecol 1987;157:4-9
Intrauterine Transfusion
RBC Selection and Processing

- Compatibility with maternal sample
- "CMV safe" - leukoreduced or CMV negative
- Fresh as possible RBCs
- Reconstituted with FFP to prevent dilutional coagulopathy (Hct 50 – 80%)
- Washing: fluid status patient, if mother’s blood used for transfusion, if AS units used
- Blood negative for Hemoglobin S
- Irradiated
Intrauterine Transfusion
Perinatal Survival

- Overall perinatal survival: 84%
- Survival with fetal hydrops: 74%
- Survival without hydrops: 94%

Intrauterine Transfusion
Neonatal Follow-up

- 36 infants
- 50% required top-up transfusions
- Mean: 38 days (20-68 days)
- Most required 1 top-up transfusion
- Follow-up with weekly hcts and retics
- Adverse neurologic outcomes in 9.1% w/ hydrops vs 6.4% w/o hydrops

Questions to Consider

- What historical information would we want from mother of child? Did she receive Rh IgG and when? Does she have a known antibody?

- What is the differential diagnosis for DAT negative anemia in a 2 week old? Usually implies non-immune mediated process so: G-6 PD, Pyruvate kinase deficiency, Diamond-Blackfan anemia, leukemia, blood loss, or potentially immune mediated with total destruction of targeted red cells explaining DAT negative result
Questions to Consider

- What role does the blood bank have in this case and how can they help?

- What type of red cells should the patient receive for transfusion now?

- Should the transfusion be a simple one or an exchange transfusion?

- When are intrauterine red cell transfusions indicated and what type of red cell products should be transfused?
Follow-up: Case presentation patient

He was placed on rEPO due to hypoproliferative suppression of bone marrow.

He is still requiring transfusion every 4 - 5 weeks and now approximately 80 days later his IAT is negative, retic count is close to normal and he is growing well.