Cord Blood Testing and HDFN
A Case Study

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BACKGROUND

- KU Hospital policy: run ABO/Rh (front) type + Direct Antiglobulin test on cord bloods for neonates born to mothers who are:
  - Type O
  - Rh Negative
  - Have a history of a positive antibody screen for a clinically significant antibody
  - At the request of a practitioner/clinician
  - Policies vary by institution
Neonatal Hyperbilirubinemia

- AKA Neonatal jaundice
- Multiple possible pathways, predominantly (physiologically) either:
  - Increased bilirubin production (typically due to shortened RBC lifespan / intravascular hemolysis), OR
  - Decreased bilirubin clearance – more common in pre-term infants due to liver maturation
- Focus of our interest in transfusion service is ABO/Rh Incompatibility
Why do the DAT?

- About 2.6% of cord bloods have a positive DAT.
- When there is an ABO incompatibility between mother and neonate, there is a large increase in likelihood of a positive neonatal/cord blood DAT.
  - About 23% of cases where mother’s type is O and newborn’s type is A.
  - About 13% of cases where mother’s type is O and newborn’s type is B.
- (Valsami, Politou, Boutsikou, Briana, Papatesta, Malamitsi-Puchner, 2015).
Why do the DAT - continued

- Positive DAT isn’t necessarily diagnostic of impending hyperbilirubinemia / jaundice.
- Possible (and obvious) increase in diagnostic value when considering an elevated bilirubin in conjunction with an ABO incompatibility.
- Still no direct guideline for specific testing algorithm to follow.
- (Peeters, Geerts, Mullem, Micalessi, Saegeman, 2015)
The Patient

- Full Term Baby girl born to a mother with some unrelated complications
  - History of tobacco use
  - Pre-eclampsia
  - Type 2 Diabetes Mellitus
- Uncomplicated, healthy delivery.
- Routine hematocrit at birth: 42% (reference range 51-65%)
Mother's Blood Bank Testing

- Solid phase testing
- O Pos
- Negative antibody screen (3 cell)

KU Policy – cord blood sample has to be run (front type + DAT)
Blood Bank Testing - Baby

- Blood Type: B Positive
- DAT: 1+ positive in tube
  - Due to ABO/Rh incompatibility
DAY 2

- Normal behavior
- Slight feeding difficulties
- Jaundiced appearance, somewhat agitated demeanor
- Fairly unremarkable physical examination
- Total Bilirubin at 0935: 21.3 mg/dL, considered critically high (ref range for newborn = <8.0 mg/dL, anything ≥18.0 is considered critically high)
  - Panic value: close to indicated level for exchange transfusion of neonate by patient’s gestational age.
**FOLLOWING UP...**

- Total Bilirubin at 0935: 21.3 mg/dL, considered critically high (ref range for newborn = <8.0 mg/dL)
- Re-check at 1046 (baby ~36 hours old): 20.7 mg/dL
- Re-check at noon, 20.8 mg/dL
  - Hemoglobin 12.2 g/dL (normal 17.5 – 22.5 g/dL)
  - Hematocrit 36.1% - ~6% decreased from previous day
- Repeat sample (Type and Screen) drawn, DAT repeated on Type and Screen sample
  - Same results
American Academy of Pediatrics Guideline for Exchange Transfusion

- The dashed lines for the first 24 hours indicate uncertainty due to a wide range of clinical circumstances and a range of responses to phototherapy.
- Immediate exchange transfusion is recommended if infant shows signs of acute bilirubin encephalopathy (hypertonia, arching, retrocollis, opisthotonos, fever, high pitched cry) or if TSB is ≥5 mg/dL (85 μmol/L) above these lines.
- Risk factors - isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis.
- Measure serum albumin and calculate B/A ratio (See legend)
- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin
- If infant is well and 35-37 6/7 wk (median risk) can individualize TSB levels for exchange based on actual gestational age.

Source: AAP July 2004
Screening cells came back negative – so tested with A1 and B cells.

Determines antibody specificity against B cells alone (true anti-B).
CLINICAL DECISION

- Initiate IVIg and Phototherapy
- Test Bilirubin to monitor
- Perform exchange transfusion if AAP Threshold exceeded
  - Blood bank was ready for exchange transfusion
- Repeated neurological examinations
EXCHANGE TRANSFUSION GUIDELINES

- RBCs <5-7 days old
  - CPDA-1 additive
  - Hgb S negative
  - Sometimes CMV negative is indicated
- Irradiated (just prior to transfusion, preferably)
- Unit hematocrit should be ~45-60%, reconstituted as whole blood with ABO compatible plasma (replaces clotting factors lost)

EXCHANGE TRANSFUSION CONT.

- Hospital specific policy: same as AABB guidelines, except desired hematocrit of unit is 50-60%.
- Simple C1V1=C2V2 equation.
  - \((\text{initial volume})(\text{initial HCT}) = (\text{final volume})(\text{desired HCT})\)
- Aliquot made and tested in Hematology to get original and reconstituted HCT.
- End product resembles whole blood
- Viewed as last-ditch effort (rarely performed).
PATIENT’S COURSE OF TREATMENT

- Remaining day 1 labs (after initiation of therapy)
  - 1500: 20.0 mg/dL
  - 1900: 20.4 mg/dL
  - 2300: 18.1 mg/dL

  - Hemoglobin 10.9 g/dL (normal 17.5 – 22.5 g/dL)
  - Hematocrit 31.1%

- Average bilirubin declining significantly (see graph on next slide)
Average Daily Total Bilirubin, Days 2-8

Total Bilirubin (mg/dL)

Day 2 3 4 5 6 7 8
20.2 17.8 18.2 17.2 14.8 12.9 11.9
IMPROVEMENT ON TOTAL BILIRUBIN, BUT…

Hematocrit

Day 2    Day 4    Day 6    Day 8
**Patient Outcome**

- Labs slowed down to conserve blood:
  - Day 10: Total Bilirubin: 12.8 mg/dL (no supportive care – last inpatient level 12.2 mg/dL on day 8)
  - Day 12: Total Bilirubin: 9.6 g/dL
  - Patient discharged to home with outpatient follow up
  - Day 22: Hematocrit 27.1% (up from 22.9% on Day 12)
  - Day 27: Hematocrit 25.6%, Total Bilirubin 0.9 mg/dL (within normal limits)
Patient Outcome, Cont.

- Baby at home
- Recovery from anemia slowed due to feeding mechanism defect + normal growth & dip in hemoglobin/hematocrit.
- If needed, we would transfuse the baby with a CPDA unit (KU keeps stock units for neonates as needed, and can designate a unit for a neonate if necessary).
This case is a good argument for utilizing cord blood screening – early detection of ABO incompatibility could trigger a need for enhanced surveillance and laboratory analysis.

Some thought that mother’s titer could be important.

- Small cohort study in which a titer of \( \geq 512 \) for anti-A or anti-B was considered significantly high risk (90% sensitivity, 72% specificity for predicting need for therapy).
- (Bakkeheim, Bergerud, Schmidt-Melbye, Akkok, Liestol, Fugelseth, Linemann, 2009).
REFERENCES


Questions?

- Special thanks to the Blood Bank staff at KU Hospital and our manager, Laurie Wolf, for allowing me time to research this case study.