Case Studies

Elizabeth Donegan, MD

GLOBAL HEALING MODERN MEDICINE FOR THE DEVELOPING WORLD

54yo woman with peritonitis
S/F emergency exploratory laporotomy
• PSH: None

• PMH: obese, no ongoing medical care

• HPI: acute onset of abdominal pain while attending a convention, nothing to eat/drink for 2 days

• An acutely ill, disoriented woman with severe abdominal pain

• VS: BP: 140/80, 94, 20, 98% RA, 38°C

• Labs: WBC 24K, Hct 40.5% Plt 200K Na 138, K 3.8, Cl 104, CO2 24 PT/PTT 12.8/30 sec, fibrinogen 358mg/dl
• Patient was taken to the OR

• Induction of anesthesia required pressure support

• Following midline incision, fecal contents were noted in the peritoneum & a ruptured cecum exposed

• The surgeons proceeded with a partial colectomy & peritoneal washout

• 1 hr into the case: 2 liters of colloid
  1 liter of crystalloid
  urine output – none
  phenylephrine infusion running

• BP 98/68, 104, 12, 38°C

• Labs: WBC 35K, Hct 32, plt 103K
  PT/PTT 14/34 sec, fibrinogen 250mg/dl
• 2 hrs into the case: 2 liters colloid
  3 liters crystalloid
  4 units FFP
phenylephrine/norepinephrine

• VS: 86/58, 120, 16, 39°C

• LABS: WBC 38 k, Hct 28%, plt 58K
  PT/PTT 18.5/42, fibrinogen 122mg/dl

Surgery Complete: transfer to the ICU
• 6 hrs later: 2 liters colloid
  4 liters crystalloid
  8 units FFP
phenylephrine/norepinephrine infusion
• VS: 70/42, 126, ventilated 100% O2 → O2
  sat 86%, 39°C
• LABS: WBC 38 k, Hct 23%, plt 20K
  PT/PTT >100/>100, fibrinogen 58mg/dl
Diagnosis?

- Sepsis
- Disseminated intravascular coagulation
Bleeding In Surgery

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<th>DILUTION</th>
<th>DIC</th>
<th>FIBRINOLYSIS</th>
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<tbody>
<tr>
<td>PT/PTT</td>
<td>↑</td>
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<tr>
<td>PLATELETS</td>
<td>↓</td>
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<td>FIBRINOGEN</td>
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<td>d-DIMERS</td>
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(PT/PTT: HIGH = >1.5x NORMAL; PLATELET COUNT: LOW = <50-80K; FIBRINOGEN: LOW = <80mg/dl; d-DIMERS: HIGH = >1:2)

Disseminated Intravascular Coagulation

- Crush injury
- Acute hemolytic transfusion reaction
- Abruptio placenta
- Cardiopulmonary bypass
- Sepsis
Disseminated Intravascular Coagulation

- Liver disease
- Anoxia
- Acidosis
- Acute pancreatitis
- Immune complex disease
- Intravascular Emboli (fat, amniotic fluid, air)

Treatment

- Supportive:
  - Intravascular pharmacologic/volume pressure support
  - Transfusion (RBC, FFP, cryo, plts) as needed
  - No clear indications for heparin
85 yo male in the ER with abdominal pain, expanding girth

CT scan: 10cm abdominal aortic aneurysm

- PMH: HTN, hypercholesterolemia, MI
- PSH: appendectomy, 24 yrs cholecystectomy, 58 yrs

- VS: BP: 148/88, 98, 16, 98% on RA
- LAB: H/H: 9.1/24%, Plts 143K Na 140, K 3.8, Cl 108, CO2 23 PT/PTT 14/29, sample in blood bank
• On examination:
  patient is noted to have expanding abdomen

BP: 110/58, 120, 20

What should we do now?
What should we do now?

- Family
  - clarify resuscitation wishes
- Laboratory
  - notify Blood Bank of impending surgery
  - T&C 6 units RBC, thaw 8 FFP, plts
  - release 6 units O RBC to OR
- Operating Room
  - obtain adequate IV access, colloids
  - prepare for cardiopulmonary resuscitation
  - blood in room, hanging prior to incision
A male infant 2,511 gm, 40 week gestation

- the child is jaundiced
- mother had no prenatal care

• What do you want to do?
• Examine the child
• Labs: CBC
  bilirubin
direct antiglobulin test
ABO, Rh type mother and child
Causes of Neonatal Anemia & Hyperbilirubinemia

- Rh disease
- ABO incompatibility
- Idiopathic Hyperbilirubinemia
- Other hematologic dx:
  - G6PD, PK def, sepsis, fibrosarcoma,
  - AML, alpha-thalassemia,…

Recommendations:

American Academy of Pediatrics 1994:

- Phototherapy
- Exchange Transfusion: > 48 hrs old with evidence of hemolysis: 20mg/dl
  w/o evidence of hemolysis: 25mg/dl
Hemolytic disease of the newborn

• Destruction of fetal/neonate RBCS by maternal antibodies

• Mother antibody stimulated by a previous pregnancy or transfusion (rare 1st pregnancy)

• Historically, ~95% of cases do to anti-RH\textsubscript{0}(D)

HDN: Disease Mechanism

• Maternal antibody destroys fetal RBCs
• Only IgG antibodies are actively transported across placenta (IgM, IgA, and IgE are not)
• the IgG antibodies are directed against fetal RBC Ags inherited from father
Rh HDN

Fetomaternal Hemorrhage →
Maternal antibodies formed against paternally derived antigens →
During subsequent pregnancy, placental passage of
maternal IgG antibodies →
Maternal antibody attaches to fetal RBCs →
Fetal RBC hemolysis → Anemia

HDN Antigenic Exposure

• 50-65% of pregnant women have fetal cells in their blood
• In most, fetomaternal hemorrhage is small (but 1.0 mL RBCs can immunize)
  - miscarriage/abortions can immunize
• Fetomaternal hemorrhage during later pregnancies → significant ↑ in maternal Abc titers → worse
HDN: Host Factors

- Individual Aby response to Ag exposure varies, depending upon complex genetic factors.

- Exposure to Rh D Ag is very stimulating:
  1 u Rh\(^+\)RBCs into Rh\(^-\) : \(\sim 80\%\) develop anti-D

- \(\sim 10\%\) of Rh-negative moms develop anti-D after Rh-positive pregnancy if no RhIG is given.

HDN: Antibody Specificity

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<thead>
<tr>
<th>Common</th>
<th>Rare</th>
<th>Never</th>
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<tbody>
<tr>
<td>Anti-D</td>
<td>Anti-Fy(^a)</td>
<td>Anti-Le(^a)</td>
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<tr>
<td>Anti-D + C</td>
<td>Anti-s</td>
<td>Anti-Le(^b)</td>
</tr>
<tr>
<td>Anti-D + E</td>
<td>Anti-M</td>
<td>Anti-I</td>
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<tr>
<td>Anti-C</td>
<td>Anti-N</td>
<td>Anti-IH</td>
</tr>
<tr>
<td>Anti-E</td>
<td>Anti-S</td>
<td>Anti-P(_1)</td>
</tr>
<tr>
<td>Anti-c</td>
<td>Anti-e</td>
<td>Anti-K</td>
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GLOBAL HEALING
HDN: Influence of ABO Group

- Mother-fetal major ABO incompatibility → (e.g., mom = O; fetus = A)
- Detectable fetomaternal hemorrhage ↓
- Rh immunization ↓
- ? Hemolysis in maternal circulation of Rh⁺ fetal RBCs before sensitization

HDN: Hemolysis, Anemia, and Erythropoiesis

- RBC destruction: antibody titer/specificity
  # of fetal RBC Ag sites
- Fetal RBCs destruction → compensatory
  ↑ erythropoiesis in marrow, spleen and liver
HDN: Hyperbilirubinemia

- RBC destruction: Hbg → *indirect* bilirubin
- *In utero*: maternal hepatic excretion of *indirect* bilirubin (no clinical disease in fetus)
- After delivery, accumulated bilirubin can cause major problems - *kernicterus*
  - neonatal liver immature (bilirubin not well metabolized/excreted)

HDN: Serologic Testing

- A “type and antibody screen” at the first antenatal visit (preferably during 1st trimester)
HDN: ABO/Rh

- ABO and Rh testing (for D antigen) are very important
- Rh test: include weak D, (weak D$^+$ = “Rh$^+$")

HDN: Antibody Detection

- Prenatal testing: must detect clinically significant IgG antibodies reactive at 37° C
- Use $\geq$ 2 reagent screening cells
- Use an antibody enhancing medium (e.g., LISS or albumin)
HDN: Antibody Detection

- Can eliminate immediate spin and RT incubation
  - Use anti-IgG (not broad spectrum) antiglobulin reagent to eliminate IgM reactions

- If antibody screen is NR, repeat at 20-24 weeks, and at delivery.

HDN: Early Delivery/Phototherapy

- Early delivery:
  - Once: method of choice for mod-severe disease
  - Now: repeated, frequent IUTs generally allows delivery after fetal lung maturity

- Phototherapy: Following delivery, often eliminates need for exchange transfusions in infants with mild-to-moderate hemolysis
**HDN: Newborn Transfusions**

- Newborns with HDN may need small aliquots of RBCs and/or entire exchange transfusions.
- Exchange transfusions:
  - *primarily* remove high levels of bilirubin.
  - Also to remove IgG and sensitized RBCs.
  - To replace incompatible RBCs.
  - Suppress erythropoiesis.

**HDN: Newborn Transfusions**

- Premature infants > term infants to need exchange transfusions.
- Hbg < 12 g/dL → may require transfusion.
- Hbg < 8 g/dL → severe anemia requiring exchange transfusion.
HDN: Newborn Transfusions

- Blood Selection: Exchange Transfusion
  - Group O
  - Negative for antigens involved
  - CMV-seronegative/Irradiated (sometimes), leukoreduced
  - CPDA-1
  - Relatively fresh (i.e., ≤ 5-7 days old), when possible
  - Screened for sickle trait
  - Reconstituted with FFP (usually AB type); Hct 40-55%

Rh Immune Globulin

- RhIg attaches to Rh⁺ fetal RBCs in maternal blood
- Antibody-coated RBCs are trapped in maternal spleen, activating suppressor cells or causing production of blocking antibody (or both)

ABO Hemolytic Disease of Newborn

- ABO incompatibility between mom and fetus can cause HDN, since ABO antibodies of IgG class may cross placenta;
- Now the most common cause of HDF/N;
- Destruction of fetal RBCs leading to severe anemia is rare
- ABO HDF/N usually is treatable, after delivery, by phototherapy, alone.

4yo with SCD presents to the ER with a painful abdomen
• PSH: none

• PMH: neonatal dx of SCD

• HPI: well and in NAD distress until last night when his mother noted that he seemed to have a painfull abdomen when she put him in bed for the night

• VS: 72/48, 110, 18, 90%RA
• Crying, o/w healthy appearing male child
  HEENT: nl
  Lungs: clear
  CV: RR, w/o murmur
  ABD: enlarged, painful
Lab: WBC 10.2K, Hbg 5, Hct 15%, Plt 86K
What Is Going On?

What Should We Do?
What should we do?

- O2 by face mask or blow-by
- T&C 2 units, leukoreduced when possible (phenotype matched: ABO, D, C, E, K)
- Maintain with intravascular fluid, as needed
- Establish urine output

Normal Forms of Hemoglobin

<table>
<thead>
<tr>
<th>Form</th>
<th>Neonate</th>
<th>Adult</th>
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<tbody>
<tr>
<td>HgbA ($\alpha_2\beta_2$)</td>
<td>30%</td>
<td>97%</td>
</tr>
<tr>
<td>HgbA$_2$ ($\alpha_2\delta_2$)</td>
<td>0.5%</td>
<td>1.5-3.5%</td>
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<tr>
<td>HgbF ($\alpha_2\gamma_2$)</td>
<td>70%</td>
<td>&lt; 1%</td>
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Sickle Cell Disease

- Hgb S (deoxyggenated) aggregates and polymerizes (goes from liquid to gelatinous)

- usually reversible but repeated episodes → membrane damage → irreversible sickling

- Consequences:
  - Chronic hemolytic anemia
  - Occlusion of small blood vessels
Sickling triggered by fever, infection or hypoxia → multiple crises:

- pain due to musculoskeletal or tissue ischemia
- splenic/pulmonary sequestration (chest syndrome)
- aplastic crisis transient viral marrow suppression
- leg ulcers, priapism, tissue infarction, and stroke

Treatment

- No cure, care is supportive
- Most patients usually asymptomatic → routine transfusion unnecessary
- Transfusion goals in SCD:
  ↓ risk of stroke: ↓ % of Hbg S RBCs but avoid ↑ in blood viscosity
Treatment, cont.

- Major indications for blood transfusion:
  - improve O2 carrying capacity by:
    - diluting circulating sickle red cells to improve microvascular perfusion

- Chronic RBC transfusions
  - treat tissue hypoxia
  - suppress endogenous Hgb S production
  - reduce recurrent pain crises
    - risk of stroke
    - other complications
• Rapid destruction of sickle cells → anemia, jaundice, and gallstones

• SCD patients: highest rates of alllmmunization of any patient group

• RBC alloimmunization: disease severity
  - age at 1st transfusion
  - number of transfusions
  - ethnicity of donors/recipientns

Transfusion Practices

• Common practice: ↓ potential alloimmunization
  - phenotype patient’s RBCs prior to transfusion
  - provide antigen-negative units
• Most common: screen units for C, E, and K
• Helpful: Kidd and Duffy negative units
• Screen blood for Hgb S
Monitoring

- Avoid raising Hct >35%: hyperviscosity

- ↑ Hct without a ↓ % of sickle cells: can ↑ viscosity negating transfusion benefit