“D”Windling Rh Type

A Case Study Involving Weakening of D Antigen in Malignancy
July 11, 2012

- Blood bank received an order to Type and Crossmatch 2 units for LL, an 82 year old female Oncology patient.

- Patient’s Hemoglobin was 6.2 gm/dL

- Prior history check
  - O Positive and no alloantibodies detected
  - Last RBC transfusion at LMH on May 5, 2010
  - Received 27 units of RBCs between Dec 2006 and May of 2010
Gel Technology Reactions
LL's ABO/Rh by gel testing

![Image of gel testing results]

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**Legend:**
- **A**: Sample
- **B**: A- Probe
- **D**: B- Probe
- **Ctl**: Control
- **Buf**: Buffer
Mixed field D Reaction

What’s with that?
Trouble Shooting Mixed Field Reactions

- Recent Transfusions
- Transplantation
- Fetomaternal Hemorrhage
- Twin or dispermic chimerism
Recent Transfusions

- Is this an O Negative patient who was given Rh Positive red blood cells in an emergency situation? OR

- Is this an O Positive patient who has been given O Negative red blood cells?
Transplantation

- Has this patient had a bone marrow or stem cell transplant?

- Is the patient’s Rh type changing to that of her donor?
Fetomaternal Hemorrhage

Is this an OB patient who has experienced a large fetomaternal hemorrhage and her Rh type is mixed field due to contamination with baby’s blood?
Twin or Dispermic Chimerism

- In dispermic chimeras, two eggs that have been fertilized by two sperm fuse together.
- Dispermic chimeras demonstrate a dual-cell population in disparate body tissues derived from different germ layers.
- Chimerism in humans is a rare phenomenon usually identified at the time of blood group determination when mixed field agglutination on the cell typing is noted.
Investigation of LL’s Rh type

- Oncology physician was called
- Patient had not been transfused at another facility
- Patient had not received a bone marrow or stem cell transplant
- Patient was 82 - fetomaternal hemorrhage ruled out
- Patient had previously demonstrated 4+ reactions with anti-D reagent
Investigation Continued

- Did this specimen belong to LL or another patient?
- Did the specimen somehow get contaminated?
  - Redrawn specimen from LL demonstrated the same mixed field reaction
- If the reason for mixed field D reaction cannot be resolved, what type of blood do we give LL?
  - Crossmatched 2 units of O Negative
Article Reviews

- Red blood cell antigen changes in malignancy: case report and review
  J.L. Winters and D. S. Howard
  http://www.redcross.org/cgi-bin/pubs/171sm.pdf

- Loss of red cell A, B, and H antigen is frequent in myeloid malignancies
  Tina Bianco, Belinda J. Farmer, Robert E. Sage, and Alexander Dobrovic
  http://bloodjournal.hematologylibrary.org/content/97/11/3633.full.html
Changes in RBC Antigens with Malignancy

- Loss or diminished expression of RBC antigens have been reported to occur in a number of malignancies, both hematologic and solid.
- For hematopoietic diseases, the loss predominantly results from a mutation within a stem cell that affects antigen production.
- Some antigens reported to be altered by malignancy include, ABO, Rh, Lewis, Ii, MNSs, LW, Colton, Cromer, Cartwright, Dombrock, JMH, & Tn.
Loss or Weakening of the D Antigen

- Is the second most commonly reported change in blood group antigens after ABO

- Loss or weakening of other Rh system antigens including C and E have been reported. Frequently, this has occurred with concurrent loss or weakening of D.

- Patients present either with complete loss of selected Rh antigens or with development of a mixed population or antigen-positive and antigen-negative cells

- Thought to be a disruption or mutation of the RHD gene
Reported Cases

- In 3 reported cases of loss of the D antigen, chromosomal abnormalities involving either the entire chromosome 1\(^26\) or the short arm of chromosome 1\(^20,23\) were seen on cytogenetic analysis.
  - Chromosomal abnormalities are thought to be responsible for the loss of antigen expression through deletion or disruption of the RHD gene.
- Another case involved sequencing of the RHD gene that revealed a single base pair deletion of the gene.
More Findings

- One reported case was associated with development of anti-D. This patient suffered from myeloid metaplasia.

- Lost expression of the D antigen at age 37; had been typed as D+ at age 33

- Twenty years later, he was still found to be D- but had developed anti D as well as anti-C
And yet another case

- 48 year old Caucasian woman diagnosed with CML was being evaluated for a stem cell transplant

- Her twin sister was to be the donor and molecular studies revealed them to be identical twins

- ABO and Rh typing of the patient was A Negative while her sister typed as A Positive

- Additional testing was performed with new specimens and confirmed the previous ABO and Rh typings

- History obtained revealed the patient had been typed as Rh Positive at the birth of her child and also at four whole blood donations
These antigen changes have been reported to mirror the course of the disease.

When a patient enters remission, their original Rh phenotype returns, whereas antigen negative cells reappear during relapse.
Patient LL’s Diagnosis

Myelodysplastic Syndrome (MDS) w/thrombocytosis

- Initial transfusion in December of 2006
  - Hemoglobin was 7.6
  - Platelets were 1,368,000
Myelodysplastic Syndromes (MDSs)

- MDSs are a group of acquired hematologic disorders characterized by progressive cytopenias in the peripheral blood. All are a result of proliferation of abnormal stem cells.
- The mutated stem cell produces a pathologic clone of cells that expands in size at the expense of normal cell production.
MDS Findings

- Blood cells fail to mature normally
- Cells that are produced may not function normally
- The marrow eventually becomes filled with the immature cells and there is not room for the normal cells and in this case caused anemia
- May evolve into acute leukemia
- Median age at diagnosis is 70 (LL was 76)
Peripheral Blood Smear in MDS
Patient LL

- First mixed field reaction in July 2012
  Initially gave 2 O Neg RBCs and again with next transfusion
  Later discussed with Medical Director again and decided to
give O Positive going forward since patient was not of child
bearing age

- D reaction continued to be mixed field until April of 2013 when
  4+ reaction returned

- In October of 2013, mixed field reactions once again appeared
  and continue currently

- Has received 31 O Positive units since initial discovery of MF
  reactions and has not developed anti-D