O Brother, Where Art Thou?

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Community Blood Center
Typical January Day...

- 62 y/o male
- Initial evaluation for bone marrow transplantation
- MDS secondary to esophageal cancer diagnosed in June of 2012
- Received treatment at Cancer Treatment Centers of America in Tulsa
Lab Values
1-14-14

- Hematology
  - WBC 1.3 (4.5-11.0 K/UL)
  - HGB 8.5 (13.5-16.5 GM/DL)
  - PLT 50 (150-400 K/UL)
- HLA Class I & II typing
- Bone marrow biopsy to confirm diagnosis
- Blood bank sample
# The University of Kansas Hospital

## Antibody Detection

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## Diagnosis

Transfusion Hx/Medications:  
Report:  
Additional Billing: AABI, AGIS, Other:  
Antibody Registry: FND  
NFND  
Entered  
Tech:  
Date: 1-14-14

Reviewed by:  
Date:  

BB 2.3.2, 04/13
What Do We Know?

- Patient’s plasma was reactive with all cells tested
  - SPRCA
  - Gel
  - PEG IAT
- Auto control and DAT = negative
- Patient’s plasma was reactive with available nulls
  - k-, S-s-, Fy(a-b-), Le(a-b-)
Meanwhile...

- Patient history is everything
  - Cancer Treatment Centers of America in Tulsa
    - 11-10-13 – ABSC negative, received 2 units of RBCs
  - Primary oncologist follow up visit
    - 12-31-13 – ABSC positive, sent to their Immune Reference Lab which was sent to LA-ARC
LA-ARC Immunohematology Reference Lab Report

- Patient had been recently transfused
  - RBC phenotype might not be reliable
    - No mixed field
- Patient RBCs were coated with complement only
  - Prepared acid Eluate was nonreactive
- Patient’s plasma contains alloantibodies
  - Anti-E
  - Anti-Jkα
  - Anti-LAN
Our Ballgame Just Changed…

- How will transplantation be affected?
  - Engraftment issues due to alloantibodies?
- How necessary is this transplant given this new information?
  - Other treatment alternatives?
- How will we support the patient with product?
  - Frequent transfusion requirements
  - Availability of RBC products
So I Made A Phone Call...

- ...to Kirkegaard at our Immuno Ref Lab at CBC
- Give patient history
- Question blood availability
- Get advice on how to proceed
- Help?
1-16-14 Hospital Consultation

• Spoke with Laurie regarding patient history
  – Discussed patient history
  – Which laboratory identified antibodies?
    • Important if getting blood from ARDP
    • Did we need to re-identify antibodies

• Availability of Lan- blood
  – Had another patient in Sept 2013 that needed Lan-blood.
    • American Rare Donor Program (ARDP) did not have any responses to request for blood at that time.
    • Found some frozen units at New York Blood Center
Hospital Consultation Continued

• Options for E-, Jk(a-), Lan- blood
  – Send request to ARDP
    • Not helpful the last time looking for just Lan- units
  – Make some phone calls to friends at other blood center reference labs
    • Check with NY Blood Center see if their Lan- units are also E- and Jk(a-)
    • Check with select other blood Centers
  – Check if any siblings available
E-, Jk(a-), Lan- blood

• No units at LA Red Cross, Life Share Louisiana, Heartland Blood Center Illinois, Blood Center of Wisconsin
  – Either no Lan- blood or Lan- units were E+ or Jk(a+)

• NY Blood Center “have a few” group O frozen units that are E-, Jk(a-), Lan-
  – Donor is now too old to donate anymore
Lan Blood Group System

• First reported in 1961
• Named after first antigen negative proband to make anti-Lan (Mr. Langeries)
• Promoted from 901 Series of High-Incidence antigens to a System in 2012
  — Shown that homozygosity for ATP-binding cassette, sub-family B, member 6 (ABCB6) null alleles define the Lan- phenotype
• Only one antigen in system: Lan
Lan Blood Group System

• ABCB6 binds heme and poryphyrins and functions in their ATP-dependent uptake into the mitochondria
  – High expression in heart, skeletal muscles, fetal liver
  – Also in mitochondrial membrane, eye and Golgi apparatus

• Eye developmental defect coloboma is associated with changes in ABCB6
  – Lan – individuals appear healthy
Lan Blood Group System

- Autosomal recessive inheritance
  - Must get recessive gene from each parent
- 16 different mutations reported that result in Lan- phenotype
  - All mutations present in homozygous or compound heterozygous state
- 4 altered phenotypes
  - Leads to Lan+$^w$ or Lan+$^w/-$ phenotype
- Lan- phenotype frequency is 1 in 20,000 people
Lan Blood Group System

• Lan- phenotype found in Blacks, Caucasians and Japanese

• Clinical significance:
  – Transfusion reactions: no to severe hemolytic
  – Hemolytic disease of the newborn: no to mild
Patient’s antibodies

• Anti-E, anti-Jk\(^a\) and anti-Lan are all clinically significant

• Incidence of E- is:
  – 71% in Caucasians
  – 78% in Blacks
  – 61% in Asians

• Incidence of Jk(a-) is:
  – 23% in Caucasians
  – 8% in Blacks
  – 27% in Asians
E-, Jk(a-), Lan- blood

• Lan- phenotype found in 1 in 20,000
  – 1/20,000 is .00005%

• Frequency of antigen negative blood in Caucasians
  – .00005 x .71 x .23 = .00008.17% or 8.17 x 10^{-6}
So I Made Another Phone Call...

- Informed our Medical Director and our BMT physicians
  - Alloantibodies
  - Lack of red cells available
- Poor prognosis
- Proceed with stem cell transplant regardless of new information
MDS: Myelodysplastic Syndrome

- Group of clonal stem cell disorders
  - Ineffective hematopoiesis/marrow failure
  - Variable tendency to progress to AML
- Types of MDS
  - Primary
    - Etiology is unknown
  - Secondary
    - Usually caused by past chemotherapy and radiation
    - Related to accumulation of mutations in a hematopoietic stem cell
- Diagnosed with bone marrow biopsy and cytogenetic studies
MDS: Myelodysplastic Syndrome

- Risk factors
  - Age at presentation
  - Karyotype
    - Perform cytogenetic studies to determine structural chromosome abnormalities
  - Monosomal Karyotype
    - 2 or more distinct monosomies (unpaired chromosome) or a single monosomy in the presence of other structural abnormalities
    - Poor prognosis
Normal vs Abnormal Karyotypes

Human Male Karyotype

[Diagram of human male karyotype showing chromosomes numbered 1 to 22 with X and Y chromosomes]
Case Study’s Clinical Presentation

- Bone Marrow
  - Myelodysplastic syndrome (refractory cytopenia with multilineage dysplasia)
  - Hypercellular marrow

- Cytogenetic Studies
  - Structural chromosome abnormalities
    - Majority of the chromosome metaphases were hypodiploidy (monosomic karyotype)
    - Monosomies of chromosomes 5 and 7
O Brother, Where Art Thou?
1-16-14

- Donor evaluation of brother
- Lives in New Mexico
- 58 y/o with an unremarkable past medical history
- Routine labs collected including samples for HLA Class I & II typing
- ...decided to take a chance...
O Brother, Where Art Thou?
1-16-14

- O POS
- Negative antibody screen
- E-negative, Jk(a-) phenotype

Hmmmm...
Wonder if he’s LAN-negative like his brother?
GUESS WHAT?

Brother’s E-, Jk(a-) cells were compatible with our patient!
O Brother, Where Art Thou?
1-16-14

- Made more phone calls to Medical Director, BMT physician, transplant coordinator...

- At the very least, investigate directed donation!
1-17-14

• Got a call from Beth BMT coordinator at KU
  – Dr. Tilzer wants to collect 2 units from patient’s brother for transfusion to patient

• Got details on patient and potential donor
  – Patient
    • Current hemoglobin (hgb) is 8.5 and holding
    • Anticipating hgb to drop quickly once chemotherapy starts 1/23.
    • Stem cell collection will be infused 1/30
1-17-14 continued

• Donor (brother)
  – Current hgb is 18.6 grams
  – Weight is 84.5 Kg
  – Staying at residence near KU
  – Scheduled for stem cell collection 1/30
  – Has good arm veins and hand veins
    • KU would prefer to collect stem cells from arm vein
  – Already been tested for infectious markers for stem cell collection so should pass donor testing
  – No qualifying hgb levels for stem cell collection
    • Whatever donor happens to be at the time of collection
1-17-14 CBC Discussion

- Coordinated with Therapeutic Services, Quality Management, VP of Technical Services and Medical Director
  - What units could be drawn?
    - FDA regulations
    - Whole blood or apheresis collections
    - Do we have SOPs in place to collect units
    - Directed donor units
  - Would they be licensed?
    - CBC is in MO, KU is in Kansas
  - Timing of donation if 2 units needed?
    - Should more than 2 units be drawn while donor is available?
  - Could units be frozen?
    - Freeze units first
      - Frozen units are fragile. Run the risk of being broken in process
    - Freeze units if not used for transfusion
1-17-14 CBC Discussion

• Should donor take iron prior to donations?

• Conclusions:
  – Units should be directed donations
    • Ok to collect per regulations and have SOPs in place
  – Dr. Menitove would have to give medical approval to collect units so close together and would have to do physical assessment of donor each donation
  – Collect 2 whole blood donations
    • Can’t freeze double apheresis collections at this time
    • Draw units on 1-20 and 1-24
  – Need Special Donations form filled out and faxed back to CBC prior to collection of units
Communication with BMT Coordinator

• Spoke back with Beth and told her all the information
• Told her Dr. Menitove would communicate with Dr. Tilzer about units being collected
• Faxed Special Donations form to Beth to fill out
• Discovered Beth had left for the day and the BMT office is closed on Monday
  – Beth would have form completed and faxed to CBC by Tuesday morning
Communication with BMT Coordinator

• First donor collection would be 1-21 instead of 1-20 as originally planned
• Beth could only communicate with Donor through the patient cell phone number
• Asked Beth to tell donor to take over the counter iron
• Donor collection appointment set for afternoon of 1-21
  – Had to make sure Dr. Menitove would be available at the same time
Directed Donor units collected

• First unit collected 1-21-14
  – Donor hgb was 19.4
    • Donor lives in mountains in New Mexico. So hgb is high due to elevation
  – SOPs upper limit for hgb is 19
  – Dr. Menitove had to approve collection of unit
  – Rest of donation went smoothly

• Second unit collected 1-24-24
  – All went smoothly

• Both units pass testing and are released to KU
The Stem Cell Collection
1-30-14

Donor (brother) was serologically compatible with our patient

Donor and recipient are an HLA 8 of 8 match

AND donated two RBCs for our patient’s supportive care during engraftment

Donor’s stem cells were collected without incident and infused the same day
Case Study

- Two directed donor units were received and allocated
- Order placed to transfuse
- After multiple phone calls, Medical Director/BMT physicians agreed to split the units
Supportive Care

Hemoglobin & Transfusion

- 29-Jan: 6.1
- 30-Jan: 6.5
- 31-Jan: 5.9
- 1-Feb: 4.6

Records indicate transfusions:
- ½ unit on 2-Feb
- ½ unit on 3-Feb
- ½ unit on 4-Feb
Thursday 2-6-14

• Communication with KU
  – Patient has gotten first unit. Will be getting 2\textsuperscript{nd} unit soon
  – What can be done to get more units?
    • One of two sisters provided blood sample but was incompatible
      – Received at KU and tested 1-31-14
  • Frozen units in NY
    – Due to different glycerolization process, NY would have to deglyce units and ship on direct flight to KC. Only a few direct flights from NY to KC. Timing is critical since units outdate in 24 hours once thawed. Thawing process takes about 2 hours. Would take time to coordinate and not easily done on a weekend.
2-6-14 continued

• Collect more units from brother
  – Brother has returned home to NM
  – Brother would have to travel back to KC to donate or would have to arrange donation at blood center in his area
  – Not easily arranged on a weekend

  – No evidence of engraftment of stem cells in patient
  – Patient hgb down to 4.6 g
The Power of Communication

• 2-6-14 15:21
  – Dr. Menitove contacts Medical Director and Regional Director at United Blood Systems in Albuquerque NM to ask them to draw more units from brother at their facility

• 2-6-14 16:12
  – UBS agrees to draw directed donation from brother and wave hemoglobin requirements
  – UBS wants to draw a double unit and ship it prior to testing being complete
  – Dr. Menitove faxes Special Collections Request form to UBS
2-6-14 continued

• 16:33
  – UBS contacts brother (donor)
    • He lives in Red River which is 4 hours from Albuquerque. He has no mode of transportation
    • Currently experiencing bad weather especially where the donor lives
  – UBS is trying to arrange staff to go pick up donor and bring him to donor center to donate then take him back home
2-6-14 continued

• 18:05
  – UBS plan
    • Staff will go pick up donor and drive him to center to donate on Friday 2-7
      – 8 hour round trip drive
    • UBS will draw donor in evening and put him up in a hotel that night
    • UBS will drive donor back home to Red River on Saturday 2-8
  – Donor agrees to the plan
  – Dr. Menitove gives his approval
Monday 2-10-14

• Plan went well
• Double unit was drawn on Friday evening at UBS
• Units were delivered directly to KU on Saturday 2-8 early afternoon
• Patient had gotten last aliquot of final unit collected at CBC
  – Hgb is 5 g
• Patient going to receive one of the units from UBS
Supportive Care

Hemoglobin & Transfusion

- 29-Jan: 6.1
- 30-Jan: 6.5
- 31-Jan: 5.9
- 1-Feb: 4.6
- 2-Feb: 4.5
- 3-Feb: 5.0
- 4-Feb: 5.2

Transfusion: ½ unit
Supportive Care & Follow up

- Received two units from UBS
  - Both units unlicensed
    - Collected, processed, shipped
    - Infectious disease testing was incomplete
  - One split for transfusion on 2-11 & 2-17
- As of 2-26-24, evidence of serologic engraftment…albeit microscopic
- As of 2-28-14, engraftment analysis showed engraftment of the stem cell transplant
  - 99% donor and 1% recipient
- Second directed donor unit not transfused
  - Shipped directly from KU back to UBS for freezing
Follow Up

- As of 4-10-14, the patient’s HGB is 13.1g/dL
- Treated at our Cancer Center on an outpatient basis
- Brother recently had a doctor’s visit and felt ready to donate again if needed

Happy, happy ending!
Community Blood Center
Save a Life. Right Here, Right Now.

savealifenow.org
References

- [http://bloodjournal.hematologylibrary.org/content/116/13/2224.short](http://bloodjournal.hematologylibrary.org/content/116/13/2224.short)
- Rodgers, G; Young, N. *Handbook of Clinical Hematology*. 2005.
- Lomis-Francis, C; Reid, M. *Antigens Factsbook*. 2004.
O Brother, Where Art Thou?

QUESTIONS?

...Thank You