



# O Brother, Where Art Thou?

Laurie Wolf MLS(ASCP)SBB  
University of Kansas Hospital

Julie Kirkegaard MT(ASCP)SBB  
Community Blood Center

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# 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

INITIAL  
BMT EVAL

THE UNIVERSITY OF KANSAS HOSPITAL

ABO/RH	Cell Typing							Reverse Typing		
Interpretation	Phase	Anti-A	Anti-B	Anti-A,B	Anti-D	Anti-D	Mono Cont	A1 Cells	B Cells	A2 Cells
B POS										

Antibody Detection				
Cell	Echo	Neo	Gel	
I		3+		
II		3+		
III		3+		
AC			0	

Direct Antiglobulin			
Poly	IgG	C3	Saline
0+			

Other Cell Typings					
Anti-	Anti-	Anti-	Anti-	Anti-	Anti-

Phenotype:

Antibody Identification																			
Source	Phase				Source	Phase				Source	Phase								
ORTHO					1MM					1MM					1MM				
Lot #	VR	AKO	Gel		Lot #	49153	RT	182		Lot #	46107	RT	182		Lot #	43051	RT	182	
1			2+		I		0			1		0	H		3-5-18		0	H	
2			2+		II		0			le(a-b)	2		0	H					
3			2+		AC		+			le(a-b)	3		0	H					
4			2+		I-		0			le(a-b)	4		0	H					
5			2+							5		0	H						
6			2+							6		0	1+						
7			2+							7		0	1+						
8			2+							8		0	1+						
9			2+							9		0	1+						
10			2+							I-	15		0	1+					
11			2+							le(a-b)	20		0	H					
										AC	0		0+						

Diagnosis \_\_\_\_\_  
 Transfusion Hx/Medications \_\_\_\_\_  
 Report \_\_\_\_\_  
 Additional Billing: AABI \_\_\_\_\_ AGIS \_\_\_\_\_ Other \_\_\_\_\_

Antibody Registry: FND  NFND  Entered

Tech LU  
 Date 1-14-14

# 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-Jk<sup>a</sup>
  - 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 porphyrins 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+<sup>w</sup> or Lan+<sup>w</sup>/- 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<sup>a</sup> 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
  - $.00005 \times .71 \times .23 = .000008.17\%$  or  $8.17 \times 10^{-6}$

# 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

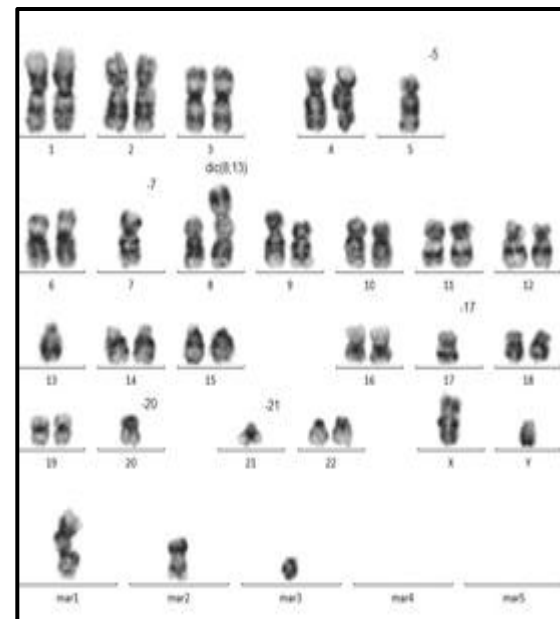
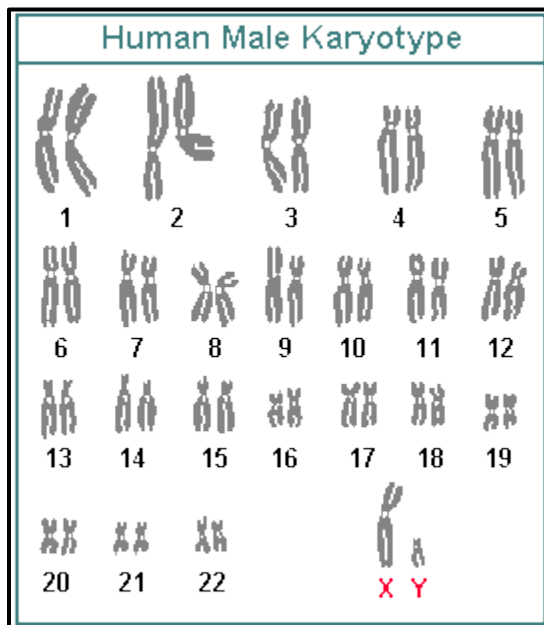
# MDS: Myelodysplastic Syndrome

- 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



# 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

# ○ 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?

# ○ Brother, Where Art Thou?

1-16-14

## **GUESS WHAT?**

Brother's E-, Jk(a-) cells were compatible  
with our patient!

# ○ 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

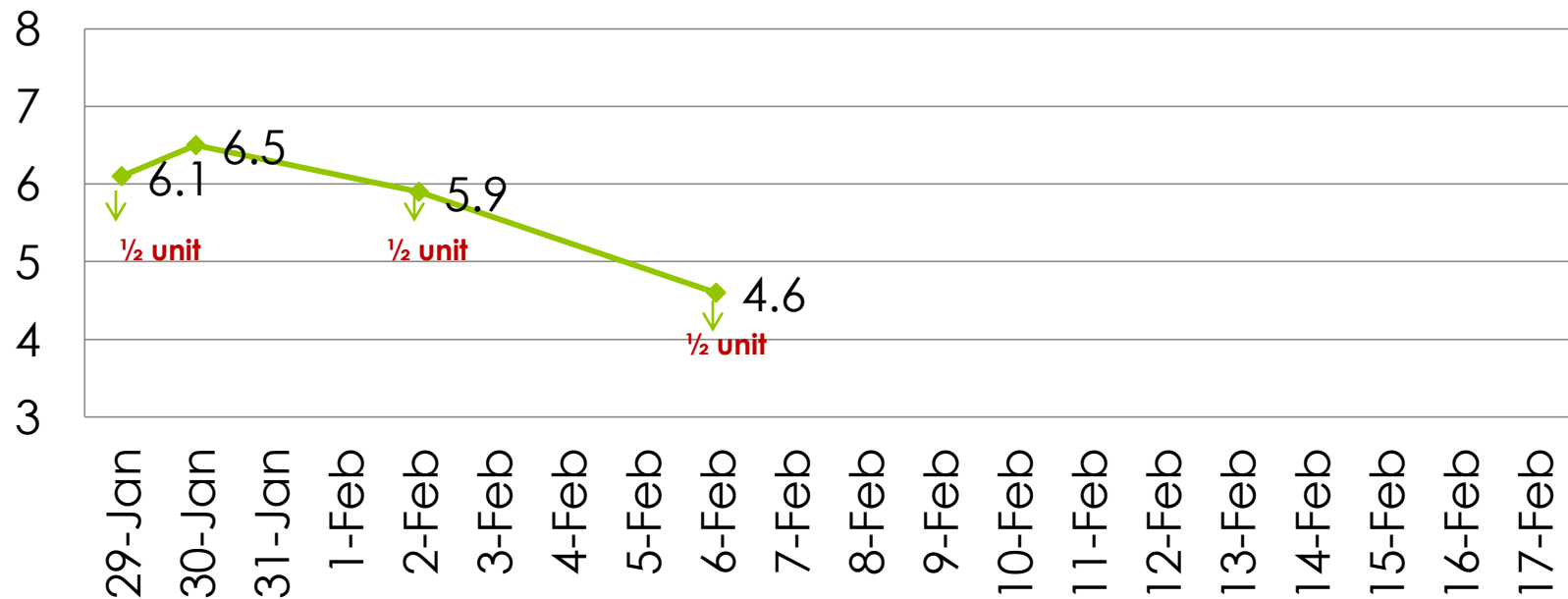
- Donor (brother) was serologically compatible with our patient
- Donor and recipient are an HLA 8 of 8 match
- AND donated two RBCs for our patient's supportive care during engraftment
- Donor's stem cells were collected without incident and infused the same day

# 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



# Thursday 2-6-14

- Communication with KU
  - Patient has gotten first unit. Will be getting 2<sup>nd</sup> 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

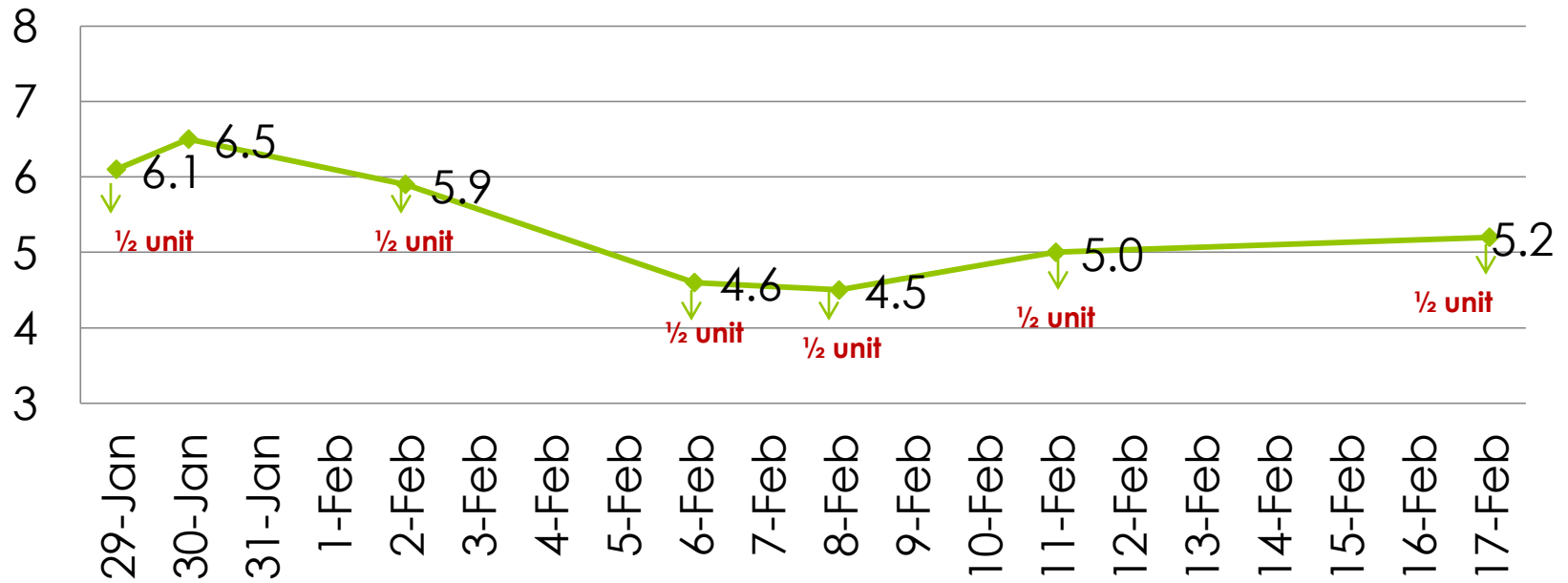
- 18:05
  - UBS plan
    - Staff will go pick up donor and drive him to center to donate on Friday 2-7
      - 8 hour round trip drive
    - UBS will draw donor in evening and put him up in a hotel that night
    - UBS will drive donor back home to Red River on Saturday 2-8
  - Donor agrees to the plan
  - 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



# 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 13.1 g/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](http://savealifenow.org)



# References

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○ Brother, Where Art Thou?

**QUESTIONS?**

**...Thank You**