PILOT STUDY OF ANTIGEN MATCHING FOR AUTOIMMUNE HEMOLYTIC ANEMIA

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CENTRALIZED TRANSFUSION SERVICE

- Antibody identification
- Antibody titer
- Antigen typing
- Cold agglutinins
- Compatibility Testing
- DAT (poly & C3)
- Elutions
- Kleihauer
- R sets
- Sickle cell screening
BLOOD MANAGEMENT

RBC Units per Discharge

EVOLUTION OF TRANSFUSION PRACTICE

- Eliminated minor crossmatch
- Replaced antiglobulin XM with IS XM unless antibody present
- Eliminated IS XM if qualify for electronic XM
- Eliminated reading antibody screen after IS
- Eliminated autocontrol for pretransfusion testing
- Eliminated weak D testing except for cord bloods
- Eliminated multiple antibody panels under different conditions
- Eliminated repeat panels on patients with known antibody
EVOLUTION CONTINUED

- Limited elutions on DAT positive samples to Tx within 3 mos
- Eliminated cold antibody screens for open heart surgery
- Eliminated antigen typing for insignificant antibodies
- Substituted R-set for full panel for patients with positive Ab & possible RhIg
- Replaced separate anti-A & -B with anti-A,B for O unit confirmation
- Eliminated repeat Rh typing of Rh+ units; only confirm Rh neg units
- Eliminated routine cord blood typing & DAT on infants born to Group O moms
- Eliminated elutions on cord blood with positive DAT
Our Latest Idea

Undertake a pilot project to determine if we could decrease our time and labor in providing blood for patients with autoantibodies.
WHAT ARE AUTOANTIBODIES?

• Reactivity of the patient’s serum/plasma with their own cells.
  • May indicate the presence of a cold/warm autoantibody, drug induced antibody production, allo antibody production from a recent blood transfusion, or antibodies to the test method (LISS/PEG/Gel/Solid phase)

• A Direct Antiglobulin Test (DAT) determines if the patient’s cells are coated with complement or immunoglobulin (IgG).
  • A positive DAT does not always mean cellular hemolysis, but is used in the evaluation of AIHA.
  • Patients with AIHA, especially Warm AIHA will react with all cells tested and at the IgG phase.
PROBLEMS WITH TRANSFUSION

• How are clinically significant antibodies detected in WAIHA?

• Reactivity is enhanced with PEG/Gel/enzymes to a lesser extent with LISS.

• Patient’s with AIHA have shortened red cell survival, so may require more frequent transfusions.

• How do you manage a transfusion?

• Phenotype to determine what antibodies can be made?

• Need to balance the risk and clinical need for the transfusion and these patients need to be monitored carefully throughout the transfusion.
INCIDENCE OF POSITIVE DAT IN BLOOD DONORS

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Incidence</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1978</td>
<td>Worledge</td>
<td>1 in 9000</td>
<td>BJH 1978;39:157</td>
</tr>
<tr>
<td>1980</td>
<td>Gorst</td>
<td>1 in 14,000</td>
<td>Vox Sang 1980;38:99</td>
</tr>
<tr>
<td>1982</td>
<td>Beck</td>
<td>1 in 12,800</td>
<td>Clinics Hematology 1984;13:167</td>
</tr>
<tr>
<td>1983</td>
<td>Habibi</td>
<td>1 in 13,000</td>
<td>BJH 1983;54:493</td>
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</tbody>
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Most donors were hematologically normal at donation and at 1 year follow-up
AUTOANTIBODIES IN HOSPITALIZED PATIENTS

Incidence in hospitalized patients

- 0.5 to 1.5% of hospitalized patients have a positive DAT
- Incidence of AIHA is 1 in 50,000 to 80,000 individuals

Chief concern

- Underlying alloantibody masked by autoantibody
- Transfusion of RBCs with antigen corresponding to alloantibody
- Acceleration of hemolysis
- Misdiagnosis of AIHA exacerbation
PREVALENCE OF ALLOANTIBODIES IN AIHA

• 32% of patients with AIHA had alloantibodies
  - Petz and Branch, Transfusion 1999;39:6-10

• 40% of patients with AIHA have alloantibodies
  - Shirey et al. Transfusion 2002;42:1435-41

• 20-25% of alloimmunized hematology patients develop additional antibodies after subsequent transfusion
  - Schoneville, Transfusion 2009;49:453-7
ALLOANTIBODY SPECIFICITY IN AIHA

<table>
<thead>
<tr>
<th>Specificity</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-E</td>
<td>46%</td>
</tr>
<tr>
<td>K, C, Fy(^a), Jk(^a), c</td>
<td>10-20%</td>
</tr>
<tr>
<td>Jk(^b), S, D, e, M</td>
<td>5-9%</td>
</tr>
<tr>
<td>Other antibodies</td>
<td>2-4%</td>
</tr>
</tbody>
</table>

202 antibody containing sera from 418 patients with AIHA
Frequency in antibody containing sera
Los Angeles Red Cross reference laboratory

<table>
<thead>
<tr>
<th>Number of Alloantibodies</th>
<th>Percent of Sera</th>
</tr>
</thead>
<tbody>
<tr>
<td>One</td>
<td>40%</td>
</tr>
<tr>
<td>Two</td>
<td>30%</td>
</tr>
<tr>
<td>Three</td>
<td>20%</td>
</tr>
<tr>
<td>Four or more</td>
<td>10%</td>
</tr>
</tbody>
</table>

Garratty & Petz, Transfusion 2002;42:1390-92
PROBLEMS WITH ADSORPTION TO IDENTIFY ALLOANTIBODIES

- Collection of large volume blood from anemic patient
- Transfused RBCs may adsorb alloantibody → false negative result
- Incomplete adsorption may mimic alloantibodies & delay transfusion
- Weak alloantibodies may not be detected
- Antibody to high frequency antigen may be adsorbed
- Procedure is labor intensive & time consuming
- Procedure is expensive
- Blood may not be available urgently
ALTERNATIVE APPROACH IS TO PROVIDE PROPHYLACTIC ANTIGEN MATCHED RBCS

- Use adsorption to identify alloantibodies during 1st admission
- Phenotype patients for c, C, D, E, e, K, Jk\(^a\), Jk\(^b\), Fy\(^a\), Fyb, S & s
- If extended phenotype not available, type for Rh, Kell & Kidd
- Transfuse leukoreduced prophylactic antigen matched (PAM) RBC
- Confirm presence of autoantibody on subsequent admissions
  - Transfuse PAM without adsorptions
- PAM promoted patient safety by preventing alloimmunization and DHTR
- PAM RBCs have survival time equal to autologous RBCs
- Shirey et al. Transfusion 2002;42:1435-41
SHIREY STUDY OUTCOMES

- 20 patients with AIHA
- 40% had alloantibodies of clinical significance
- Reliable phenotype obtained in 60% of patients
- 12 patients transfused with PAM RBCs
- None of 12 patients developed new alloantibodies
- Expected post-tranfusion hemoglobin achieved
- No hemolytic transfusion reactions occurred
WOULD PAM WORK IN A COMMUNITY HOSPITAL?

• Shirey study suggested PAM was feasible & safe in a large academic medical center
• Feasibility & cost effectiveness of PAM in community hospital has not been reported
• SLH started pilot study on January 1, 2013
OLD SLH TRANSFUSION SERVICE PROCEDURE

- Specimens from AIHA patients sent to blood center consultation lab for adsorption studies to identify alloantibodies
- Blood center performed XM with adsorbed plasma
- Testing was repeated every 3 days while patient was being transfused
- Transfusion service tested RBCs with adsorbed plasma
- Protocol was expensive
- Often resulted in delayed transfusions, especially on weekends & holidays
NEW SLH PROCEDURE—JANUARY 2013

- Initial workup performed at blood center
- Adsorption, antibody ID, XM, antigen negative blood, phenotyping
- If XM ordered, performed with adsorbed plasma
- Phenotype included E, C, e, c, K, Jk^a, Jk^b, Fy^a & Fy^b
  - Shirey also matched for S & s
- If complete phenotype not available, then requested
  - Rh match first
  - Kidd match second
  - Kell match third
  - Duffy match fourth
NO CONSENSUS ON PAM

• Lack of consensus even for sickle cell disease patients
• Survey of 1182 transfusion services in North America
• Majority matched only for ABO & D for unsensitized SCD patients
• One third matched for C, E & K antigens
• One seventh matched for Kidd and Duffy
• Few performed extended phenotype

Osby & Shulman, Arch Pathol Lab Med 2005;129:190-3
NEW SLH PROCEDURE CONTINUED

- If warm autoantibody confirmed, PAM RBCs were transfused
- Compatibility testing performed with original plasma & antigen matched RBC
- XM testing through antiglobulin phase
- If XM incompatible, physician signed Emergency Release Form
- If patient had history of autoantibody & had not been transfused, sample sent to blood center q3 months to identify new alloantibodies
- If patient was recently transfused, sample sent to blood center q4 weeks to detect new alloantibodies
PILOT STUDY OUTCOMES

- 16 patients presented with AIHA from Jan 1, 2013 through August 2013
- 7/16 patients had alloantibodies – E, C, c, K, S
- 3/16 patients with history AIHA, had undetectable auto & allo antibodies
- 12 patients presented only one time & 3/12 were transfused once
- 4 patients returned for additional workups and/or transfusion
  - 1 patient transfused on 8 of 8 episodes
  - 1 patient transfused on 4 of 6 episodes
  - 1 patient transfused on 4 of 4 episodes
  - 1 patient transfused on 1 of 2 episodes
- 7 patients transfused with 39 RBC units during 20 transfusion episodes
Initial workup consisted of adsorptions, antibody ID, XM, antigen negative blood selection & phenotyping
- Charges for initial workup ranged from $1000 to $2100

Subsequent workup for antigen typing cost $100 per unit

New procedure saved $1100 to $2000 per transfusion episode

Patient transfused during 8 episodes over 4 months had 2 adsorptions
- Savings amounted to $5800

One patient returned 3 times for additional transfusions
- Each time was outside of our 4 week window
- Adsorption performed each time
- No alloantibodies were detected
SLH OUTCOMES CONTINUED

• One patient transfused 3 times
  - Made anti-S after second transfusion
  - S typing was not included in our procedure
• Achieved expected post-transfusion hemoglobin (0.9 – 1.2 g/dL)
• No evidence of hemolysis & no transfusion reactions reported
• Extended PAM provided for all patients
• PAM RBCs available in 2-3 hours when adsorption not required
• Initial workup required 12 to 24 hours
PILOT STUDY UPDATES—SINCE AUGUST 2013

• In October, 2013, S matching was added to the SOP.

• In January 2014, LISS testing was added to the SOP, after the initial identification was verified.

• Study has expanded to 21 patients.
PILOT STUDY UPDATES—SINCE AUGUST 2013

- 4/5 patients had allo antibodies
- 1/5 patients with history of AIHA, had undetectable auto & allo antibodies
- 1 patient presented only one time and was crossmatched but not transfused
- 4 patients returned for additional workups and/or transfusion
  - 1 patient transfused 6/7 episodes
  - 1 patient transfused 2/3 episodes
  - 1 patient presented twice and was crossmatched but not transfused
  - 1 patient transfused 1/2 episodes
- 3 patients transfused with 16 RBCs during 8 transfusion episodes
SUMMARY

• Conclusion
  - PAM protocol appears safe and cost effective
  - We will continue the study

• Questions that need to be answered
  - Since 2/3 patients presented one time, should we wait until second episode to request PAM?
  - If patients lose autoantibody, should they be removed from procedure?
  - Is 4 week interval for requesting repeat adsorptions optimal?
  - If a patient has not been transfused, is it necessary to repeat adsorption at 3 months?
  - Do we need to expand to include other disease states such as Myelodysplastic Syndrome?
WAIHA CASE STUDY

• Patient #1
• History: on 1/1/2013 Pregnant admission for delivery
  • Admitted with a 5.7 hemoglobin.
  • Physician orders a TX for 2 units.
  • Patient types as A negative and the ABSCRN is positive with both screening cells.
  • Antibody Panel is positive with all cells and the autocontrol.
  • Since 2010, patient has a history of a WAIHA and anti-S... sent to CBC for workup and units.
  • Patient is transfused with 2 units.
• On 2/14/13 presents with dizziness and shortness of air.
  • Admitted with a 4.8 hemoglobin.
  • Based on our new SOP, do we send or not send?
WAIHA CASE STUDY

- Patient #2
- History: admitted on 1/5/14 for GI bleed
- TX for 2 units ordered.
  - Patient types as A Positive and ABSCRN is positive with both screening cells
  - Antibody Panel is positive with all cells and the autocontrol.
  - No history found sent to CBC for a workup.
  - CBC identifies anti –E, Jka, and a Warm Auto
  - Patient is not transfused.
- On 2/6/14 patient is going for surgery. The physician orders another TX for 2 units.
  - Based on our new SOP, do we send or not send?
WHAT ABOUT OTHER PATIENT POPULATIONS?

• Patient with MDS presents 2/25/14 with a hemoglobin of 7.9
  • Patient types as O Positive and ABSCRN is negative.
  • Transfusion history since 11/2010 with negative ABSCRNs.
  • Patient is transfused on 2/25/14 with 1 unit of RBCs.

• On 3/20/14, patient has a 7.7 hemoglobin and another request to transfuse is ordered.
  • Patient types as O Positive and ABSCRN is positive.
  • Eluate indicates an anti-E.
  • A delayed serological transfusion reaction is reported

• Is this the next group to look at PAM??
So what does WAIHA really stand for?

*Why Adsorb? Instead Honor Antigen matched blood!*