Managing platelet refractory patients: case studies

Presented by Paul F. Lindholm, M.D.
Platelet transfusion

Thrombocytopenia/transfusion goals

Prophylactic >10K/mL to prevent serious bleeding (prophylactic)

Therapeutic >40-50K/mL to treat bleeding or before invasive procedure
>75-100K/mL for CNS bleeding/procedure
Patient with multiple myeloma

Received allogeneic stem cell transplant and later developed sepsis and engraftment failure.

Platelet transfusion goal: > 20,000/µL for bleeding

Corrected count increments were less than 5,000 M^2/µL following 2 platelet transfusions; 9 poor at 18-24 hours.

Platelet antibody screen positive 10/13 cells
Compatible units obtained with testing: 4/6, 8/12, 6/6, 6/20
HLA antibody screen – non-reactive
HLA and crossmatched platelets provided.
Platelet antibody screen and crossmatch

Figure 13-9. Solid-phase test procedure. (Courtesy of Immucor, Norcross, Georgia.)

Immucor, Inc.
HLA antibody testing methods

Lymphocytotoxicity

1. + antibodies
   - HLA-A1
   - HLA-A2
   - HLA-A3
   - HLA-A4

2. + C'
   - HLA-A1
   - HLA-A2
   - HLA-A3
   - HLA-A4

3. + vital dye
   - HLA-A1
   - HLA-A2
   - HLA-A3
   - HLA-A4

Luminex technology

- Sample
- Label Mix
- Multi-Analyte Profile


Medscape.com
Matched platelet timeline

1. Provide ABO compatible platelets
2. Obtain HLA & platelet antibody screen
   - Perform platelet crossmatch
3. Obtain HLA class I A&B typing
   - Request HLA matched platelets
4. Collect HLA matched product
5. Provide XM platelet
6. Provide HLA matched product
Platelet count (x10^3/µL)

- SDP
- HLA matched
- Crossmatched

CCI values:
- CCI = 18,100
- CCI = 5,600
- CCI = 8,400

Platelet units:

XMC: 6/6
## Platelet refractoriness

<table>
<thead>
<tr>
<th>Immune refractoriness</th>
<th>Non-immune refractoriness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Majority HLA Class I A and B</td>
<td>Splenomegaly (sequestration)</td>
</tr>
<tr>
<td>Platelet-specific antibodies</td>
<td>Sepsis</td>
</tr>
<tr>
<td>ABO compatibility</td>
<td>Fever</td>
</tr>
<tr>
<td>Patients may have both immune and nonimmune factors</td>
<td>Bleeding</td>
</tr>
<tr>
<td></td>
<td>DIC</td>
</tr>
<tr>
<td></td>
<td>Medications</td>
</tr>
<tr>
<td></td>
<td>Venoocclusive disease</td>
</tr>
<tr>
<td></td>
<td>Graft-versus-host disease</td>
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<tr>
<td></td>
<td>Platelet storage age</td>
</tr>
</tbody>
</table>
### Clinically Important Factors Affecting Transfusion Outcomes

<table>
<thead>
<tr>
<th>Factor</th>
<th>1 hour platelet increment/μL</th>
<th>18 to 24 hour platelet increment/μL</th>
<th>Days to next transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall response</strong></td>
<td>24,900</td>
<td>12,000</td>
<td>1.75</td>
</tr>
<tr>
<td><strong>Clinically Important change</strong></td>
<td>≥ 5,000</td>
<td>≥ 2,400</td>
<td>≥ 0.35</td>
</tr>
<tr>
<td><strong>Improved platelet response</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Splenectomy</td>
<td>+ 24,800</td>
<td>+12,400</td>
<td>-</td>
</tr>
<tr>
<td>ABO compatible</td>
<td>+4,600</td>
<td>+6,300</td>
<td>-</td>
</tr>
<tr>
<td><strong>Decreased platelet response</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytotoxic antibody*</td>
<td>-9,300</td>
<td>-4,000</td>
<td>-0.36</td>
</tr>
<tr>
<td>Female ≥ 2 pregnancies* or male</td>
<td>-8,900</td>
<td>-5,700</td>
<td>-0.40</td>
</tr>
<tr>
<td>Palpable spleen</td>
<td>-3,500</td>
<td>-4,400</td>
<td>-0.23</td>
</tr>
<tr>
<td>Heparin*</td>
<td>-</td>
<td>-3,800</td>
<td>-0.37</td>
</tr>
<tr>
<td>Bleeding*</td>
<td>-1,700</td>
<td>-3,100</td>
<td>-0.33</td>
</tr>
<tr>
<td>Fever*</td>
<td>-1,600</td>
<td>-2,000</td>
<td>-0.25</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>-2,700</td>
<td>-2,500</td>
<td>-0.28</td>
</tr>
<tr>
<td>DIC</td>
<td>-</td>
<td>-</td>
<td>-0.40</td>
</tr>
</tbody>
</table>

* Factor also affected platelet refractory rate.

Platelet increment outcomes

- Non-refractory
- Non-immune refractory
- Immune refractory
Patient with end-stage liver disease

Patient with cirrhosis, splenomegaly, ascites and hydrothorax developed pancytopenia and refractoriness to platelet transfusions

Platelet transfusion goal: > 50,000/µL for bleeding and procedures

Corrected count increments were less than 5,000 M^2/µL following 7 consecutive platelet transfusions

Platelet antibody screen positive 10/13 cells
1 platelet unit compatible of 6 tested
HLA antibody screen – 100% PRA
HLA type performed and matched platelets provided
Platelet count (x10^3/μL)

- Crossmatched
- HLA matched

CCI = 12,000
CCI = 6,200
CCI = 3,500

Platelet units:

- 5
- 2
- 2
- 3
- 1
- 1
- 1
- 3
- 1
- 2
- 5
- 3
- 2

XMC:
- 2/29
- 6/46
- 4/28
- 7/36
Summary

Our first patient with platelet specific antibodies had one excellent response to crossmatched platelets followed by intermittent modest responses with matched platelets.

Our second patient had had highly reactive HLA and platelet antibody screens and obtained initial excellent responses that decreased over time, partly compensated by large platelet doses.
Northwestern platelet refractoriness study

- Retrospective review, 2 years (2012, 2014)

- Platelet refractoriness studies had both anti-HLA and platelet antibody screen/crossmatch

- Review platelet count increments for all XM or HLA-matched platelet transfusions.
  - Prophylactic response, to $\geq 10K/\mu L$
  - Therapeutic, to $\geq 40K/\mu L$

- Best transfusion responses determined for XM/HLA in each case
Platelet refractoriness test results

85 samples in 83 patients

<table>
<thead>
<tr>
<th>HLA Antibody</th>
<th>Negative</th>
<th>Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>35 (41%)</td>
<td>15 (18%)</td>
</tr>
<tr>
<td></td>
<td>No special units needed</td>
<td>Crossmatch-compatible units</td>
</tr>
<tr>
<td>Positive PRA &gt; 20%</td>
<td>12 (14%)</td>
<td>23 (27%)</td>
</tr>
<tr>
<td></td>
<td>HLA-matched units</td>
<td>Crossmatched or HLA-matched units</td>
</tr>
</tbody>
</table>
Best transfusion responses by unit type

- Therapeutic: (→ ≥ 40K/ml)
  - Crossmatched: 10
  - HLA-matched: 7

- Prophylactic: (→ ≥ 10K/ml)
  - Crossmatched: 7
  - HLA-matched: 8

- Not Therapeutic: Pre >10 → < 40K/ml
  - Crossmatched: 2
  - HLA-matched: 4

- Not Prophylactic: (not → ≥ 10K/ml)
  - Crossmatched: 8
  - HLA-matched: 1

(Percent in Category)
Patients receiving both HLA and cross-matched platelets

![Bar graph showing corrected count increment (CCI) for crossmatched and HLA matched platelets. Crossmatched CCI is 4870, HLA matched CCI is 5660.](image-url)
# Transfusion responses: ABO effect

<table>
<thead>
<tr>
<th>Category</th>
<th>ABO compatible</th>
<th>ABO incompatible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-T/P</td>
<td>21</td>
<td>5</td>
</tr>
<tr>
<td>Prophylactic</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Therapeutic</td>
<td>31</td>
<td>1</td>
</tr>
<tr>
<td>ABO compatible</td>
<td>33</td>
<td>20</td>
</tr>
<tr>
<td>ABO incompatible</td>
<td>33</td>
<td>20</td>
</tr>
</tbody>
</table>

- **Crossmatched**:
  - 100% ABO compatible
  - 100% ABO incompatible

- **HLA matched**:
  - 100% ABO compatible
  - 100% ABO incompatible

Percent in Category:

- 0%
- 10%
- 20%
- 30%
- 40%
- 50%
- 60%
- 70%
- 80%
- 90%
- 100%

Crossmatched and HLA matched categories show 100% compatibility across all subcategories.
Meta-analyses of HLA and crossmatched platelet transfusions

HLA: 30 studies selected, 1 randomized control trial

HLA-matched platelets led to better 1-hour post-transfusion platelet count increments than crossmatched or unmatched

K Pavenski and ICTMG Collaborators. Transfusion 2013

Crossmatched platelets: 20 studies selected

Cross-matched platelets improved platelet count increments versus random or pooled platelets

RR Vasallo and ICTMG Collaborators. Transfusion 2014

Effect of matched platelets on bleeding and mortality outcomes not available

Studies heterogeneous – prospective trials needed
Conclusions

Almost 60 percent (50/85) of platelet-refractory studies were positive by solid-phase or HLA antibody screen.

Crossmatched platelets were readily available and useful for patients with platelet antibodies.

HLA-matched platelets tended to yield higher platelet increments.

Prophylactic or therapeutic responses were obtained with 61% of ABO compatible matched units versus 36% not receiving ABO compatible.