Septic Reactions from Apheresis Platelets

What have we learned from 10 years of hemovigilance?

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Disclosures

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• The opinions expressed are my own and not those of the US government or American Red Cross
### Septic Transfusion Reactions

**American Red Cross Hemovigilance, 2004 - 2014**

<table>
<thead>
<tr>
<th>Onset within 4 h of transfusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any of the following clinical signs</td>
</tr>
<tr>
<td>• Fever &gt; 39°C (102.2°F) or change of ≥ 2°C (3.6°F)</td>
</tr>
<tr>
<td>• Rigors</td>
</tr>
<tr>
<td>• BP increase or decrease ≥ 30 mmHg</td>
</tr>
<tr>
<td>• Tachycardia ≥ 120 bpm or change in HR ↑ or ↓ ≥ 40 bpm</td>
</tr>
</tbody>
</table>

- Cultures of residual product and patient with identical isolates (**definite**) OR
- Culture of residual product (not lab contamination) (**probable**)

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Hemovigilance definitions reflect the *final classification* of definite and probable cases, not the triggers for investigation. Any change in condition or suspicion for sepsis after transfusion should be reported and investigated.

Investigate Suspected Sepsis after Transfusion

Clinical triggers for investigation

1. Fever defined as temperature $\geq 38^\circ$ C ($100.4^\circ$ F) with a rise of $\geq 1^\circ$ C ($1.8^\circ$ F) from the pretransfusion value PLUS any of the following signs and symptoms:
   - Rigors
   - Hypotension
   - Shock
   - Tachycardia (rise of $>40$ beats/minute from pre-transfusion value)
   - Dyspnea
   - Nausea/vomiting

2. Any change in clinical condition leading to a suspicion of sepsis, even in the absence of fever or other typical signs and symptoms of sepsis.

BacT Confirmed-Positive Aph Plt Donations

March 1, 2004 to December 31, 2014
960 Confirmed-positive cultures (4.7 million Aph Plt Donations)

- Coagulase-negative Staph
- *Staphylococcus aureus*
- *Streptococcus spp.*
- *Enterococcus spp.*
- *Bacillus spp.*
- Other gram-positive
- *E. coli*
- *Klebsiella spp.*
- *Serratia spp.*
- *Listeria monocytogenes*
- *Enterobacter spp.*
- Other Gram-negative

March 1, 2004 to December 31, 2014
960 Confirmed-positive cultures (4.7 million Aph Plt Donations)

- 75%
- 36%
- 31%
- 8%
Septic Transfusion Reactions, APLTs

American Red Cross Hemovigilance, 2004 - 2014

<table>
<thead>
<tr>
<th>Culture Volume</th>
<th>NA</th>
<th>4 mL</th>
<th>8 mL</th>
<th>8 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diversion</td>
<td>NA</td>
<td>39%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Septic RATE</td>
<td>1:36,000</td>
<td>1:66,000</td>
<td>1:109,000</td>
<td>1:108,000</td>
</tr>
</tbody>
</table>

Eder et al, Transfusion 2009,49:1554 (Period 1 & 2); Eder et al. Transfusion, 2014;54:857-862
Implicated Bacteria in STRs

- Coag-neg staphylococcus
- Staphylococcus aureus
- Streptococcus spp.
- Enterococcus faecalis
- Enterobacter spp.
- Klebsiella spp.
- Acinetobacter spp
- Pseudomonas fluorescens
- Bacillus spp.
- Clostridium perfringens
- Ralstonia pickettii

Streptococcus spp. (9%)
Staphylococcus aureus (22%)
Coag-neg Staph (52%)

March 1, 2004 to December 31, 2014
> 8 million distributed Apheresis Platelets

Eder et al. Transfusion, 2014;54:857-862
Delayed Septic Reactions

• Active surveillance = plate cultures (100 uL) before transfusion; retrospective chart review
• 7 year period; 20 of 51,440 platelet units had positive cultures;
• 5 reactions/sxs identified; 4 confirmed, all delayed onset (>9hrs)

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age, y/sx</th>
<th>Diagnosis</th>
<th>In/out patient</th>
<th>Onset, h</th>
<th>Presentation</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>63</td>
<td>56M</td>
<td>MM PBSCT</td>
<td>Out</td>
<td>24</td>
<td>Hypotension syncope</td>
<td>Moderate</td>
</tr>
<tr>
<td>68</td>
<td>62M</td>
<td>AML BMT</td>
<td>In</td>
<td>12</td>
<td>Cardiac arrest multiorgan failure</td>
<td>Fatal</td>
</tr>
<tr>
<td>70</td>
<td>78M</td>
<td>NHL</td>
<td>Out</td>
<td>9</td>
<td>Fever (39.5°C), rigors</td>
<td>Life-threatening</td>
</tr>
<tr>
<td>72*</td>
<td>22F</td>
<td>AA</td>
<td>Out</td>
<td>18</td>
<td>Hypotension</td>
<td>Moderate</td>
</tr>
<tr>
<td>76</td>
<td>7M</td>
<td>ALL</td>
<td>Out</td>
<td>16</td>
<td>Fever (39.5°C), rigors</td>
<td>Severe</td>
</tr>
</tbody>
</table>

AA, aplastic anemia; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; BMT, bone marrow transplant; MM, multiple myeloma; NHL, non-Hodgkin lymphoma; PBSCT, peripheral blood stem cell transplant.

*Posttransfusion blood culture was negative.

Hong et al. Blood 2016;127: ePub Ahead of Print
Blood Collectors:
• Primary testing (apheresis platelets and prestorage pools, single units whole blood platelets)
• Additional Considerations for Blood Centers
  • Secondary testing, Day 4 and Day 5 platelets

Transfusion Services:
• Primary testing platelet components, if not done by blood center
• Additional Considerations for Transfusion Services
  • Inventory management to minimize day 4 and 5 transfusions
  • Secondary (rapid) testing on day 4 or 5
  • Secondary (culture) testing on day 4 for transfusion on day 5
  • Recommendations for testing required for 7 day storage, when cleared by FDA

Summary

• Bacterial sepsis after apheresis platelets is the leading infectious risks associated with blood component transfusion in the US
• The current residual risk of sepsis after apheresis platelet transfusion is ~1:108,000 distributed components based on reporting to the Red Cross
  • All apheresis platelet components implicated in septic transfusion reactions have been from prestorage culture-negative donations

• Clinical recognition and immediate reporting of suspected transfusion reactions to transfusion service and blood supplier is essential to intercept other contaminated units from same donation