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Disclosures

• None
Objectives

• Define and categorize transfusion reactions
• Describe clinical manifestations of specific transfusion reactions
• Discuss patient evaluation and management when transfusion reaction is suspected
Introduction

- DDx of any untoward clinical event should always consider adverse sequelae of transfusion, even when transfusion occurred weeks earlier
- No pathognomonic S/Sx that differentiates a transfusion reaction from other potential medical problems
  - Vigilance- during and after transfusion
- Transfusion reactions are common, BUT uncommonly fatal
  - FDA receives ~40 reports/yr of fatalities attributable to transfusion

Introduction

• Transfusion reactions may be defined by case type, timing, severity, and imputability (the causal relationship of a reaction to transfusion)

• Other classification schemes differentiate reactions by mechanism
  – Immunologic/non-immunologic
  – Type of blood component

Background

The AABB Center for Patient Safety, a federally listed Patient Safety Organization, is dedicated to improving outcomes associated with blood transfusion. Membership provides access to blinded blood transfusion benchmark reports focused on the identification and reduction of risks and hazards associated with patient care.

National Healthcare Safety Network
Biovigilance Component
Hemovigilance Module
Surveillance Protocol

https://patientsafety.aabb.org/
NHSN Biovigilance Component Hemovigilance Module Surveillance Protocol v2.4 www.cdc.gov/nhsn
## Timing and manifestations of transfusion reactions

<table>
<thead>
<tr>
<th>Reaction Type</th>
<th>Typical Timing in Relation to Transfusion (Range)</th>
<th>Presenting Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hemolytic</td>
<td>During (up to 24 h after)</td>
<td>Fever, chills, dyspnea, hypotension, tachycardia, infusion site pain, back pain, hemoglobinuria, hemoglobinemia, indirect hyperbilirubinemia, renal failure, disseminated intravascular coagulation</td>
</tr>
<tr>
<td>Febrile nonhemolytic</td>
<td>During (up to 4 h after)</td>
<td>Fever, chills, rigors</td>
</tr>
<tr>
<td>Allergic</td>
<td>During (up to 4 h after)</td>
<td>Urticaria, pruritus, flushing, angioedema, dyspnea, bronchospasm, hypotension, tachycardia, abdominal cramping</td>
</tr>
<tr>
<td>Transfusion-associated circulatory overload</td>
<td>Within 2 h (up to 6 h)</td>
<td>Dyspnea, tachycardia, hypertension, headache, jugular venous distention</td>
</tr>
<tr>
<td>Septic</td>
<td>During (may be subclinical)</td>
<td>Fever, chills, hypotension, tachycardia, vomiting (may be delayed several hours after transfusion)</td>
</tr>
<tr>
<td>Hypotensive</td>
<td>During</td>
<td>Isolated hypotension</td>
</tr>
<tr>
<td>Transfusion-related acute lung injury</td>
<td>Within 2 h (up to 6 h)</td>
<td>Dyspnea, hypoxemia, fever, hypotension</td>
</tr>
<tr>
<td>Transfusion-associated graft-versus-host disease</td>
<td>8–10 d after (up to 6 wk)</td>
<td>Fever, erythroderma, bloody diarrhea, pancytopenia, liver function abnormalities</td>
</tr>
<tr>
<td>Posttransfusion purpura</td>
<td>5–12 d after</td>
<td>Purpura, hemorrhage</td>
</tr>
</tbody>
</table>

Approximate risk of select transfusion complications, as compared with select societal risks. VCJD, Variant Creutzfeldt-Jakob disease.

Transfusion-related acute lung injury

• The leading cause of transfusion-related death reported to the FDA

• Symptoms
  – Mild dyspnea → severe noncardiogenic pulmonary edema
    • Patients require O2 support (many require mechanical ventilation)
    • Pulmonary edema is non-cardiogenic → classically no ↑ in cardiopulmonary pressures.
  – Chills
  – Fever
  – Hypotension

• Because TRALI is hard to distinguish from fluid overload without CVPs, it is not straightforward to diagnose
TRALI- 2 Hit Event

• 1st hit- underlying clinical condition → sequestration and priming of neutrophils in the lung tissue


  – Previously pregnant women make anti-HNA and anti-HLA antibodies  


• Other antibody-independent mechanisms of TRALI


TRALI- Management

• HLA/HNA reactions are usually donor specific and should not recur with a different donor

• Treatment is **supportive**
  – Donors clearly implicated in TRALI reactions should be **permanently deferred** from blood donation
Transfusion-associated circulatory overload

• Hydrostatic transudate accumulation in the lungs
• Consider in pts who develop sudden signs of fluid overload during transfusion including but not limited to:
  – Dysepsnea
  – Jugular venous distention
  – Tachycardia
  – Congestive heart failure
• At risk pts: compromised cardiopulmonary status → R/L sided heart failure (infants, elderly, pts with renal/heart failure)
TACO - Management

  – ~1/100 transfusions
• If TACO is suspected, the transfusion should be stopped ➔ diuretics
• For concerning pts:
  – Divide the product into aliquots for separate transfusions
  – Infusions in adults ≤ 3 mL/kg/hr (Pediatrics pts max 5ml/kg/hr)
• The initial stages of TACO may be difficult to distinguish from other transfusion related reaction ➔ N-terminal pro-brain natriuretic peptide (NT-pro-BNP)
  – NT-pro-BNP is at least 50% higher after transfusion than pre-transfusion levels
Transfusion-associated graft versus host disease

- Immunologically competent lymphocytes are introduced into a host who cannot inactivate the donor lymphocytes
  - The immunocompetent donor lymphocytes engraft → host HLA is presented to donor lymphocytes → activated lymphocytes attack host tissues
- Occurs after transfusion of non-irradiated cellular blood components
- Much higher fatality rate than HSCT-related GVHD
  - Donor lymphocytes → recipient BM aplasia in addition to typical liver, gut, and skin manifestations of acute GVHD
  - In GVHD after BMT, the BM is of donor origin, and BM aplasia does not occur.
  - > 90% of cases are fatal 2/2 recipient BM aplasia
TA-GVHD Management

- **Presentation**
  - 8-10 days after transfusion
  - S/Sx: N/V, anorexia, fever, diarrhea, liver dysfunction, and erythroderma
  - Pts often die of infection and hemorrhage (3-4wks)
- **NO EFFECTIVE TX** (possible exception of BMT)
- Using irradiated blood (2500 cGy) is recommended (pt receive directed blood transfusions from their relatives)
- Leukocyte-reduction filters **SHOULD NOT** be used as prophylaxis
Post-Transfusion Purpura

• RARE → ~1/100,000 transfusions
• Sudden onset, self-limited thrombocytopenia
  – 5-10 days s/p transfusion; resolved in 14 days
  – Pts lacking a specific platelet antigen (usually HPA-1a (GPIIIa, CD61))
    (Metcalfe P. Platelet antigens and antibody detection. Vox Sang 2004;87(Suppl 1):82–6.)
  – H/o sensitization with prior transfusions or pregnancies (~85% of cases occur in women)
• After re-exposure with transfusion → develop Abs against the PLT-specific antigen they are lacking but which is present on donor PLTs
  – These PLT Abs often have a high titer and can fix complement, destroying the pt’s own PLTs through indiscriminant adsorption of the antigen or immune complexes on their own PLTs
PTP- Management

• Severe thrombocytopenia (<10,000/mL) can distinguish PTP from heparin-induced thrombocytopenia
• Consider if platelet refractoriness persists despite transfusion of HLA-matched PLTs
• Treatment options
  – IVIg
  – Plasma exchange
  – Steroids
  – Splenectomy
• Pts with acute bleeding → PLT-specific antigen negative PLTs
  – Random donor PLTs → severe inflammatory reactions
Additional Resources


• *NHSN Biovigilance Component Hemovigilance Module Surveillance Protocol v2.4* [www.cdc.gov/nhsn](http://www.cdc.gov/nhsn)

• [http://www.aabb.org/research/hemovigilance](http://www.aabb.org/research/hemovigilance)

• [http://www.bbguy.org/](http://www.bbguy.org/)
Thank you for listening...