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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

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</th>
<th>Preceding Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Hemolytic</td>
<td>During day 0 (6 h)</td>
<td>Fever, chills, dyspnea, hypotension, tachycardia, unexplained hemolysis, microangiopathic hemolytic anemia, renal failure, disseminated intravascular coagulation</td>
</tr>
<tr>
<td>Allergic</td>
<td>During day 0 (6 h)</td>
<td>Urticaria, pruritus, flushing, angioedema, dyspnea</td>
</tr>
<tr>
<td>Transfusion-associated</td>
<td>After 2 h (6 h to 1 h)</td>
<td>Diaphoresis, tachypnea, hypotension, headache, goose bumps, flushing</td>
</tr>
<tr>
<td>Trauma</td>
<td>During day 0 (6 h)</td>
<td>Fever, chills, tachycardia, worsening hypotension</td>
</tr>
</tbody>
</table>

Transfusion-related acute lung injury

- The leading cause of transfusion-related death reported to the FDA
  - 2010-2014, 41% (72 of 176) of reported fatalities to the FDA were due to TRALI
  - 1/10,000 transfusions is complicated by TRALI

- Symptoms
  - Mild dyspnea → severe noncardiogenic pulmonary edema
  - Patients require O2 support (many require mechanical ventilation)
  - Develops within 6 h of starting a transfusion (typically within 2 h)
  - No cardiopulmonary pressures
  - Pulmonary edema is non-cardiogenic; classical 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
- 2nd hit: transfusion of blood products containing anti-HLA or anti-human neutrophil antigen (HNA) antibodies activate neutrophils in the lung parenchyma

- Previously pregnant women make anti-HNA and anti-HLA antibodies
- Removal of female donors from the plasma pool → ~50% reduction in TRALI
- Aged blood products → accumulated bioactive lipid soluble mediators (CD40 L) that hamper chemokine scavenging ability of RBCs

TRALI- Management

- HLA/HNA reactions are usually donor specific and should not recur with a different donor
- Treatment is supportive
  - Glucocorticoids and diuretics have not been established to help (a positive fluid balance is a risk factor for TRALI)
  - 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:
  - Dyspnea
  - 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**

- Vastly underreported; ~1/100 transfusions
- If TACO is suspected, the transfusion should be stopped
- 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 reactions
  - NT-pro-BNP is at least 50% higher after transfusion than pre-transfusion levels
  - NT-pro-BNP is sensitive and specific for TACO

**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 presented to donor lymphocytes activated lymphocytes attack host tissues
- 2010-2014: 2 fatalities were reported to the FDA
  - 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
  - Marked pancytopenia, gut, skin, and liver
  - 5% 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)
- Haplo-identical directed donor units of blood post-transfusion GVHD even in immunocompetent recipients, when donor and recipient share HLA types
- 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)) which is not present on donor PLTs
  - 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.aabb.org/research/hemovigilance
- http://www.bbgu.org/
Thank You

Thank you for listening...