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Complications of Transfusion

M2 Hematology/Oncology Sequence
Robertson Davenport, MD

Winter 2009
Transfusion Reactions

- Acute (intravascular) hemolytic reaction
- Delayed (extravascular) hemolytic reaction
- Febrile non-hemolytic reaction
- Allergic (urticarial) reaction
- Bacterial contamination
- Transfusion-related acute lung injury
- Transfusion-associated circulatory overload
- Post-transfusion purpura
- Graft-vs.-host disease
Hemolytic Transfusion Reactions

• Acute
  – Presentation within 24 hrs
  – Intravascular hemolysis
  – Prototype: ABO incompatibility

• Delayed
  – Presentation > 24 hrs
  – Typically extravascular but may be intravascular
  – Prototype: Rh
Clinical Presentation of HTR

• Intravascular
  – Fever, chills, pain, hemoglobinemia, hemoglobinuria, dyspnea, vomiting, shock
  – Complications: renal failure, DIC, ARDS, death
  – Mortality: ~10%

• Extravascular
  – Fever, chills, leukocytosis, anemia
  – Complications: renal failure, DIC, sickle cell crisis
  – Mortality: rare
Recognition of HTR

- Free serum hemoglobin, positive DAT
- New red cell antibody
- Patient or sample misidentification
- Bleeding, hemoglobinuria in an anesthetized patient
Febrile Non-Hemolytic Transfusion Reactions

• Incidence
  – 1:250 transfusions

• Presentation
  – Fever and/or chills

• Mechanisms
  – Leukocyte antibodies in recipient
  – Cytokines released in unit during storage
Allergic Reactions

• Incidence 1-3:100 transfusions
• Presentation
  – Hives, flushing, dyspnea, vomiting
• Mechanisms
  – Antibody to allergen or plasma protein
  – Passive transfer of donor antibody
Anaphylaxis

• Presentation
  – Hypotension, bronchospasm, stridor, shock

• Mechanism
  – IgA deficiency with anti-IgA
  – Haptoglobin deficiency with anti-haptoglobin

• Prevention
  – IgA deficient plasma, washed RBC & platelets
Bacterial Contamination

• Incidence in platelet concentrates
  – 1:5000 culture positive
  – 1:10,000 cause reactions
  – 1:75,000 cause mortality

• Organisms involved
  – Platelets: Gram neg. rods, Gram pos. cocci
  – RBC: Yersinia, Pseudomonas

• Sources
  – Contaminated equipment, nonsterile procedure
  – Donor skin
  – Donor blood
Bacterial Contamination

- **Symptoms:** fever, chills, rigors, hypotension, shock, DIC
- **Differential:** hemolytic transfusion reaction, sepsis
- **Work-up:** Gram stain, culture
Transfusion Related Acute Lung Injury (TRALI)

- Incidence 1:5000 transfusions
- Presentation: non-cardiogenic pulmonary edema
- Mechanisms
  - Donor antibody to recipient neutrophil-specific or HLA antigen
  - Production of platelet activating factor-like lipid during storage
  - Release of CD40L from platelets during storage
- Mortality: 10 - 20%
- Differential: Hemolytic reaction, allergic reaction, fluid overload, acute lung injury
- Reduction strategy
  - Plasma components from male donors
  - Antibody screening
Transfusion Associated Graft-vs.-Host Disease

- Incidence: rare
- Presentation: rash, fever, diarrhea, liver dysfunction, cytopenia
- Mechanism: engraftment of transfused T-cells
- Mortality: very high
- Differential: viral infection, drug reactions
Patients at risk for TA-GVHD

• Severe cellular immunodeficiency
  – Congenital immunodeficiency
  – Intrauterine transfusion
  – Bone marrow transplantation
  – Hodgkin’s disease, NHL, high dose chemotherapy

• Homogenous populations

• Recipients of donations from first degree relatives
Mechanism of Engraftment in Normal Recipients

- HLA homozygous donor
- HLA heterozygous recipient
- Shared haplotype

<table>
<thead>
<tr>
<th>Donor</th>
<th>Recipient</th>
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Different

Same

R. Davenport
Transfusion-Associated Circulatory Overload (TACO)

• Incidence: Variable
• Presentation: Dyspnea, hypoxemia, pulmonary edema
• At-risk patients: heart disease, renal failure
• Mortality: ~double underlying disease
• Differential: Hemolytic reaction, allergic reaction, TRALI, cardiac or pulmonary disease
Other Adverse Effects of Transfusion

• Iron overload
• Alloimmunization
• Non-immune hemolysis
• Hypotensive reaction
• Acute pain reaction
Transfusion-Transmitted Diseases

- Hepatitis (B, C, G)
- HIV/AIDS
- Cytomegalovirus
- HTLV
- Parvovirus
- Chagas’ disease
- Malaria
- Babesiosis
- Leishmaniasis
- Variant CJD
Hepatitis B

- Jaundice 2 -3 months after transfusion
- Chronic carrier rate 5-10%
- 25% active hepatitis in carriers
- Complications
  - Cirrhosis
  - Hepatocellular carcinoma
Hepatitis C

• Acute infection usually nonicteric
• 70% develop chronic hepatitis
  – 10 - 20% progress to cirrhosis
• 0.5% of first time blood donors are HCV+
Sources of Infection for Persons With Hepatitis C

- Injecting drug use: 60%
- Sexual: 15%
- Transfusion (before screening): 10%
- Occupational: 4%
- Other: 1% *
- Unknown: 10%

* Nosocomial; iatrogenic; perinatal
Posttransfusion Hepatitis C

% of Recipients Infected

Year


All volunteer donors
HBsAg

Donor Screening for HIV Risk Factors
Anti-HIV
ALT/Anti-HBc
Anti-HCV

Improved HCV Tests

Source Undetermined
Transfusion Transmitted HIV

Year of Transfusion

Incidence

Source Undetermined
Estimated HIV/AIDS Cases 2006

- MSM: 59%
- IDU: 16%
- MSM+IDU: 7%
- Heterosexual: 17%
- Other: 1%
- Other: 1%
Outcome of Transfusion Transmitted HIV

- Rate of progression similar to other cohorts
- Progression rate independent of donor status
- Older recipients progress more rapidly than younger recipients
Estimated Current Risks

• Hepatitis C
  – 1:1,800,000

• HIV
  – 1:2,300,000

• Hepatitis B
  – 1:1,500,000
Cytomegalovirus

- Enveloped DNA Herpes virus
- Usually asymptomatic in immunocompetent patients
- Latent in monocytes and other cells
- High prevalence in donor populations
Patient Populations at Risk of CMV Disease

- Fetuses
- Premature infants
- Bone marrow transplantation
- HIV infection
- Congenital cellular immunodeficiency
- Solid organ transplantation
CMV and Blood Transfusion

- Transmission rate by seropositive cellular components: 0.4 - 10%
- Seronegative blood components equivalent to background rate
- Leukocyte reduced components are as effective as seronegative in prevention
Parvovirus B19

• Non-lipid enveloped DNA virus
• Clinical associations
  – Erythema infectiosum (Fifth disease)
  – Arthritis
  – Red cell aplasia
  – Non-immune hydrops
Parvovirus and Blood Transfusion

• Per unit risk 1:1,000 - 1:5,000
• Seroconversion rate: 80%
• Detected in factor concentrates, pooled plasma and donor sera by PCR
• Seroprevalence 50%
West Nile Virus

• Latent period 3-15 days
• No chronic carrier state
• Blood donor prevalence: ~1:10,000
• Transfusion risk: <1:1,000,000
2008 WNV Blood Donor Viremia
Chagas Disease

• US prevalence: ~100,000 persons
• Seroprevalence: ~1:5000 in Los Angeles
• Infectivity: 60% of seropositive bloods are PCR positive
• Transfusion transmission: 9 cases in US and Canada
• Prevention: leukocyte reduction, antibody screening
Chagas Confirmed Positive Blood Donors
CJD

• UK vCJD experience
  – 18 donors with 66 components transfused
  – 3 recipients developed vCJD 5-10 years after transfusion
  – Background mortality: 0.24/million/year

• US sCJD and fCJD experience
  – 32 donors with 395 components transfused
  – 1663 person-years follow-up
  – No evidence of transmission to date
Other Transfusion-Transmitted Diseases

- Human T-Lymphotrophic Virus
- Hepatitis G
- Epstein-Barr Virus
- Malaria
- Babesiosis
- Leishmania
Informed Consent for Transfusion

• Indications for the transfusion
• Possible risks
• Possible benefits
• Alternatives
• Possible consequences of not receiving the transfusion
Emergency Transfusion

- Judgement of patient’s preference
- Implied consent
- Do not delay transfusion in life-threatening situations
- Document circumstances in medical chart
Additional Source Information
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Slide 16: Robertson Davenport
Slide 22: Centers for Disease Control and Prevention
Slide 23: Source Undetermined
Slide 24: Source Undetermined
Slide 25: CDC Cases of HIV infection and AIDS in the United States and Dependent Areas, 2006
Slide 34: Centers for Disease Control and Prevention
Slide 36: American Association of Blood Banks