Transfusion Reactions

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Types of reactions

- Hemolytic transfusion reactions
- Febrile non-hemolytic transfusion reactions
- Allergic reactions/ Anaphylactic reactions
- Transfusion related acute lung injury (TRALI)
- Transfusion associated circulatory overload (TACO)
- Post transfusion purpura
Hemolytic Transfusion Reactions

- They may be acute (occurring within 24 hours of transfusion) or delayed (when signs of red cell destruction do not occur until 4 to 10 days after transfusion).

- These patients usually have been exposed to the antigen through previous pregnancies or transfusions.
Acute Hemolytic Transfusion Reaction

- Definition: RBC destruction < 24 hrs of transfusion
- Occurs mainly with RBCs and whole blood, but can occur with any plasma-derived products (plts, FFP, cryo, etc…)
- Fatal 1 in 100,000 – 600,000 units transfused
- Most common cause: incompatible RBCs leading to intravascular hemolysis
Acute Hemolytic Transfusion Reaction

- Pathophysiology

  \[
  \text{Donor RBC} \quad \text{recipient Ab (ABO, Kell, Kidd, Duffy)}
  \]

  complement activation

  Cell lysis
Acute Hemolytic Transfusion Reaction

- Complement activation leads to:
  - Hypotension (C3a and C5a anaphylotoxins)
  - Vasoconstriction and renal ischemia
  - Activation of plts and coag cascade leading to DIC
Acute Hemolytic Transfusion Reaction

- Clinical
  - Depends on antigen involved, quantity of RBCs infused, and titer of the Ab
  - Clinical presentation also varies depending on premorbidity factors, so use common sense when evaluating your pts., i.e., if pt is paralyzed then you won’t see chills/rigors
  - AIHA with either warm or cold Abs may look like AHTR clinically AND these pts may also develop alloantibodies and that makes our job even harder…
  - TTP, HUS, DIC, Heart valves, congenital hemolytic anemias (hereditary spherocytosis, G6PD, sickle cell anemia) also mimic AHTRs
Acute Hemolytic Transfusion Reaction

- Signs and Sxs:
  - Fever
  - Chills/rigors
  - Anxiety
  - Flushing
  - Chest/ abdominal/ back pain
  - N/V/D
  - Dyspnea
  - Hypotension
  - Hemoglobinuria
  - Pallor
  - Icterus
  - Oliguria/anuria
  - Pain at transfusion site
  - Diffuse bleeding jaundice
Acute Hemolytic Transfusion Reaction

- **Lab Dx:**
  1. Make sure that the right patient got the right blood product
     - Reconfirm ABO/RH type and antibody screen results
  2. Direct and indirect Coombs test (usually yields mixed field reactions b/c of combination of pt and donor RBCs only one of which is sensitized)
  3. Direct evidence of hemolysis
     - Pretransfusion blood sample is compared with posttransfusion sample for visible evidence of hemolysis. Free serum hemoglobin appears as a pink color in the serum in a clotted centrifuged specimen. This may be observed with as little as 5-10 mL of hemolyzed blood.
Acute Hemolytic Transfusion Reaction

- Labs:
  - CBC w/plts
  - UA
  - bilirubin, BUN/CREATININE

Coags: PT/PTT/FSP/fibrinogen/haptoglobin
Acute Hemolytic Transfusion Reaction

- Serum bilirubin peaks in 3-6 hours as the free hemoglobin is metabolized.
- Haptoglobin binds to hemoglobin and the serum hemoglobin level falls, reaching its nadir in 1-2 days.
- Examine urine for hemoglobinuria.
- A repeat CBC fails to show the expected rise in hematocrit in patients developing intravascular or extravascular hemolysis.
Acute Hemolytic Transfusion Reaction

- Prevention:
  - Make sure that pt really needs transfusion (treat the patient and not the labs!)
  - Accurate clerical function (patient ID, sample collection, sample and unit labeling, unit ID, patient testing, component handling…)
  - Don’t add meds to blood
  - Blood is stored at proper temperature
  - Blood is not exposed >37°C
Acute Hemolytic Transfusion Reaction

- **Management:**
  - If suspected, STOP transfusion! And maintain IV access
  - Make initial rapid assessment of pt and requirements for basic and advanced support
  - Notify blood bank, collect transfused units (full or partial), tubing, etc. and return them to BB
  - Reconfirm identity of blood units & pt
  - Collect appropriate patient blood specimens
Acute Hemolytic Transfusion Reaction

- Supportive approaches:
  - IV fluid resuscitation for hypotension
  - Maintain IV fluids
  - Diuretics: Make efforts to maintain urine output at 30-100 mL/h.
  - Low dose dopamine
  - Replace procoagulant factors and fibrinogen with FFP and cryo; also plts as needed
Acute Hemolytic Transfusion Reaction

- Non-immune mediated acute hemolysis:
  - Bacterial contamination
  - Mechanical trauma during infusion
  - Thermal hemolysis
  - Osmotic lysis from reconstitution of blood components with hypotonic solutions
Delayed Hemolytic Transfusion Reaction

- Pathophysiology same as acute EXCEPT:
  - Low titer of reactivity so undetected on initial screen
  - Repeat post-transfusion sample will show the Ab
Delayed Hemolytic Transfusion Reaction

- Symptoms:
  - Milder than in acute
  - Fever
  - Unexplained anemia
  - Jaundice
  - Hemoglobinuria
  - Rarely DIC and ARF
Delayed Hemolytic Transfusion Reaction

- Any antibody can cause it, but most common culprits:
  - Rh
  - Kidd
Delayed Hemolytic Transfusion Reaction

- **Prevention:**
  - More sensitive antibody screens
  - Medical records of Ab maintained for pts
  - Pts with multiple transfusion histories, i.e., sickle cell dz., should undergo extensive Phenotyping

- **Treatment same as for acute**
Delayed Hemolytic Transfusion Reaction

- 3-10 days after transfusion of blood that initially appeared to be serologically compatible
- Previously transfused or pregnant and Ab not detected on pretransfusion sample
Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Incidence:
  - 0.5% - 1.4% of nonleukoreduced red blood cell transfusions
  - 43-75% of all transfusion reactions
Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Nonhemolytic febrile reactions are due to WBCs, WBC antibodies, or cytokines elaborated by either donor or recipient
- Granulocyte and human leukocyte antigen 5 (HLA5) antibodies
- Cytokines accumulate during storage so to prevent this all samples are leukoreduced prior to storage
Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Symptoms
  - Fever (increase of temp 1°C from baseline)
  - Chills

In absence of other causes of fever
Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Treatment
  - Discontinue transfusion
  - Antipyretics
  - Supportive care
Febrile Nonhemolytic Transfusion Reactions (FNHTR)

- Prevention:
  - Antipyretics
  - Prestorage leukoreduced blood products

- Of course…
  - Make sure to exclude a Hemolytic transfusion reaction
Uncomplicated Allergic Reactions

- Incidence:
  - 1-3% of transfusions
  - 45% of all transfusion reactions
Uncomplicated Allergic Reactions

- Pathophysiology:
  - IgE directed against soluble donor antigens
Uncomplicated Allergic Reactions

- Symptoms:
  - Local or diffuse urticaria
Uncomplicated Allergic Reactions

- **Treatment**
  - Discontinue transfusion
  - Antihistamines
  - If urticaria resolved, then can restart transfusion
Uncomplicated Allergic Reactions

- Prevention:
  - Antihistamines
Anaphylactic Reactions

- **Incidence:**
  - 1-3% of all transfusion reactions

- **Pathophysiology:**

Donor plasma \( \rightarrow \) IgA \( \rightarrow \) Transfused recipient

Recipient Plasma anti-IgA
Anaphylactic reactions

- Anaphylactic reactions most often are observed in those patients with a hereditary immunoglobulin A (IgA) deficiency.
- Some of these patients have developed complement-binding anti-IgA antibodies that cause anaphylaxis when exposed to donor IgA.
Anaphylactoid Reactions

- Subclass, allotypic or specific anti-IgA in patients who have demonstrable levels of IgA
- Donor products may also have anti-IgA
- Difficult to identify these patients b/c of an infinite number of specific IgA proteins
Anaphylactic Reactions

- **Symptoms:**
  - In anaphylactic reaction, symptoms usually occur with less than 10 mL of blood transfused and only rarely occur more insidiously.
  - Tachycardia
  - Flushing
  - Urticaria
  - In more severe cases, wheezing, laryngeal edema, and hypotension
Anaphylactic Reactions

- **Treatment:**
  - Stop transfusion immediately.
  - Support airway and circulation as necessary.
  - Administer epinephrine, diphenhydramine, and corticosteroids.
  - Maintain intravascular volume.
Anaphylactic Reactions

Prevention

- IgA deficient patients should avoid plasma-containing products or donations from other IgA deficient donors
- Washed RBCs
Transfusion Related Acute Lung Injury (TRALI)

- Incidence:
  - rare
Transfusion Related Acute Lung Injury (TRALI)

- Noncardiogenic pulmonary edema associated with:
  - Transfer of donor granulocyte Abs directed against the patient’s WBCs
  - Agglutination of Ab-antigen complex within the pulmonary vasculature

- By-products of neutrophil activation result in:
  - Altered vascular permeability
  - Capillary leak syndrome and thus pulmonary edema

- Clinical picture resembling ARDS
TRALI

- Can occur with:
  - FFP
  - RBCs
  - Whole Blood
  - Platelets
  - Granulocytes
  - Cryoprecipitate

- Not reported with:
  - Albumin
  - IVIG
  - RhIg
  - Coagulation factor concentrates
TRALI

- Clinically similar to ARDS, but TRALI:
  - Better prognosis
  - Lower mortality (10%)
  - More rapid resolution (3-7 days)
  - Lower likelihood of permanent pulmonary sequelae
TRALI

- Signs and symptoms
  - Acute onset of respiratory distress and hypoxemia with clinical and X-ray evidence of acute pulmonary edema
  - Hypotension
  - Fever
  - Chills

- Diagnosis of exclusion, fluid overload and cardiac failure must be ruled out
TRALI

- Treated with supportive care:
  - Ventilatory support
  - Supplemental oxygen
  - Pressors

- Important to recognize
  - Donor specific phenomenon
  - Donor will not be permitted to donate plasma-containing blood components

- Blood donor center will evaluate unit for:
  - HLA granulocyte-specific antibodies in the donor
  - HLA granulocyte-specific antibodies in the recipient
  - Reverse lymphocyte crossmatches (pt’s lymphocytes with donor serum)
Transfusion Associated Circulatory Overload (TACO)

- Incidence:
  - 1 in 100 transfusions

- Pathophysiology:
  - High rates of infusion
  - High volume of infusion
  - Underlying cardiovascular of pulmonary pathology
TACO

- Symptoms:
  - Dyspnea
  - Orthopnea
  - Cough
  - Tachyacardia
  - Hypertension
TACO

- **Treatment:**
  - Stop or slow rate of infusion
  - Diuretics
  - Oxygen if necessary
  - Supportive care
TACO

- Prevention:
  - Vigilant assessment of pt’s ins/outs
  - Slow rates of infusion
  - Pretransfusion and/or intratransfusion diuretic administration
Post-transfusion purpura

- Incidence:
  - Rare
  - 200 cases reported

- Pathophysiology
  - Profound thrombocytopenia 1-2 wks post transfusion
  - Transfusion of donor platelets with a platelet antigen lacking in the recipient
  - Human platelet specific alloantigen 1a (HPA-1a)
Post-transfusion Purpura

Donor Platelets

HPA-1a

HPA-1a

HPA-1a

Recipient antibodies

HPA-1a

HPA-1a

HPA-1a

HPA-1a
Post-transfusion Purpura

- **Treatment**
  - IVIG (mechanism of action ?)
    - Reticuloendothelial blockade
    - Nonspecific adherence to target antigen blocking access by specific antibody
  - Plasmapheresis if poor response
  - If the pt doesn’t die from hemorrhage, then it’s self-limited with recovery within 4-5 days of therapy
Post-transfusion Purpura

Prevention:
- Avoid antigen positive platelet transfusion in pts in whom this has previously occurred