DELAYED TRANSFUSION REACTIONS
Shan Yuan, MD
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I. Delayed Hemolytic Transfusion Reaction (DHTR)
   A. Incidence: 1:5,000 to 1:11,000
   B. Etiology/Pathophysiology
      o Primary Alloimmunization
         ♦ Antibody production begins 7 – 10 days to weeks or months after antigen exposure
         ♦ May decrease survival of transfused foreign cells in circulation – monitor by decrease in Hgb
         ♦ Usually not clinically significant; manifests as positive DAT and antibody detectable in patient’s serum and eluate
      o Anamnestic Response
         ♦ Occurs in previously immunized patient, secondary response to RBC Ag
         ♦ Primary response undetectable
         ♦ Rapid rise in IgG antibody titer in 3 – 7 days following exposure to the offending antigen
         ♦ Hemolysis generally extravascular, occasionally intravascular (particularly DHTRs due to Kidd antibodies)
   C. Signs/Symptoms
      o Usually very mild, unremarkable except falling hgb, hct without other explanation
      o But may see fever, mild jaundice, decreased haptoglobin, occasional hemoglobinuria, acute renal failure in severe (rare) cases
      o Often no symptoms
         ♦ If asymptomatic and without lab findings (including Hgb changes) other than newly positive antibody screen, may be called “delayed serologic reaction (DSTR)”
   D. Action/Evaluation
      o Post-transfusion DAT should positive. Negative only if all antigen positive cells have been cleared.
      o Perform an eluate to determine antibody specificity; correlate with serum antibody screen/identification
      o Consider phenotyping transfused units to gauge the amount of transfused RBCs that are antigen positive
      o Communicate with clinicians: monitor hgb/hct level, assess if there are other reasons for the Hgb level to drop, follow serial hemolysis labs

II. Transfusion-Associated Graft versus Host Disease (TA-GVHD)
   A. Mechanism: Transfused T lymphocytes see host tissues as foreign, proliferate and attack the immunocompromised host, who is unable to “inactivate” the transfused lymphocytes
   B. Clinical presentation:
o Fever, skin rash, GI involvement, liver damage.

- Hallmark of TA-GVHD: Bone marrow aplasia -> pancytopenia, death. This is not seen in GVHD associated with bone marrow transplant, as the bone marrow is not recognized as "self" and escapes the attack.

C. Treatment: No effective treatment if bone marrow aplasia develops (except bone marrow transplant?), near 100% fatality.

D. Prevention: Irradiation of lymphocyte-containing blood products given to at risk patients, including RBCs, platelets, and granulocytes.
  - Dose: 25Gy midplane, 15Gy minimum any point
  - Irradiation causes DNA damage of the donor lymphocytes, rendering them incapable of proliferating and attacking the host.
  - Irradiated RBC will expire in 28 days due to increased K+ leakage following irradiation. No effect on platelet and granulocyte products’ shelf life.

E. At risk patients
  - Congenital cellular immunodeficiencies (Classic example: DiGeorge’s)
  - Hodgkin’s disease
  - Intrauterine transfusion
  - Premature neonates (birth wt <1200g per AABB)
  - Stem cell transplant recipients/candidates (hence most patient with hematologic malignancy)
  - Recipients of blood components donated by relatives
  - Recipient donor pairs from genetically homogenous populations (e.g. all cellular products in Japan are irradiated)
  - Recipients of HLA matched cellular products
  - Debatable whether at risk due to lack of case reported, however TA-GVHD is often a missed diagnosis:
    - Solid organ transplant recipients
    - Recipients of “high-dose” chemotherapy or irradiation

III. Post-Transfusion Purpura
A. Incidence: Rare.
B. Etiology/Pathophysiology
  - Formation anti-\( \text{PL}^A1 \) (HPA-1A) is classic and most commonly involved
    - Almost everyone is \( \text{PL}^A1 \) positive, so \( \text{PL}^A1 \) negative patients are easily exposed to this platelet antigen through pregnancy or transfusion
    - Transfusion after antibody is formed leads to devastating destruction of platelets (both transfused \( \text{PL}^A1 \) positive, and autologous \( \text{PL}^A1 \) negative platelets). Possibly due to:
      - Absorption of the \( \text{PL}^A1 \) (HPA-1A) onto the recipients own platelets
      - Adherence of immune complexes to antigen negative platelets
      - Possibly due to production cross-reactive autoantibodies early in the immune response
  - Multiparous females especially at risk, associated with DRw52 HLA
Triggering transfusion does not have to be platelets – the small amount of platelets in RBC units can be sufficient to trigger the reaction. PTP cases have been reported to occur even after plasma transfusion.

C. Signs/Symptoms
- Marked thrombocytopenia in about one-three weeks (mean= 9 days) following transfusion (may be below 10,000/μL), can be accompanied by bleeding
- Thrombocytopenia may persist for several weeks. Self limited
- Mortality ~10-15%

D. Therapy/Evaluation
- IVIG successfully reverses the process (replacing therapeutic plasma exchange as the treatment of choice)
- Steroids, splenectomy may also help
- Plasmapheresis for refractory patients
- Platelets should not be transfused, antigen negative platelets will be destroyed quickly just like patient’s own platelets
- Blood bank work-up involves testing for platelet specific antibodies and determination of implicating antibody
- Prevention:
  - Avoid platelet transfusion. Transfusion of antigen-negative platelets considered only in dire scenarios (e.g. intracranial bleeding).
  - RBCs should be washed to remove residual platelet membraned fragments
  - Some recommend limiting transfusion of plasma to avoid adsorption of the PL^A1 (HPA-1A) onto the patient’s own platelets

IV. Iron Overload
- Each unit of RBCs contains 200 mg iron
- Risk Lifetime load of approximately 150 units in a 70 kg person
- Becomes a concern in chronically transfusion-dependent individuals
- Deposition causes liver, pancreas, gonad and cardiac dysfunction
- Treatment and prevention:
  - Deferoxamine (Desferol), Exjade. Oral agents have improved compliance and efficacy
  - Exchange transfusion rather than simple transfusion