

Transfusion complications

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Immediate Transfusion Reactions

- ➤ Begin within minutes to hours.
- ➤ Immediate transfusion reactions may be hemolytic, febrile, or caused by contaminated blood.
- ➤ The symptoms may not reflect the severity of the reaction.

- Chills
- Fever
- Urticaria
- Tachycardia
- Dyspnea
- Nausea Vomiting
- Tightness in the chest
- Chest and back pain
- Hypotension
- Bronchospasm
- Angioneurotic edema
- Anaphylaxis Shock
- Pulmonary edema
- Congestive failure

In the anesthetized patient undergoing surgery

- immediate transfusion reaction may manifest itself as:
 - generalized oozing of blood from the operative site
 - shock that is not corrected by the administration of blood

Acute Hemolytic Transfusion Reactions(AHTR)

- ➤ The patient in this clinical case illustrates the typical presentation of an acute hemolytic transfusion reaction: pain at the administration site, fever, chills, back pain, dark urine, and laboratory evidence of intravascular hemolysis.
- ➤ Often, fever is the only initial sign.
- ➤ The serologic hallmark of an acute hemolytic reaction is a positive DAT.
- ➤ DIC may occur.

- **Why does it happens?**
- (1) Most commonly incompatibility in the ABO, causes intravascular destruction of the transfused RBCs which can manifest as hemoglobinemia and hemoglobinuria
- (2) Activation of complement leads to the release of cytokines, including
- tumor necrosis factor, accounting for fever and chills.
- ➤ It usually occurs after pack cell transfusion but very rarely is seen after platelet transfusion too.

- **Lab testing for ATHR:**

- ➤ Repeat ABO compatibility
- ➤ Serum and urine inspection for pink color
- ➤ Hemolysis testing (haptoglobin,LDH , bilirubin)
- ➤ Coombs testing
- ➤ DIC testing
- ➤ Electrolytes (Hyperkalemia)
- ➤ Bun / Cr

- **Management of ATHR**
- ➤ Two **major effort**:
 - ➤ *control of bleeding*
 - ➤ *prevention of ATN.*
- ➤ Immediate termination of the transfusion
- ➤ Institution of fluids and vasopressors for hypotension and maintenance of urine output (Systolic blood pressure should be maintained above 100 mm Hg)
- ➤ Correct the bleeding diathesis.

- **Prevention of ATHR**

-  Systems errors or failure to follow established hospital procedures remains the most common cause of acute hemolytic transfusion reactions; therefore:
-  The importance of definitive bedside patient identification, both at the time that type and screen specimens are obtained and at the time that the product is ready to be administered, cannot be overemphasized.

- **Febrile Reactions**

- ➤ Hemolytic reaction
- ➤ sensitivity to leukocytes or platelets
- ➤ bacterial pyrogens
- ➤ unidentifiable causes

- ➤ *The decision to stop the administration of blood in a febrile reaction is a difficult one.*
- ➤ Many but not all febrile reactions can be tolerated by the patient with supportive care, such as antipyretics and antihistamines.

- ➤ A chill, however, may herald a more serious reaction, such as a hemolytic reaction, or may be the result of grossly contaminated blood.
- ➤ Reliable guidelines are not available to help ***Clinicians should exercise their best judgment***
- ➤ *Do not hesitate to stop the transfusion if there is any doubt about the cause of the reaction.*

Febrile non-hemolytic transfusion reaction(FNHR)

- ➤ Febrile nonhemolytic transfusion reactions typically manifest during or within 4 hours of transfusion with fever (defined as an increase in temperature of 1°C above the patient's baseline, typically to $>38^{\circ}\text{C}$) with or without chills and/or rigors.
- ➤ Temperature continues to rise for 2 to 6 h after cessation of transfusion, *may persist for 12 h.*

WHY DOES IT HAPPEN?

- 1) Multiparous women and multiply transfused patients develop antileukocyte antibodies that cause febrile nonhemolytic reactions to RBC or platelet transfusions.
- 2) During the storage of blood, clinically significant quantities of cytokines (IL-1, IL-6, IL-8, and tumor necrosis factor) are sometimes liberated from donor-derived leukocytes present in platelet and RBC products.

- ➤ Usually at least seven transfusions are required to induce sensitization to leukocyte antigens in *men, nonparous women, or children.*
- ➤ In gravid or parous women, reactions may occur with the first or second transfusion.

Management of FNHR

- ➤ *Symptoms are usually self-limited*
- ➤ *Respond to symptomatic therapy, which includes antipyretics for fever and chills and meperidine for rigors.*

Prevention of FNHR

- ➤ Use leukoreduced products.
- ➤ Pre-storage leukoreduction is more effective than post-storage bedside leukofiltration, due to less accumulation of biologic mediators.
- ➤ Routine use of premedication to prevent febrile-nonhemolytic transfusion reactions, but many clinicians premedicate with acetaminophen or glucocorticoids if fever is bothering and repeating.

Transfusion-Related Lung Injury (TRALI)

Noncardiogenic Pulmonary Edema

- ➡ clinical picture is acute lung injury with noncardiogenic pulmonary edema with dyspnea, hypoxemia, hypotension, fever, and a chest x-ray showing bilateral infiltrates with pulmonary edema.



Fig 1: Pre and Post transfusion X-rays of our patient with TRALI. Bilateral Lung infiltrate with pulmonary edema is an essential criteria for the clinical diagnosis of TRALI.

- ➤ TRALI is a potentially life-threatening reaction with a 5% to 10% fatality rate.
- ➤ The frequency of this reaction has been estimated as *1 in 5000 transfusions*.
- ➤ TRALI can be difficult to distinguish from the manifestations of a patient's underlying medical problems, particularly those of cardiac origin, such as congestive heart failure and fluid overload from the transfusion. (timing is important)
- ➤ TRALI usually occurs during or within 6 hours of transfusion.

Why does it happen?

- ➤ It is caused by passive transfusion of donor antigranulocyte antibodies, cytokines, biologically active lipids, or other substances.
- ➤ Almost 25 % of multiparous women donors have leukoagglutinins and lymphocytotoxicins that can cause these reactions.
- ➤ TRALI may occur after any plasma-containing blood product transfusion (ie, RBCs, platelet concentrates, platelet apheresis units, and plasma)

- Management of TRALI
- ➤ Aggressive pulmonary support, 100% of patients require oxygen support with approximately 70% requiring mechanical ventilation.
- ➤ Approximately 80% of patients improve within 48 to 96 hours.
- ➤ *Pulmonary infiltrates clearing within 4 days.*

Prevention of TRALI

- ➤ Once blood from a particular donor is implicated in a case of TRALI, that donor is excluded from the donor pool.
- ➤ Preventing the first cases of TRALI by those donors, however, requires the elimination of all blood donors whose plasma contains anti-HLA or antineutrophilantibodies.
- ➤ For plasma, this is achieved by excluding female donor from the plasma donor pool because multiparous female are the most likely among a healthy donor population to have anti-HLA antibodies as a result of sensitization during pregnancy.
- ➤ Because platelets are chronically in short supply, excluding all

Transfusion Associated Circulatory Overload(TACO)

- ➤ Dyspnea with or without hypoxia during or after transfusion, accompanied by signs of volume overload—such as an increase in blood pressure, jugular venous distention, and elevated pulmonary arterial wedge pressure—represents transfusion-associated circulatory overload (TACO).

- ➡ TACO and TRALI may be difficult to distinguish from each other.
- ➡ TACO accounted for 24% of transfusion-related fatalities reported and is the second most common cause of reported death due to transfusion in this time period (after TRALI).

- **➡ Risk factors for TACO include:**
- ➤ Extremes of age
- ➤ History of cardiac disease
- ➤ Renal failure
- ➤ Transfusion of multiple blood components within a short period of time
- ➤ Patients with severe chronic anemia (Hb<4), such as those with pernicious anemia

- **Management and prevention of TACO**
- ➤ Slow administration in a semi-upright position.
- ➤ Monitor venous pressure.
- ➤ Therapy consists of diuretics and decreased blood administration rate.
- ➤ Transfusion given at a rate of 2 ml /kg /h

- **Urticarial transfusion reaction (Allergic transfusion reactions)**
- ➤ Minor allergic reactions manifested by urticaria and pruritus are frequent.
- ➤ Occasionally there may be bronchospasm, angioneurotic edema, or anaphylaxis.

- **Why does it happen?**
- ➤ The cause is poorly understood.
- ➤ Sensitivity to plasma proteins or other agents
- ➤ Antibodies to leukocytes or platelets do not seem causally related to urticarial reactions.

- Management and prevention
- ➤ Antihistamines generally alleviate symptoms of allergic reactions.
- ➤ Many urticarial reactions do not recur with subsequent transfusions.
- ➤ If a recipient experiences multiple urticarial reactions, premedication with antihistamines (particularly non-sedating ones) can be considered.

- ➤ Washed products may be considered in severe cases.
- ➤ Although removing plasma through washing mitigates allergic reactions, washing platelets impairs platelet function and leads to accelerated clearance after transfusion.

A dangerous allergic reaction!

- ➤ Severely IgA-deficient patients may make anti-IgA antibodies that can cause anaphylactic reactions, but this is a rare occurrence.
- ➤ serious reactions require the prompt parenteral administration of epinephrine.
- ➤ Washed RBCs, washed platelets, and/or platelet and plasma products from IgA-deficient donors should be transfused only when a patient has severe IgA deficiency (<0.05 mg/dL) and a concern for anaphylactic reactions.

Infection:

- ➤ All donated blood is extensively screened for transfusion-transmitted infections; as a result the risk of acquiring infection is extremely low.
- ➤ *Infections can occur at the time of collection or donor bacteremia at the time of donation.*
- ➤ *The risk of bacterial contamination of products is much greater than the risk of viral transmission.*

- **Bacterial Contamination**

- ➤ Blood may be contaminated by cold-growing gram negative microorganisms (*Yersinia enterocolitica* organisms, *Pseudomonas*).
- ➤ These microorganisms utilize citrate and may result in clotting.
- ➤ *Visual inspection of the blood unit may reveal clots and suggest the presence of contamination.*

- ➤ Bacterial contamination of blood is an uncommon complication to be 2 per 1,000,000 u.
- ➤ This transfusion hazard is significant with platelets because this product is stored at room temperature.
- ➤ Platelets are typically contaminated by gram-positive cocci, such as coagulase-negative staphylococci.

- ➤ The reaction may start with ***shaking chills*** following a latent period of 30" or more.
- ➤ As little as 10 ml of blood may contain sufficient microorganisms to produce the reaction.
- ➤ Rapid diagnosis is essential and can be made by drawing a small sample of residual donor blood from the container or administration tubing.
- ➤ The plasma smeared on a slide and gram stained.
- ➤ If the blood contaminated, several organisms can be identified in fields.

- ➤ Septic shock is a complex disorder comprehensive supportive therapy is essential
- ➤ Treatment is often ineffective.
- ➤ The fatality rate with this type of overwhelming shock is estimated to be from 50 to 80 %.

Transfusion-associated graft-versus-host disease

- ➤ Patients develop signs and symptoms of classic transplantation-associated GVHD, including skin rash, diarrhea, liver function test abnormalities, pancytopenia and its related symptoms such as infection and bleeding.
- ➤ Usually symptom start 4-30 days after transfusion.

- **➤ Why does it happen?**
- **➤** The pathophysiology of TA-GVHD involves engraftment of small numbers of donor-derived passenger leukocytes into a host whose immune system is unable to recognize these cells as foreign and/or unable to eliminate them.
- **➤** The infusion of any cellular blood product can theoretically cause

- **Management and prevention of TA-GVHD**
- ➤ When TA-GVHD develops, mortality approaches 100% as a result of complications of severe pancytopenia.
- ➤ Irradiation of all cellular blood products before transfusion—but not conventional leukoreduction—virtually eliminates the risk of TA-GVHD.

TABLE 177-3 TRANSFUSION-ASSOCIATED ADVERSE REACTIONS

ADVERSE REACTION	RISK PER UNIT INFUSED
Delayed serologic reactions	1 in 1600
Delayed hemolytic reactions	1 in 6700
Transfusion-related acute lung injury	1 in 8000
Graft-versus-host disease	Rare
Fluid overload	1 in 20
Febrile, nonhemolytic transfusion reactions	1 in 20-200
Allergic reactions	1 in 30-100
Anaphylactic reactions	1 in 150,000
Iron overload	After 80-100 U
Post-transfusion purpura	Rare
ABO-incompatible blood transfusions	1 in 30,000-60,000
Fatalities	1 in 600,000
Storage lesions	Unknown
Immunosuppressive effects	Unknown

