COMPLICATIONS OF BLOOD TRANSFUSION

DR AMIR HASAN MATINI MD. AP/CP

- Any unfavorable consequence is considered an adverse effect of blood transfusion. It is also referred to as a Transfusion Reaction
- Transfusion reactions occur in up to 10% of patients.
- Most common adverse side effects are usually mild and non-life-threatening

NON-INFECTIOUS COMPLICATIONS OF TRANSFUSIONS

- □ Acute (< 24°)
- □Immunologic □Non-immunologic
- □ Delayed (> 24°)
- □Immunologic □Non-immunologic

ACUTE (< 24°) IMMUNOLOGIC

- □ Hemolytic
- □ Fever/chills, non-hemolytic reaction
- □ Urticarial/Allergic
- □ Anaphylactic

ACUTE (< 24°) NON-IMMUNOLOGIC

- Hypotension associated with ACE inhibition
- Transfusion-related acute lung injury (TRALI)
- Circulatory overload
- Nonimmune hemolysis
- Bacterial/Sepsis

HEMOLYTIC REACTION

- Acute hemolytic transfusion reactions (AHTRs), by definition, present within 24 hours of transfusion.
- AHTRs are most commonly caused by transfusion of RBC units that are positive for an antigen against which the recipient has formed antibodies.
- AHTRs may also be seen with transfusion of antibodies (in donor plasma or IVIG) into recipients whose RBCs bear the antigen recognized by those antibodies

- Presenting signs include fever and chills, nausea, vomiting, pain, dyspnea, tachycardia, hypotension, bleeding, and hemoglobinuria.
- Fever is the most sensitive initial sign of an AHTR. Therefore, any increase in temperature of 1°C or greater should result in a transfusion being stopped and a laboratory evaluation initiated.

- Renal failure is a later complication. Pain during an AHTR has been reported as localizing to the flanks, back, abdomen, chest, head, and infusion site.
- A subjective feeling of distress is reported sometimes. Unexpected bleeding may be due to DIC. During surgery, hypotension and excessive bleeding may be the only signs of an AHTR

- Laboratory findings in AHTRs include hemoglobinemia, hemoglobinuria, elevated lactate dehydrogenase, hyperbilirubinemia, and low haptoglobin. The blood urea nitrogen and creatinine will be elevated if renal injury has occurred.
- The direct antiglobulin test (DAT) may show positive results with a mixed-field pattern if transfused incompatible red cells are present in the circulation
- ABO incompatibility due to a clerical error is the most common cause of AHTRs

- In the event of an AHTR, the transfusion should be discontinued and intravenous access maintained.
- The identity of the patient and the unit or units of RBCs should be reconfirmed, and other units of RBCs that have been dispensed for the patient should be located and quarantined. The reaction must be reported to the blood bank promptly. If a misidentification is discovered, another patient (e.g., with a similar name) may also be at risk for receiving incompatible blood.

DIFFERENTIAL DIAGNOSIS

- AIHA
- Nonimmune hemolysis
- Microangiopathic hemolytic anemia
- Drug-induced
- Infections

TREATMENT&PREVENTION

- Stop transfusion
- Supportive care to maintain renal function
- Goal of urine O/P 100 mL/hr. in adults for at least 18- 24 hours
- Treatment of DIC (Heparin – direct anticomplement effect)
- Prevention of clerical/human errors

FEBRILE NONHEMOLYTIC REACTIONS

- A febrile transfusion reaction is defined as a rise in temperature of 1°C or greater, possibly accompanied by chills or rigors.
- Symptoms usually occur during the transfusion but may be delayed for up to 1 hour after the procedure has been completed.
- A patient who is hypothermic at the start of a transfusion and then manifests an expected temperature rise to normal, without symptoms, is not having a febrile reaction

- Etiology
- □ Reaction □ Between recipient WBC antibodies (HLA, WBC antigens) against transfused WBC in product
- □ Cytokines that accumulates in blood bag during storage

- It is important to rule out a hemolytic transfusion reaction or bacterial contamination of the unit.
- Antipyretics, such as acetaminophen (325 to 500 mg) can be administered. Antipyretics are not necessarily required, as the fever of nonhemolytic transfusion reactions is self-limited and usually resolves within 2 to 3 hours.
- Diphenhydramine (25 to 50 mg) is commonly administered in this setting but probably has no effect on the course of febrile reactions

URTICARIAL/ALLERGIC REACTION

- Mild – urticarial
- "Anaphylactoid"
- Severe – anaphylactic
- Incidence : 1-3% of all transfusion reaction.
- Signs/Symptoms : Uriticarial/hives – upper trunk and neck
- Pulmonary signs (10%) – hoarseness, stridor , bronchoconstriction
- No cutaneous involvement
- GI – N/V, abdominal pain, diarrhea
- Circulatory – tachycardia, hypotension

- Etiology : Circulating antibodies against soluable material in the blood : Proteins in donor plasma , Binds to preformed IgE ab on mast cells
- Release of histamine , Vasoactive substances, C3a, C5a, leukotrienes
- Differential Diagnosis:
- Hemolytic
- Bacterial
- TRALI

TREATMENT/PREVENTION

- Discontinue transfusion
- Antihistamine/steroids
- Washing of blood products, pretreatment,leukoreduction?

SEVERE ALLERGIC (ANAPHYLACTIC) REACTIONS

- In addition to the signs of typical milder allergic reactions, anaphylactic or anaphylactoid reactions manifest cardiovascular instability, including hypotension, tachycardia, loss of consciousness, cardiac arrhythmia, shock, and cardiac arrest.
- Respiratory involvement with dyspnea or stridor may be more pronounced than is seen usually in typical allergic reactions.

- Patients with IgA deficiency who develop IgE anti-IgA can have anaphylactic reactions .
- Patients who have significant allergic reactions should be evaluated for their quantitative IgA levels.
- Recent transfusion may elevate serum IgA levels falsely
- However, if IgA deficiency has been established, anti-IgA testing should be done, usually by a reference laboratory. IgA-deficient plasma can be obtained from rare donor registries, if necessary.
- Red cells and platelets can be washed to remove sufficient amounts of IgA to prevent reactions.

- Patients with haptoglobin deficiency can have similar anaphylactic transfusion reactions due to IgG or IgE antihaptoglobin . Haptoglobin deficiency is rare in North American populations but is more common than IgA deficiency among Japanese patients suffering anaphylactic reactions.

TREATMENT&PREVENTION

- If an anaphylactic reaction occurs, the transfusion should be discontinued and intravenous access maintained. Supportive care, including intubation, oxygen, intravenous fluids, and placement of the patient in the Trendelenburg position, should be instituted promptly.
- Epinephrine should be available immediately.
- An antihistamine such as diphenhydramine, 50 to 100 mg, can be given intravenously, particularly when there are cutaneous manifestations such as urticaria. Aminophylline (6 mg/kg loading dose) may be useful when there is bronchospasm

HYPOTENSIVE REACTIONS

- Transfusion-associated hypotension is defined as hypotension that occurs during transfusion in the absence of signs or symptoms of other transfusion reactions, such as fever, chills, dyspnea, urticaria, or flushing.
- The degree of hypotension required for the diagnosis is controversial but could be defined reasonably as a drop of at least 10 mm Hg in systolic or diastolic arterial blood pressure from the pretransfusion baseline.
- if the immediate pretransfusion blood pressure is elevated from the patient's typical blood pressure and the arterial pressure does not fall below the patient's usual blood pressure, this should not be considered a hypotensive reaction.

- Hypotension begins during the transfusion and resolves quickly when the transfusion is discontinued. If hypotension persists beyond 30 minutes after discontinuation of the transfusion, another diagnosis should be strongly considered.
- Hypotensive reactions have been associated with red cell and platelet transfusions.
- Some reactions have been associated with the use of bedside leukocyte reduction filters

- If hypotension occurs, the transfusion should be discontinued and intravenous access maintained. The patient should be positioned with head down and feet elevated (Trendelenburg position), and isotonic fluids should be administered.
- The cause of transfusion-associated hypotension has not been established definitively. However, the condition is most likely due to the release of bradykinin through activation of the contact pathway of coagulation. Some reactions have been associated with angiotensin converting enzyme (ACE)–inhibitor drugs in the recipient and/or the use of leukocyte-reduction filters. ACE is the major enzyme that breaks down bradykinin in the circulation

- Some bedside filters, particularly those with a net-negative surface charge, appear to cause activation of kallikrein and cleavage of high molecular weight kininogen, which results in the release of bradykinin

TRANSFUSION-RELATED ACUTE LUNG INJURY

- Transfusion-related acute lung injury (TRALI) usually presents during or within hours of transfusion. Its symptoms include dyspnea, hypoxemia, tachycardia, fever, hypotension, and cyanosis.
- Profound hypoxemia PaO2/FiO2 < 300 mmHg
- PA wedge pressure 18 mmHg
- .Fever and hypotension, when present, are usually moderate and respond quickly to antipyretics and fluids. Characteristically, there is a lack of abnormal breath sounds. A chest x-ray usually shows pulmonary edema, most commonly in a generalized pattern rather than only along the major vasculature, as seen in cardiac failure.

- Patients with hematologic malignancy or cardiac disease appear to be at higher risk for TRALI .
- This may reflect the fact that these patient groups receive the majority of platelet transfusions.
- Reported mortality is approximately 20%, depending on the severity of the lung injury and the underlying clinical status of the patient

- The differential diagnosis includes circulatory overload, bacterial contamination, allergic reactions, acute respiratory distress syndrome (ARDS), pulmonary embolism, and pulmonary hemorrhage.
- The diagnosis is established by findings of noncardiogenic pulmonary edema. Pulmonary artery wedge pressure is not elevated. An increase in brain natriuretic peptide (BNP) from pre- to post-transfusion is found in circulatory overload, but not in TRALI.

- Characteristically, TRALI resolves within 48 to 96 hours from outset . Failure of the patient to improve substantially after this time should call the diagnosis into question.
- Although chest x-ray findings may persist beyond 7 days, no permanent pulmonary sequelae are evident, unlike with ARDS
- A decrease in leukocyte or platelet count may be a useful clue in TRALI caused by transfusion of HLA class I antibodie

- TRALI has been attributed to the presence of antibodies in the plasma of the transfused unit that are directed against HLA or granulocyte antigens present on recipient leukocytes
- Plasma from multiparous female donors may carry a greater risk for TRALI

- The treatment of TRALI is supportive. If a transfusion is in progress, it should be discontinued, and blood bags from recently transfused units should be recovered.
- The blood bank should be consulted regarding the evaluation of TRALI. Usually, oxygen is indicated. Severely affected patients may require mechanical ventilation.
- Corticosteroids appear to be of little, if any, value. Diuresis is not indicated in the absence of signs of fluid overload.

CIRCULATORY OVERLOAD

- Acute pulmonary edema due to volume overload
- Incidence
- One of the most common complications of transfusion
- Young children and elderly at risk
- Cardiac and pulmonary compromise
- Chronic anemia with expanded plasma volume
- Infusion of 25% albumin : Shifts large volume of extravascular fluid into the vascular space

- Signs/Symptoms : Dyspnea, cyanosis, orthopnea, HTN, CHF during or soon after transfusion
- Ddx: TRALI Allergic reaction. Other causes of CHF

TREATMENT&PREVENTION

- □ Stop transfusion
- □ Supportive care
- □ Phlebotomy
- □ Diuretic
- □ Slow transfusion
- □ Usually 4 hours, can be extended to 6 hours

NONIMMUNE HEMOLYSIS

- Lysis of RBCs as a result of storage, handling, or transfusion condition
- Incidence : Rare
- Signs/Symptoms :
- Transient hemodynamic
- Pulmonary impairment
- Renal impairment
- Hemoglobinemia and hemoglobinuria
- Hyperkalemia (renal failure)
- Fever

DIFFERENTIAL DIGNOSIS

- Immune Hemolytic
- Bacterial/sepsis
- PNH, drug-induced, oxidative stress, etc.
- Diagnosis of exclusion

- Stop transfusion
- Investigation of blood bag and tubing
- Investigate for hemolytic transfusion reaction.
- Check serum K
- Supportive care
- Maintain urine O/P