IN THE NAME OF GOD

Adverse Reactions Of Blood Transfusion

Atbin Latifi

M.D.

Pediatric Hematology Oncology Fellowship

Shahid Beheshti University of Medical Sciences

Mofid Children's Hospital

DEFINITION

- Any unfavorable transfusion-related event occuring in a patient during or after transfusion of blood components

CLASSIFICATION

Acute (Immediate) Reactions

Symptoms appear within minutes or up to 24 hours post transfusion

Delayed Reactions

Reactions occuring more than 24 hours following transfusion(up to months following)

ACUTE TRANSFUSION REACTION ETIOLOGY

- *Hemolytic Reaction (AHTR)*
- *Febrile Non-Hemolytic Transfusion Reaction(FNHTR)*
- *Allergic Reaction*
- *Anaphylaxis & Anaphylactoid Reaction*
- *Transfusion-Related Acute Lung Injury (TRALI)*
- *Transfusion-Associated Circulatory Overload(TACO)*
- *Therma Effects*
- *Bacterial Contamination*
- *Metabolic Complications*

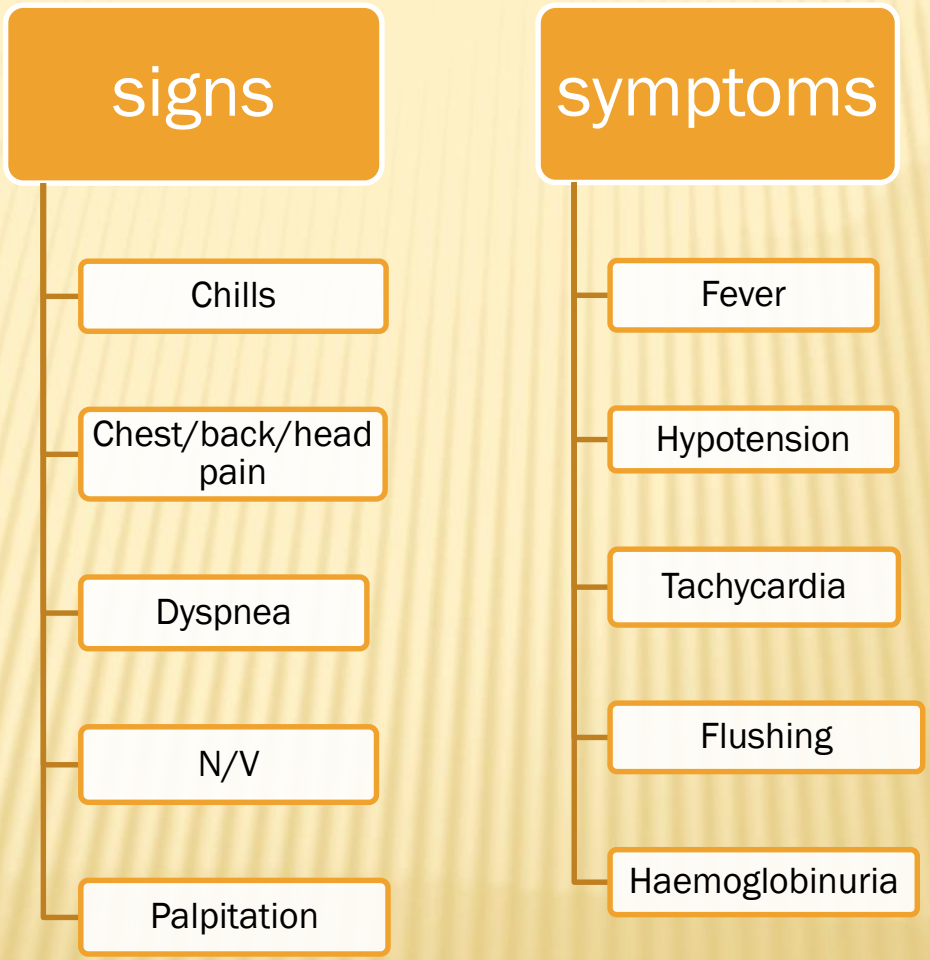
ACUTE HEMOLYTIC REACTION

- Minutes or sometime hours of initiating a transfusion
- 1/25000 Frequency
- Errors in patient identification or blood typing & compatibility testing
- Mostly due to ABO incompatibility (typically type O receiving non O blood) – may occur other blood types
- Igm mediated complement fixation leading to rapid intravascular hemolysis

ACUTE HEMOLYTIC REACTION

- Greater risk for a patient with thalassemia who travels to another center or admitted to a hospital not familiar with the case & medical history
- Two staff members check the identification of the unit and the recipient prior to beginning the transfusion
- Faster the insfusion rate, the more severe the reaction

ACUTE HEMOLYTIC REACTION



ACUTE HEMOLYTIC REACTION

Management

- Stop transfusion immediately
- Notify hospital blood bank urgently(another patient may also have been given the wrong blood !)
- The blood bank should also be alerted to the possibility of an undetected alloantibody
- Maintain an IV line
- Cardio respiratory support
- Maintain BP, HR and airway
- Ensure diuresis (Diuretic ? Dopamine ?)
- Collect first urine sample for haemoglobinuria
- Monitor blood urea & creatinine level
- Coagulation screen to rule out DIC

FNHTR

- Due to Abs in recipient against Ags of donor WBC
- Results from pyrogenes production (IL-1,IL-6,TNFa)
- Onset during or within 4 hours following transfusion
- 1/100 Frequency
- More common in multi-transfused patients

FNHTR

- Were more common in past decades , but dramatically reduced by leuco-reduction , especially pre-storage leuco-reduction , which sharply reduces cytokine accumulation and leucocyte alloimmunization
- It is important to distinguish from fever due to the patient's underlying disease or infection (check pretransfusion temperature). Fever may be the initial symptom in a more serious reaction such as bacterial contamination or haemolytic reaction.

FNHTR

Management

- If mild : Slow down the infusion / Use Antipyretics
- If severe : Stop transfusion / Antipyretics and symptomatic treatment
- Usually reactions are self limiting

ALLERGIC REACTION

- Usually due to plasma proteins
- 1/100 Frequency
- Range from mild to severe
- Milder reactions include urticaria, itching , conjunctival edema and flushing… are generally mediated by IgE
- Allergic reactions have been reported in patients who receive units of blood from donors who have been exposed to something that the patient is allergic to e.g. a donor eating strawberries donating blood to someone who is allergic to strawberries

ALLERGIC REACTION

- Occasional mild allergic reactions often can be prevented using antihistamines or corticosteroids before transfusion.
- Recurrent allergic reactions can be markedly reduced by washing the red cells to remove the plasma.

ALLERGIC REACTION

Management

Mild

- slow down rate of transfusion
- Check label & recipient identity
- Send Haemovigilance notification to blood bank
- Administer Antihistamine
- Transfusion may resume

Moderate

- Stop the transfusion
- IV fluids , oxygen , anti histamine
- Hydrocortisone considered

ANAPHYLAXIS & ANAPHYLACTIOD REACTION

Anaphylactic

- Stridor,dyspnea,bronchospasm,hypotension,shock,death

Anaphylactoid(less severe)

- Wide spread urticaria,cough,periorbital swelling,perilaryngeal edema…

ANAPHYLAXIS & ANAPHYLACTIOD REACTION

- 1/50000 Frequency
- Rapid onset ; Occurs within a few seconds to minutes following transfusion of a few ml of blood
- Especially in patients with IgA deficiency and anti-IgA antibodies (also patients with anhaptoglobinemia with anti haptoglobin antibody)
- Patients with IgA deficiency and severe allergic reactions may require blood from IgA - deficient donors

ANAPHYLAXIS & ANAPHYLACTIOD REACTION

Management :

- Stop the transfusion
- Airway support
- Adrenaline – 0.5ml (1 : 1000)
- Antihistamine(especially H2 blocker)
- Treat hypotension
- Steroids (Hydrocortisone)

TRALI

- Potentially severe complication
- 1/10000 Frequency
- Non-cardiogenic pulmonary edema
- Acute onset within 6 hours of blood transfusion
- **Delayed TRALI ; within 6 to 72 hours of blood transfusion**
- Patients at risk : cardiac surgery, sepsis, massive transfusion , induction chemo

TRALI

- Caused by specific anti-neutrophil or anti-HLA antibodies in donor plasma(from pregnancy?previous transfusion?) that activate the patient's neutrophils
- May also be due to non-antibody related accumulation of pro-inflammatory mediators during storage of donor red cells

TRALI

PATHOPHYSIOLOGY DUE TO ANTIBODY

Leukocyte Ab react with pt. leukocytes

↓

Active complements

↓

Adherence granulocyes to pulmonary endothelium with release of proteolytic enz. & toxic O2 metabolites

↓

Endothelial damage

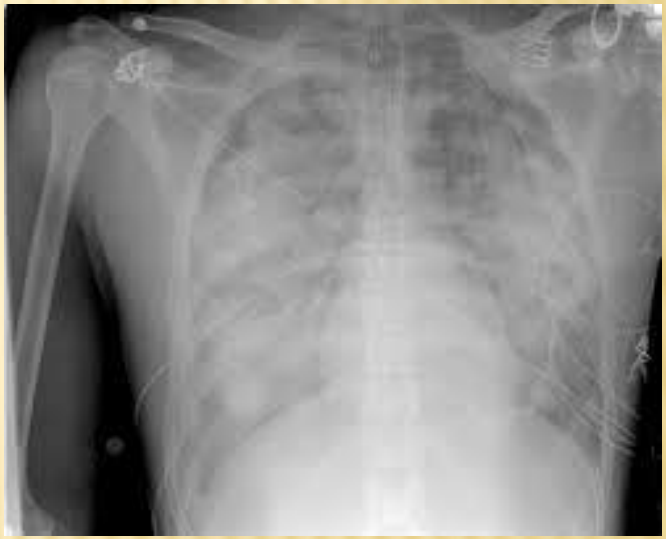
↓

Interstitial edema & fluid in Alveoli

TRALI

CLINICAL PRESENTATION

- Hypoxemia
- Fever
- Non-productive cough
- Tachypnea / Dyspnea
- Tachycardia
- +/- Hypotension
- Cyanosis
- Bilateral patchy alveolar infiltrates



TRALI

MANAGEMENT

- Supportive treatment
- 02 therapy
- Resolution within 48 to 72 hours
- But : mortality approximately 10%
- Streoids
- Diuretics may not usually helpful
- Most cases require mechanical ventilation

TACO

- In the presence of recognized or unrecognized cardiac dysfunction, or when the rate of transfusion is inappropriately fast
- Patient unable to compensate for expanded blood volume
- Acute cardiogenic pulmonary edema
- No fever
- Increased Blood Pressure

TACO

- Use appropriate transfusion rate
- Never exceed 2-4 cc/kg/hour unless bleeding
- Packed RBC slowly over 4 hours
- Not exceed 4 hours !

TACO

MANAGEMENT

- Rapid reduction of hypervolemia
- Respiratory & cardiac support
- 02 therapy
- Diuretics
- Inotropic drugs ?

THERMA EFFECTS

Hypothermia :

- Seen in recipients of large volumes of refrigerated blood products
- May lead to arrythmia
- Infants are particulary at risk
- Patients may feel cold but not shaking chills
- Warming the patient and/or blood product is needed
- Over warming blood → Hemolysis

BACTERIAL CONTAMINATION

- Transfusion of bacterially contaminated blood components
- But more frequent in platelet transfusion
- Yersinia , enterobacter , klebsiella…
- Usually within minutes of starting transfusion
- Chill , fever , N/V , hypotension , dyspnea , shock …

BACTERIAL CONTAMINATION

- Clinical features; like :

  AHTR but no hemoglobinurua

  no hemoglobinemia

  FNHTR but more severe
- Management; as :

  AHTR but add broad spectrum antibiotics
- Report immediately to blood bank(additional components must be recalled)

METABOLIC COMPLICATIONS

Citrate Toxicity

- Rapid administration of large quantities of stored blood may cause hypocalcaemia & hypomagnesemia (bind to citrate)
- More risks in liver dysfunction(inability to metabolise citrate) & neonates with immature liver function
- Causes myocardial dysfunction or coagulopathy (sign & symptoms of hypocalcemia…)

METABOLIC COMPLICATIONS

- *Management :*
- Temporarily stop the transfusion
- Give calcium
- Warming the patient
- Reassure the patient

- Use blood less than 7 days old for prevention

METABOLIC COMPLICATIONS

Hyperkalemia

- Reversible leakage of K during storage
- Clinically significant hyperkalaemia can occur during rapid, large volume transfusion of older red cell units in small infants and children

Use blood less than 7 days old for prevention

DELAYED REACTIONS

- *Delayed Hemolytic Transfusion Reaction(DHTR)*
- *TA-GVHD*
- *Alloimmunization*
- *Autoimmunization(Auto immune hemolytic anemia)*
- *Transfusion Transmitted Infections (TTI)*
- *Post Transfusion Purpura (PTP)*

DHTR

- Usually occur 5-14 days after transfusion
- May be due to an alloantibody that was not detectable at the time of transfusion or to the development of a new antibody
- Antibodies often Rh , Kidd , Duffy , Kell

DHTR

- Unexpected levels of anaemia, malaise and jaundice
- Renal impairment may occur in severe cases
- Less severe than Acute HR (no complement activation)
- Most DHR extravascular
- Positive DAT
- Increased LDH & bili and decreased haptoglobin
- Rare hemoglobinemia & hemoglobinuria

DHTR

- DHTR can not be predicted
- A sample should be sent to the blood bank to investigate the presence of a new antibody and to repeat cross-matching of the last administered unit(s)
- Good patient record & blood bank records are essential
- Clinical treatment usually not necessary
- Give Ag nagative units in future

TA-GVHD

- Caused by viable lymphocytes in donor red cell units that engraft and recognize host histocompatibility Ag and attack host tissues
- Rare but often fatal
- Immunosuppressed patients are at particular risk
- May also occur in immunocompetent recipients of red cells from a haploidentical donor such as a family member (when donor is homozygous for one of the patient's HLA haplotypes)
- Usually within 1-4 weeks of transfusion
- Characterized by fever, rash, liver dysfunction, diarrhoea and pancytopenia due to bone marrow failure

TA-GVHD

- Poor response to standard IST(ATG, cyclosporine,Ivig,glucocorticoid…)
- No success with MTX,Pentoxifylline,Thalidomide…
- Rituximab , Ibrutinib , Photophresis ; investigational??
- HSCT can be performed , but many limitations

- Prevention is the key
- To reduce the risk of TA-GVHD, donated blood from a family member should be avoided or if used should always be irradiate before transfusion.
- Leucodepletion alone is inadequate

ALLOIMMUNISATION

- Common complication
- Occurring in 10-20% of patients with thalassaemia
- More common in children who begin transfusion therapy after 1-3 years of age than in those who begin transfusion therapy earlier
- Some evidence suggests that new alloantibodies develop more frequently after splenectomy
- Important for females with child-bearing potential as these antibodies can cause severe haemolytic disease of the newborn during pregnancy

ALLOIMMUNISATION

PATHOPHYSIOLOGY

1st exposure

- Moderate production IgM & igG antibody by foreign antigens

2nd exposure

- Rapid production of large amounts of IgG

ALLOIMMUNISATION

- Difficulty in finding compatible blood
- The use of extended antigen matched donor blood is effective in reducing the rate of alloimmunisation

AUTOIMMUNISATION

- Very serious complication
- Usually but not always in patients with alloantibodies
- May be unrelated to transfusion
- Destruction of both the donor's and the recipient's red cells
- The serologic evaluation usually shows an antibody that reacts with a wide range of test cells and fails to show specificity for a particular antigen
- Steroids, immunosuppressive drugs and intravenous immunoglobulins are used for the clinical management

AUTOIMMUNISATION

- Occurs more frequently in patients who begin transfusion therapy later in life
- Should be carefully considered before instituting transfusion therapy for teenagers and adults with thalassaemia intermedia

PTP

Rare delayed transfusion reaction

Dramatic & sudden thrombocytopenia (platelet counts <10000 in 80% of cases)

Typically 7 to 10 days after a blood transfusion

Bleeding from mucous membranes and the gastrointestinal and urinary tracts is common

Concern about intracranial haemorrhage

Thrombocytopenia is expected to last approximately two weeks(usually self limiting)

Patients usually have a history of sensitisation by either pregnancy or transfusion with five times more female patients affected than males

PTP

- This reaction is due to antibodies to platelet-specific antigens, most human platelet antigen 1a (HPA-1a), however antibodies to HPA-1b, other platelet antigens and human leucocyte antigen (HLA) have also been implicated
- Intravenous immunoglobulin at 1 g/kg as a single dose and repeat as necessary with the platelet count expected to rise within the next four days

  Steroids and plasma exchange may be tried in refractory cases

- Platelet transfusion ; not effective

TRANSFUSION TRANSMITTED INFECTIONS

- Including

  Viruses(Hepatitis,HIV,Parvovirus,CMV,Prion…), Bacteria(Gram - & + , Syphilis…) Parasites(Malaria,Toxo,Chagas…)
- Major risk in blood transfusion
- Even in countries where residual risk of transmission through blood transfusion of clinically significant pathogens (HIV, HBV, HCV and syphilis) has been reduced to minimal levels, problems continue to exist or emerge

TRANSFUSION TRANSMITTED INFECTIONS

- Lab tests may fail to identify viruses during the window period or because of imperfect sensitivity
- The clinical significance of newly identified infectious agents is not always completely clarified and donors are not screened for these agents
- Currently no evidence that SARS-COV-2 is transmitted by blood transfusions, however, donor deferral due to recent illness or the logistics of donation during a pandemic (approximately 14 days from being infected ?)has affected blood stocks in many countries
- Absence of widely accepted or routine tests for bacterial, viral and other pathogens (Yersinia enterocolitica, hepatitisA, toxoplasmosis, malaria …)

TRANSFUSION TRANSMITTED INFECTIONS

- Growing interest in the use of pathogen inactivation/reduction technologies
- Greater development in platelet and plasma products and there are ongoing studies in the use of such technologies for red cell products

Transfusion of blood ???

consider when ;

the benefits clearly overweight risks

Thanks for your attention