Transfusion Reactions: Identifying and Providing Patient Care

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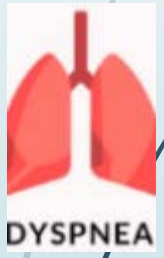
Learning Objectives

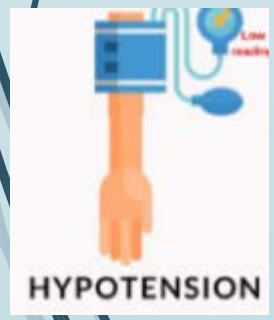
- Discuss the risks of blood product transfusions
- Discuss the signs and symptoms of a blood transfusion
- Review the common transfusion reactions and their causes
- Review clinical cases: discuss the management and the investigation results

Transfusion Reaction Symptoms

- **Fever, Chills/rigors, back pain**
  - Febrile non-hemolytic transfusion reaction (FNHTR)
  - Bacterial Sepsis or contamination
  - Acute hemolytic reaction

- **Dyspnea, hypoxemia, tachypnea, ^HR, ^BP, Hypotension**
  - Transfusion related acute lung injury (TRALI)
  - Transfusion-associated circulatory overload (TACO)
  - Transfusion Associated Dyspnea (TAD)





- **Urticaria, pruritus, flushing, bronchospasm, facial edema**
  - Minor allergic reaction
  - Severe allergic reaction

- **A hemolysis after Transfusion**
  - Acute hemolytic transfusion reaction
  - Hemolysis not related to RBC alloantibodies
  - Delayed hemolytic transfusion reaction

Callum JL., Pinkerton, PH., Lima, A., Lin, Y. (2016). Bloody Easy 4

Clinical Case I

- 58F with newly diagnosed AML
- On chemotherapy via Hickman line
- PMHX: HTN, hypothyroidism, and uterine fibroids. Daily fever
- Hb 74
- PLT 4
- WBC 0.3
- Received a pool of O Neg platelet on July 31, 2020 (exp. July 31, 2020 @MN)

- Transfusion started at 10:48
- Reaction noted at 11:31
  - Chills/ Rigors
  - T 39, P 108, RR 18, BP **80/49**

	Bacterial Contamination	Symptomatic Septic Reactions	Fatal Bacterial Sepsis
Buffy coat platelet pool	1 in 1,000	1 in 10,000	1 in 200,000
1 unit of RBC	1 in 50,000	1 in 250,000	1 in 500,000

Clinical Interventions and Investigation

Received O-negative Platelet on July 31, 2020. Start time 10:48; End time 11:31		
Pre-transfusion Vitals	T 37.9, P 85, RR 18, BP 107/63	
Post-Tx reaction Vitals	T 39, P 108, RR 18, BP **80/49**	
Clinical Symptoms	Chills and rigors	
Treatment	➢ Stop transfusion ➢ Repeat Vital signs ➢ Check patient's ID and Blood compatibility label ➢ Repeat G&S ➢ Notify MD	➢ Saline bolus ➢ Antipyretics ➢ Antibiotic
Investigation	• Blood Culture (PIV, CVAD) • Product sent to BB for culture • No growth was detect both patient and product culture	• No serological incompatibilities identified • CBS notified - investigation completed • CBS classified as FNHTR

Result of Investigation and Conclusion

Conclusion	Febrile Non-hemolytic Transfusion Reaction
Relationship	Possible
Severity	Grade 1 (non-severe)
Outcome	Minor or No Sequelae

Febrile Non-Hemolytic Transfusion Reaction (FNHTR)

- 38^0 C and $> 1^0$C from baseline
- Fever is not always present - chills/rigors alone
- Common - 1/300 RBC and 1/20 platelets
- **Cause**
  - cytokines from WBC, soluble proteins in plasma
  - alloimmunized patients more susceptible
- **Management**
  - Fever only and $<39^0$ – MD assessment, Acetaminophen, continue cautiously – max 4hours from issue (low risk fever)
  - *With fever $>39^0$ or associated symptoms – consider bacterial contamination or acute hemolytic reaction until proven otherwise (high risk fever)*
  - Demerol for rigors but do not restart transfusion
- **Prevention**
  - Premed with antipyretic if recurs

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Clinical Presentation Suspected Bacterial Sepsis

- Fever > 39^0 C (fever > 38^0 C with rigors + hypotension)
- Bacterial Sepsis or contamination
  - Fever, chills/rigors tachycardia, hypotension, N/V, dyspnea
  - Occurs most commonly with Platelet transfusion
  - Accounts for 10% of transfusion associated death

1 in 10,000	Symptomatic **bacterial sepsis**, per pool of platelets. Sepsis is when you get an infection in your bloodstream or tissue
1 in 40,000	Wrong ABO (blood) group, per unit of red blood cells
1 in 40,000	**Anaphylaxis**, which is an extreme sensitivity to a drug or substance that can result in death
1 in 200,000	Death from **bacterial sepsis**, per pool of platelets
1 in 250,000	Symptomatic **bacterial sepsis**, per unit of red blood cells
1 in 500,000	Death from **bacterial sepsis**, per unit of red blood cells

Direct Smear Atlas: A CD-ROM of Gram-Stained Preparations of Clinical Specimens. Lippincott Williams & Wilkins.

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Management and Prevention of Suspected Bacterial Sepsis

Management

- STOP the Transfusion!
- Collect patient blood culture from a different IV site
- Return blood product back to blood bank for culture and gram stain
- Supportive therapy (broad spectrum antibiotics)
- Report to blood bank
- Report CBS (blood bank)

Prevention

- ❑ Skin is disinfected at donation site
- ❑ First 40 mL of blood collected is diverted in a pouch
- ❑ CBS/HQ culture platelets
- ❑ Proper blood storage (RBC stored @ 1-6 degrees)

Clinical Case II

- 62 year old male end-stage renal disease on peritoneal dialysis
- Admitted to SBK with hypertension and peripheral vascular ds
- PMHX: CAD, NSTEMI, HTN, PD since 2018
- S/p left femoral-popliteal bypass
- Receives EPO 4000 IU for anemia prevention
- Received RBC for Hb 76 g/L on October 19, 2020
- RBC transfusion was given over 2 hours
- 30 min post transfusion completion rapid response called due to respiratory failure

Case # 961, 2020

Clinical Intervention and Investigation

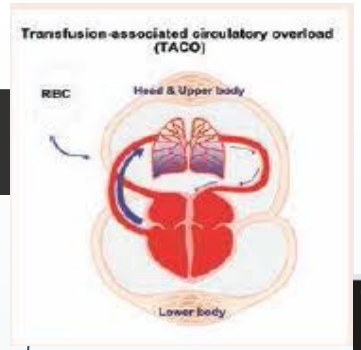
Received O-positive RBC on October 19, 2020. Start time 17:11; End time 19:12	
Pre-transfusion vitals	35.5, 87, 20 NP 2L O2 sat 93%,116/69
Post-Tx reaction vitals	35.6, 103, 24 O2 sat to 78%, NRB to 95%, 102/62
Clinical Symptoms	Hypoxemia, SOB, dyspnea, ^WOB, Decrease in O2 sat.
Treatment	Diuretics, Vasopressors, Supplementary O2, Mechanical Ventilation, Transfer to ICU,
Investigation	ECG- ST depression Lateral and Inf. Leads CXR – Severe pulmonary edema. Small bilateral pleural effusions.
Recommendation	Avoid transfusion, transfuse over 4hrs, premedicate with Lasix or remove extra 500mL during PD exchange

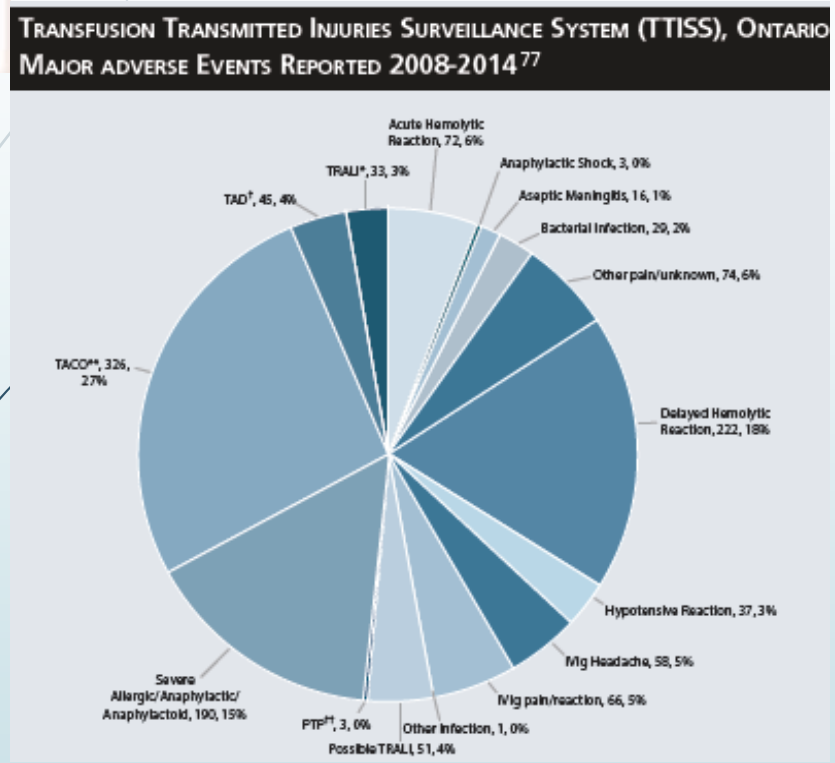
Case # 961, (2020)

Result of Investigation and Conclusion

Conclusion	Transfusion Associated Circulatory Overload
Relationship	Probable
Severity	Grade 3 (Life-threatening)
Outcome	Major or Long term sequelae (Myocardial Infarction)

Transfusion Associated Circulatory Overload (TACO)





- Circulatory volume overload temporarily associated with transfusion (within 12h) results from:
  - Impaired cardiac function, renal and pulmonary disease, sever anemia, and patients age > 70
  - Rapid rate of transfusion
  - Most commonly reported causes of transfusion-related mortality

ISBT TACO working group (2017)

Clinical Presentation of TACO

- Dyspnea, tachypnea
- Decreased O2 saturations
- Cough, cyanosis, orthopnea
- Hypertension and Tachycardia
- Increased central venous pressure
- Pulmonary edema
- Elevation in B type natriuretic peptide (NP) levels (BNP or NT-pro BNP)

JL. Callum, A. Lima, Y. Lin (2016). Bloody Easy 4; ISBT TACO working group (2017)

Management of TACO

- Stop transfusion
- Administer oxygen and diuretics as needed
- Radiographic chest imaging
- If restarting transfusion, restart at a reduced transfusion rate

ISBT TACO working group (2017)

Prevention of TACO

- Assess the patient prior to transfusion
- Consider pre-transfusion diuretics
- Monitor vital signs closely (^HR, ^BP)
- Avoid transfusion more than 1 unit at a time
- Transfuse over 4 period of time
- Component can also be divided into smaller aliquots

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ISBT TACO working group (2017)

Clinical Case III

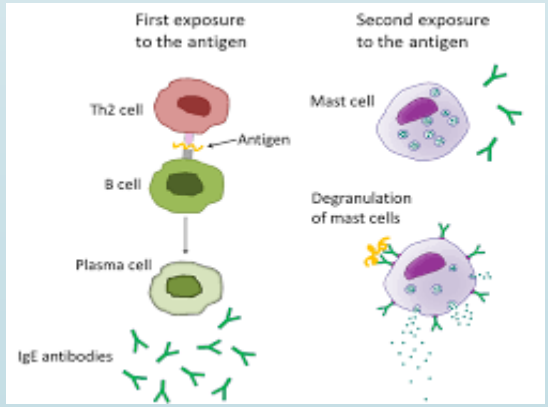
- 28M group O-positive admitted to SBK (July, 2020) for febrile neutropenia in the setting of Burkitt's Lymphoma
- Recently diagnosed with lymphoma. c/o of lower abdominal pain and ?appendicitis
- Underwent appendectomy with lymph node dissection
- Transfusion history: minor allergic reaction on Aug 2, 2020
- Hx Allergy: shrimp
- A transfusion reaction was reported on September 13, 2020 following transfusion of 1 pool of O-negative platelets.

Case # 942, (2020)

Clinical Intervention and Investigation

Platelet O Neg exp 2020-09-15. Start time: 11:55; end time: 13:10	
Pre-transfusion vitals	37.3, 92, 18 RA, 97/66
Post-Tx reaction vitals	37.7, 109, 18 RA, 106/72
Clinical symptoms	Urticaria, hives (chest), allergic associated edema (swollen lips and eyes), cough, and wheezing
Treatment	antihistamine administered, symptoms resolved within 2 hours
Investigation	Report to blood bank Report to CBS
Recommendation	The use of washed RBCs and premedicate with antihistamine prior to future platelet transfusions

Clinical Investigation cont.



- CBS did the investigation and contacted one of the donor
- Possibility of passive transfer of shrimp allergens via the transfused unit
- Serum shrimp IgE test (Shrimp ImmunoCAP f24) on patient serum
- Shrimp IgE was negative (sample drawn Sep 25)
- Recipient allergy history
- order total IgE, tryptase, and allergen specific serum IgE (ImmunoCAP f24) testing

Result of Investigation and Conclusion

Conclusion	Severe Allergic Reaction
Relationship	Definite
Severity	Grade 2 (severe)
Outcome	Minor or No Sequelae

Allergic Reaction

- 1 in 100 risk of events Minor Allergic Event (MAR)
- 1 in 40,000 risk of events Serious Allergic Reaction (SAR)

Minor Allergic Reaction Symptoms:

- Erythema, hives, flushing, swelling and pruritus. Can develop w/n seconds to several hours after receiving blood transfusion.
- ***Cause:*** *related to factors in the plasma portion of the blood component*

Severe Allergic Reaction Symptoms:

- Anaphylactic shock (tachycardia, hypotension)
- Bronchospasm (Dyspnea, SOB, wheezing, angioedema)
- Intestinal symptoms
- ***Cause***:

  - Transfusing an allergen to a sensitized patient.
  - Allergens in plasma or active allergy in donor, passive transfer of IgE (drugs or food)
  - IgA and haptoglobin deficiency

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Treatment of Allergic Reaction

- Stop transfusion temporarily & maintain IV access
- Administer antihistamine
- Administer corticosteroids
- Prevention of future allergic reaction by pre-medicating the patient with antihistamine
- Administering blood products that containing less plasma or administer washed cellular products

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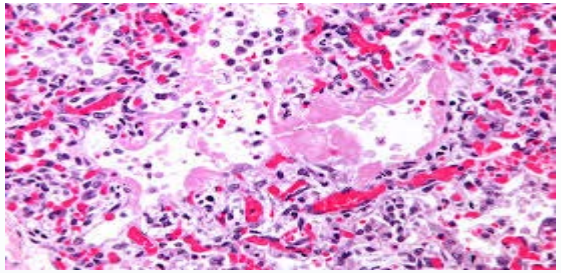
Clinical Case IV



- 69-year-old O+ female hospitalized with metastatic cholangiocarcinoma
- PMHX: stroke, NSTEMI, kidney and spleen infarcts
- She developed severe HF with increased dyspnea
- She has a history of multiple pregnancies
- No history of transfusion
- Received RBC transfusion on Oct 6th and developed severe respiratory distress → RRT

Clinical Intervention and Investigation

Received O positive RBC exp. Oct 27, 2020. Start time 01:55, end time 02:07		
Pre-transfusion vitals Post-Tx reaction vitals	37.3, 128, 40, 108/60 NP 1L - O2 sat 94% 38.1, 145, 45, 71/31, NP 1L - O2 sat 85%	
Clinical Symptoms	^WOB, tachypnea, SOB, tachycardia, hypotension, hypoxemia, O2 saturation <90%, PO2 <60 mmHg)	
CXR	Mild congestion, mild bilateral infiltrate, prominent pulmonary vasculature	
Treatment	• Stop transfusion • assessed by RRT • Supplemental Oxygen (.35 FM to 100% NRB) • Hydromorphone – improve dyspnea	• Lasix 40mg IV • Hemodynamic support (Levophed) • Fluid bolus for hypotension
Investigation & Reaction workup	• Hgb: 73, WBC 12.1 • BNP 8,249 (6,337) • Patient Cx- neg (pre-tx)	• No evidence of blood group or serological incompatibility • Product Cx neg • Anti HPA-5b detected • Anti- Fya, anti-HLA • Positive anti-neutrophil antibodies
CBS notified	TRALI form submitted	

Result of Investigation and Conclusion

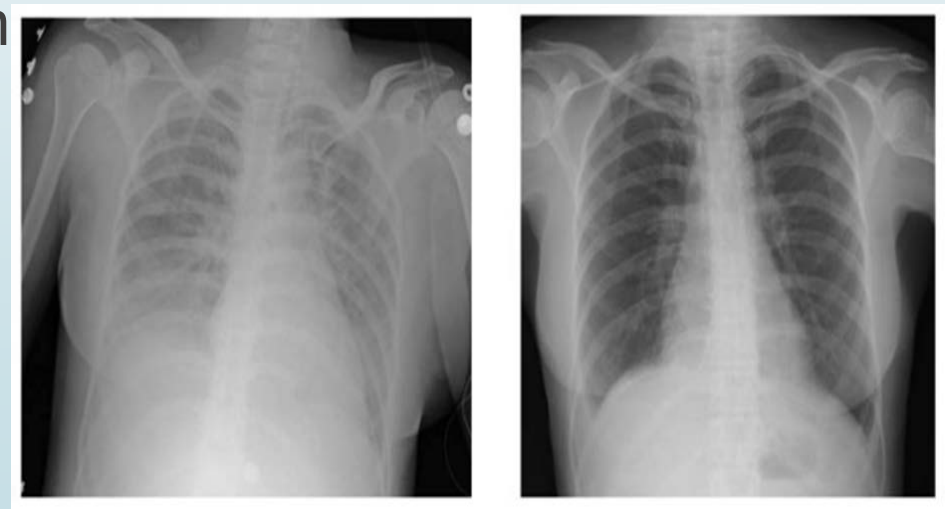
Conclusion	Transfusion Related Acute Lung Injury
Relationship	Probable
Severity	Grade 3 (Life-threatening)
Outcome	Death

Transfusion Related Acute Lung Injury (TRALI)

- A rare but serious syndrome characterized by sudden acute respiratory distress following transfusion
- In patients with no evidence of acute lung injury prior to transfusion
- Symptoms:
  - Occur during or within 6 hours of transfusion
  - No other risk factors for ALI
- **Cause**: not fully understood, multiple factors, immune mediated
  - Donor WBC/HLA/HNA antibodies – *From female donor*
  - Patient WBC/HLA/HNA antibodies
  - Bioactive substances in blood reacting with certain 'at risk' patients

Signs & Symptoms of TRALI

- Severe pulmonary edema
  - Chest X-Ray - ‘white-out’
  - CVP normal
- Copious secretions from ETT
- Hypoxia, dyspnea, cyanosis, cough
- Tachycardia
- Sometimes hypertension initially
- Hypotension (mild to mod)
- Fever 1-2^0
- Acute transient Leukopenia



Callum JL., Pinkerton, PH., Lima, A., Lin, Y. (2016). Bloody Easy 4
Polat et al. (2020). TRALI: A Case Report

TRALI Management

- Supportive care
- 70–80% need ventilatory support
- 100% need oxygen
- Diuretics and steroids not believed to be useful
- 90% recover in 2-3 days
- No permanent lung damage
- TRALI mortality -1 in 5,000 plasma containing transfusions
- Proper reporting of possible TRALI to CBS/HQ

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TRALI Prevention Strategies


CLINICAL GUIDE TO TRANSFUSION

- Follow transfusion guidelines
- Use plasma from male donors
- Use puffy coat platelet pools suspended in male plasma
- Use plateletpheresis collected from male donors
- Deferral of donors confirmed to be implicated in TRALI episode

Callum JL., Pinkerton, PH., Lima, A., Lin, Y. (2016). Bloody Easy 4

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