



Today's Agenda

- Case-based boards-based
- Thrombocytopenia
- Anemia
- RBC Transfusion Guidelines

60yo woman with DM and HTN admitted for dyspnea

- HPI: 4 days dyspnea, T 98.2F, BP 140/86, O2 sat 89% RA, breath sounds decreased at bases, +1 LE edema
- BNP 8320, trop T <0.01, creatinine 1.9
- CXR: Bilateral infiltrates (pulmonary edema)
- Echo: LVEF 55%, RV dysfunction
- V/Q scan: Mismatched perfusion defects consistent with bilateral PE









Thrombocytopenia: Work-up

- Peripheral blood smear:
 - Pseudo-thrombocytopenia: Platelet clumping
 - Microangiopathic hemolytic anemia (MAHA): Schistocytes
 - Sepsis: Toxic granulation, vacuoles
 - Myelophthisic (marrow invasion): Tear drops, left-shift
- DIC panel
- PF4 (HIT) Ab
- HIV, hepatitis, EBV, CMV
- ANA, lupus anticoagulant
- Ultrasound: Spleen size



NEVER

4 T's for HIT syndrome

- Thrombocytopenia:
 - − PLTs fall >50% \rightarrow 2 pts
 - − PLTs fall 30-50% \rightarrow 1 pt
 - − PLTs fall <30% \rightarrow 0
- Timing:
 - Onset 5-10d from heparin start → 2 pts
 - Onset >10d → 1 pt - Onset <5d → 0
- Thrombosis:
 - − New clot or skin necrosis \rightarrow 2 pts
 - − Progressive or suspected \rightarrow 1 pt
 - − None \rightarrow 0
- Other causes:
 - − None \rightarrow 2 pts
 - Possible \rightarrow 1 pt
 - − Definite \rightarrow 0

- Total:
 - <3: Low suspicion
 - 3-5: Intermediate suspicion
 - >5: High suspicion
- If intermediate or high:
 - D/C all heparin including flushes
 - Reverse warfarin with vitamin K
 - Start direct thrombin inhibitor (bivalirudin or argatroban)
 - Check anti-PF4 Ab

Negative predictive value: 99%

J Thromb Haemost 2006;4:759-65

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Heparin-Induced Thrombocytopenia

- Risk factors:
 - Heparin > enoxaparin
 - Orthopedic > cardiac surgery > medical patients
- Diagnosis:
 - 4-T score: Negative predictive value 99%
 - Anti-PF4 Ab: sensitivity >97%, specificity 74-94%
 - SRA: Sensitivity 95%, specificity 95%
- Risk of VTE continues for >1 month
 - Anticoagulate 4-6 weeks if no clot
 - Anticoagulate at least 3 months with clot
 - Start warfarin after PLTs are stable or >150k

My 4 T's for Thrombocytopenia

- Thrombocytopenia:
 - PLT <5: ITP, meds, bone marrow disorders (MDS, leukemia, aplastic anemia)
 - PLT <50: TTP/HUS</p>
 - PLT 40-150: HIT, hypersplenism, infections
 - Any PLT count: Meds
- Timing of decline:
 - Acute: Meds, infection, HIT (5-10 days)
 - Subacute: Leukemia, ITP
 - Chronic: MDS, ITP
- Thrombosis: HIT syndrome, APLS, malignancy, DIC, (ITP!)
- Other causes of thrombocytopenia: ITP vs. other



- HPI: Fevers, malaise, and productive cough
- PMHx: DM, hypertension
- MEDS: Insulin, lisinopril
- Exam: Appears unwell, lethargic, T 101.4F, BP 70/30, HR 120, O2 sat 90% RA, crackles at left base, trace ankle edema
- IV fluids, norepinephrine gtt, cefotaxime, levofloxacin, and vancomycin, enoxaparin
- 3rd hospital day: Platelets fell from 340k to 90k
- WBC 11.3, HCT 34%, MCV 88, PLT 90k, PT 12.6, INR 1.0, PTT 32, fibrinogen 290, BUN 30, creat 1.2



- What is the most likely cause of her thrombocytopenia?
- A) HIT
- B) ITP
- C) DIC
- D) Drug-induced thrombocytopenia
- E) MDS

66yo woman with DM, HTN, pneumonia: Thrombocytopenia

- What is the most likely cause of her thrombocytopenia?
- A) HIT
- B) ITP
- C) DIC
- D) Drug-induced thrombocytopenia
- E) MDS

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Drug-Induced Thrombocytopenia

- Suspect: Antibiotics especially...
 - TMP-SMX, penicillins, cephalosporins, vancomycin
 - Quinine, quinidine
 - Oxaliplatin, gemcitabine
 - Carbamazepine, phenytoin
 - Heparin
- Consider drug-specific platelet antibodies
- Onset: 1-2 weeks
- Recovery: Within 1 week (possibly up to 4 weeks)

36yo woman with no PMHx: Thrombocytopenia

- HPI: URI previous week, then developed rash
- PMHx: None
- MEDS: None
- Exam: Afebrile, 110/80, HR 80, O2 sat 98% RA, petechiae and ecchymoses
- WBC 7.6, HCT 38%, MCV 88, PLT 2k, PT 12.6, INR 1.0, PTT 32, fibrinogen 290, BUN 30, creat 1.2
- Smear: Confirms severe thrombocytopenia

*36yo woman with no PMHx: Thrombocytopenia

- WBC 7.6, HCT 38%, MCV 88, PLT 2k, PT 12.6, INR 1.0, PTT 32, fibrinogen 290
- What treatment should be tried first?
 - A) Dexamethasone
 - B) Prednisone
 - C) Rituximab
 - D) Plasmapheresis
 - E) Stem cell transplant

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ITP: Key Points

- Isolated thrombocytopenia: WBCs and RBCs are normal
- Diagnosis of exclusion
- WARNING: Wet purpura
- Chronic, relapses common
- Dexamethasone 40mg PO daily x4 days is standard of care







Anemia				
Low Retic count & Normal Bili/LDH	High Retic count & Normal Bili/LDH			
Hypoproliferative Anemia	Blood Loss			
Low Retic count & High Bili/LDH	High Retic count & High Bili/LDH			
Ineffective Erythropoiesis	Hemolytic Anemia			

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High Retic count & Normal Bili/LDH				
Blood Loss				
High Retic count & High Bili/LDH				
Hemolytic Anemia				





Case: 32yo woman with fever and rash

- What is the most likely diagnosis?
 - A) Iron-deficiency anemia
 - В) ІТР
 - C) Thrombotic microangiopathy (TMA)
 - D) Acute liver failure
 - E) Acute promyelocytic leukemia (APML)

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NEJM 1991;325(6):393-7

TTP: Key Points

- Mobilize troops:
 - Examine smear for schistocytes
 - STAT page Hematology & Blood Bank for plasmapheresis
 - Dialysis-bore central line
 - Don't rest until pheresis starts!
- ADAMTS13 activity and inhibitor level PRIOR TO PHERESIS

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Ineffective Erythropoiesis	Hemolytic Anemia		

Ineffective Erythropoiesis

- Erythropoiesis with early cell death
 - Can look like hemolysis, but without retics
- Etiology:
 - B12 and Folate Deficiency
 - MDS
 - Thalassemia

Case: 66yo man with dyspnea

- HPI: Exertional dyspnea worsening over 3 weeks, occasional lightheadedness
- PMHx: Osteoarthritis
- Meds: Naproxen, aspirin 81mg

Case: 66yo man with dyspnea			
LAB TEST	8 Months Earlier	Now	
WBC	6.3	8.1	
RBC	4.8	2.4	
Hb	13.2	7.5	
НСТ	41%	22.5%	
MCV	93	81	
PLT	188	480	
Retic count		1.1%	
Creatinine		0.9	

Case: 66yo man with dyspnea

- What is the most appropriate treatment for this patient?
 - A) EPO injection
 - B) Iron PO supplement
 - C) IV iron
 - D) pRBC transfusion
 - E) Hydroxyurea









RBC Transfusion Threshold RCTs

STUDY	THRESHOLDS	Ν	OUTCOMES
ICU NEJM 1999	Restrictive: Hb <7 Liberal: Hb <10	838	No difference in 30-day mortality (restrictive better in less severe patients or age <55)
TRISS (Transfusion Requirements in Septic Shock) NEJM 2014	Restrictive: Hb <7-7.5 Liberal: Hb <10-10.5	1005	No difference in mortality and ischemic events
Severe acute upper GI bleeds NEJM 2013	Restrictive: Hb <7 Liberal: Hb <9	921	Restrictive: Reduced transfusions and adverse events and improved 6-week survival
TRIGGER: Severe acute upper GI bleeds Lancet 2015	Restrictive: Hb <8 Liberal: Hb <10	936	No differences in bleeding, thrombosis, ischemic events, infections, mortality, QUALY

RBC Transfusion In Cardiac Surgery: Controversy Laid to Rest

STUDY	THRESHOLDS	Ν	OUTCOMES
TRACS: Elective cardiac surgery JAMA 2010	Restrictive: HCT <24 Liberal: HCT <30	512	No difference in 30-day mortality and inpatient complications
TITRe2: Elective cardiac surgery NEJM 2015	Restrictive: Hb <7.5 Liberal: Hb <9	2007	No difference in 3-month ischemic events, infections, hospital LOS Liberal: 30-day mortality rate lower (1.9% vs. 2.6%) – secondary outcome
TRICS III: Moderate-high-risk cardiac surgery NEJM 2017 NEJM 2018	Restrictive: Hb <7.5 Liberal: Hb <8.5 (non-ICU) or <9.5 (ICU)	5243	No differences in 1-month and 6- month mortality, ischemic events, readmission, coronary revascularization – primary outcome

Summary: RBC Transfusions

- Many RCTs, meta-analyses, systematic reviews support **RESTRICTIVE RBC transfusion**:
- Transfuse if Hb <7-8
- Saves RBC Units and \$\$\$
- No difference in outcomes
- Unresolved questions in cancer surgery patients, elderly, and orthopedics

DISCLOSURES

- Research funding: Biogen Idec, Genentech/Hoffman-LaRoche, Shire/Takeda
- Advisory Board: Bayer, Genentech, Shire/Takeda, Sigilon, Uniqure
- Consulting: Aspa, I-mAb, Sunovion