Hematology/Oncology

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HEMATOLOGY/ONCOLOGY

I. BLOOD PRODUCTS AND TRANSFUSION REACTIONS

A. Components

1. Red cells
   a. **Packed red cells** - contain rbcs, wbcs and 10% plasma. Preservative CDPA(citrate, dextrose, phosphate, adenosine)
      Volume 250 cc, Hct- 75%
   b. **Whole blood** - rarely used as produces volume overload and increased risk of transfusion reactions. Inefficient use of blood components.
   c. **Washed red cells** - RBCs without WBCs or plasma for patients with prior febrile reactions. Expensive. Time-consuming to produce.
   d. **Autotransfusion** - used in penetrating chest trauma. Returns patient’s own blood. Saves blood in major trauma centers.

2. **Platelets** - 5-10,000 increase per unit transfused. Typically give a “six-pack” to increase count to 30-60,000.

3. **Fresh Frozen Plasma (FFP)** - Contains all coagulation factors and reverses all coagulopathies. Risk of disease transmission. Typically give 2 units for every 4-6 units PRBCs

4. **Albumin** - Colloid that restores oncotic pressure. Heat treated so no risk of disease transmission. Two concentrations: -5% isotonic 500 cc bottle -25% hypertonic 50 cc bottle

B. Blood Groups

1. **Major** - ABO antigens
2. **Minor** - Rh (rhesus) 85% of the population is Rh positive

C. Compatibility Testing/Blood Ordering

1. **Type O neg** - Universal donor. Use in women of child-bearing age. Only 6% of population.
2. **Type O pos** - Safely given to males and postmenopausal women.
3. **Type specific blood** - Available in 15 min. ABO and Rh typing on recipient’s blood, but no crossmatch done. Also very safe to use.

4. **Typed and crossmatched blood** - Available in 45-60 min. ABO, Rh and antibody screen/crossmatch of donor and recipient’s blood. Must request a certain number of units that are held for patient.

5. Type and screen

D. Complications of Transfusions
1. **Acute Hemolytic Reaction** - ABO incompatibility usually due to clerical error. Presents with fever, chills, back pain, oliguria, hypotension, and DIC from immediate intravascular hemolysis. Stop the transfusion and give vigorous IV hydration to maintain renal perfusion.

2. **Delayed Hemolytic Reaction** - Minor blood group incompatibility resulting in extravascular (liver, spleen) hemolysis days later. Presents with fever, jaundice and anemia. Minimal clinical significance.

3. **Febrile Reaction** - Antibodies to donor WBCs and plasma proteins result in fever. Common. Prevent by using washed WBCs.

4. **Bacterial Contamination** - Now most common transfusion-transmitted infection.

5. **Allergic Reaction** - 2 types:
   a. IgA mediated - rare, can cause anaphylaxis
   b. IgE mediated - common, treated with antihistamines

6. **Disease Transmission**
   a. HIV - 1/600,000 units
   b. Hepatitis B - 1/200,000 units, Hepatitis C - 1/100,000 units
   c. Malaria - rare
   d. CMV, Epstein-Barr virus - usually results in subclinical infection.
   e. Chagas disease (trypanosomiasis) - problem in S. America
   f. Syphilis, Lyme disease
   g. West Nile virus

7. **Massive Transfusions**
   a. Dilutional coagulopathy and DIC
   b. Citrate intoxication with hypocalcemia
   c. Hypothermia - common, use blood warmers
   d. Microaggregates - might contribute to ARDS, CNS and renal dysfunction. Prevent with blood microfilter.

II. **COAGULOPATHIES**

   A. Thrombocytopenia

   1. Potential bleeding below 30,000 with a high risk of spontaneous bleeding below 10,000.
   2. Prolonged bleeding time. (normal < 8 min) Normal PT, PTT.
   3. Etiologies:
      a. Decreased production - e.g., aplastic anemia, chemotherapy
      b. **ITP (Idiopathic Thrombocytopenic Purpura)** - 2 types
         i. Acute- usually in children following a viral infection. Self limited, Rx with IV gamma globulin, steroids.
         ii. Chronic- usually in adults - may be autoimmune, due to drugs, SLE, HIV. Rx with steroids, immunosuppressants
sometimes splenectomy.

c. TTP (Thrombotic Thrombocytopenic Purpura, Hemolytic-Uremic Syndrome)
   i. Pentad
      - Microangiopathic hemolytic anemia with schistocytes
      - Thrombocytopenia
      - Fever
      - Renal insufficiency
      - Neurologic: HA, mental status changes, coma
   ii Treatment – plasmapheresis
   iii HUS
      - Pediatric variant
      - E. Coli 0157:H7 serotype
      - Bloody diarrhea and renal failure

B. Elevated PT

1. Coumadin therapy - reverse with FFP, vitamin K 1-10 mg orally or IV.
2. Severe liver disease (e.g., alcoholics)
3. Vitamin K deficiency - needed to make factors II, VII, IX, and X.

C. Elevated PTT

2. Hemophilia A - factor VIII deficiency
3. Hemophilia B - factor IX deficiency

D. Prolonged bleeding time

1. Von Willebrand’s disease
2. ASA therapy, NSAIDs, clopidogrel (Plavix)

III. HEMOPHILIA

A. Pathophysiology

1. Hemophilia A (Classic Hemophilia) - X linked factor VIII-C (coagulant) deficiency. 85% of hemophilies
2. Hemophilia B (Christmas disease) - X linked factor IX deficiency. 14% of hemophilies
3. Von Willebrand’s disease - Autosomal dominant deficiency of factor VIII-vWF and VIII-Ag results in platelet dysfunction. Most commonly inherited coagulopathy.
B. Clinical Presentation

1. Hemophilia - hemarthrosis, muscle hematomas, hematuria and CNS bleeds. May have severe (<1% activity), moderate (1-5% activity), or mild (5-30% activity) disease.
2. Von Willebrand’s disease - mucosal bleeding (epistaxis, gingival, menorrhagia, GI)

C. Treatment

1. Hemophilia A and Von Willebrand’s disease
   a. Cryoprecipitate - single donor
   b. Factor VIII concentrate - multiple donors
   c. Recombinant factor VIII - genetically engineered
   d. Desmopressin (DDAVP, vasopressin analog) - for minor bleeds, PO, IV, SQ

2. Hemophilia B
   a. Factor IX concentrate
   b. Recombinant factor IX
   c. Dosage for concentrates is 12.5 U/kg for minor bleeds (lacerations), 25 U/kg for moderate bleeds (hemarthrosis, muscle hematomas) and 50 U/kg for major bleeds (CNS, GI bleeds, pre-operative) and may need to be repeated q 8-12 hrs.

IV. SICKLE CELL ANEMIA

A. Epidemiology

1. Sickle cell disease - homozygous (SS) 56,000 in U.S.
2. Sickle cell trait - heterozygous (AS) 8 -10% of U.S. African Americans.

B. Pathophysiology

1. Valine substitution for glutamic acid on the beta-hemoglobin chain in the presence of deoxygenation results in irreversible cellular sickling which obstructs the microvasculature resulting in a painful vaso-occlusive crisis with tissue ischemia and hemolysis.

C. Clinical Manifestations

1. Hemolytic anemia- Hgb. 6-10 with reticulocytosis, cholelithiasis
2. Painful occlusive crisis- extremity, chest, abdominal pain often precipitated by dehydration, hypoxia, infection, trauma, stress.
3. End organ damage - CVA, priapism, leg ulcers, renal papillary
necrosis, and dactylitis.
4. **Acute Chest Syndrome** - pulmonary infarcts with chest pain, SOB, pulmonary infiltrates, hypoxia, 12% mortality – most common cause of death in SCD
5. **Aplastic crisis** - post infectious suppression of erythropoiesis
6. **Splenic sequestration** - shock in children due to microvascular obstruction resulting in splenomegaly, hypovolemia
7. **Splenic insufficiency** - in adults due to splenic infarcts. Prone to infection by **encapsulated organisms** (S. pneumonia, H. influenza, N. meningitides) and salmonella osteomyelitis.

D. Diagnosis and Treatment

1. Screening test followed by electrophoresis.
2. CBC, reticulocyte count, consider cultures.
3. Fluids, oxygen, analgesics, antibiotics as indicated.
5. Exchange transfusions for CVA, acute chest syndrome, priapism.

V. DISSEMINATED INTRAVASCULAR COAGULATION

A. Pathophysiology

1. An imbalance between **hemostasis** (excessive clotting) and **fibrinolysis** (excessive bleeding). Due to activation of the clotting cascade with consumption of clotting factors and platelets with fibrinolysis and fibrin deposition in the microvasculature causing tissue ischemia.

B. Clinical Presentation

1. Diffuse bleeding +/- tissue ischemia with an elevated PT, PTT, (d-Dimer) FSPs, and decreased platelets and fibrinogen levels.

C. Treatment

1. Treat the underlying cause
2. Replace blood, FFP, platelets
3. Consider heparin if thrombosis due to fibrin deposition

VI. SUPERIOR VENA CAVA SYNDROME

A. Introduction

1. Blockage of SVC by tumor
2. Small (oat) cell lung CA most common followed by bronchogenic (squamous cell) lung CA and lymphoma

B. Pathophysiology

1. Obstruction of the lumen by extrinsic compression, vein wall invasion by tumor or intraluminal thrombosis

C. Clinical presentation

1. Symptoms - headache, hoarseness, nausea, dyspnea, visual and mental status changes
2. Signs - facial plethora, chemosis, JVD, Stoke’s sign (increased neck collar size), caput medusae (dilated collateral veins over the trunk)

D. Diagnosis

1. Radiographs-
   a. CXR - right sided mediastinal mass
   b. CT chest

E. Treatment

1. Oxygen, elevate the head of the bed.
2. Radiation therapy - bronchogenic lung CA
3. Chemotherapy - small cell lung CA, lymphoma
4. Consider diuretics, steroids and anticoagulation

VII. HYPERCALCEMIA

A. Introduction

1. Common as it occurs in 10-20% of cancer patients.
2. Most common with prostate, thyroid, breast, lung, renal CA and multiple myeloma.
3. Median survival is only 4 weeks after diagnosis.

B. Pathophysiology

1. Mechanisms include bony metastasis, ectopic PTH, osteoclast activating factor production and immobilization.

C. Clinical Presentation

1. Nausea/vomiting, anorexia, polyuria, polydipsia, dehydration, weakness, lethargy, coma, constipation and abdominal pain.
D. Diagnosis

1. Serum calcium levels usually above 12 mg/dl. (N=8.5-10.5)
2. EKG reveals a **shortened** Q-T interval

E. Treatment

1. **Hydration** - 1-2 liters of 0.9NS in the first few hours
2. Diuresis - furosemide IV to promote Ca excretion.
3. Consider **bisphosphonates** (etidronate, pamidronate), gallium, steroids, calcitonin, mithramycin, and dialysis.

VIII. SPINAL CORD COMPRESSION

A. Introduction

1. A medical emergency.
2. Occurs in 5% of patients with systemic cancer.
3. Rapid diagnosis and treatment are essential for recovery.
4. Most common with prostate, thyroid, breast, lung, renal CA, multiple myeloma, and lymphoma.

B. Pathophysiology

1. Metastasis to vertebral body compresses the cord anteriorly. Occasionally an intervertebral mass causes compression. Rarely from an intramedullary tumor (in the cord itself)
2. Thoracic-70%, lumbar-20%, cervical-10%

C. Clinical presentation

1. **Back pain** in 96% of patients, usually localized to the level of the lesion.
2. Weakness, sensory loss, bladder dysfunction and ataxia are late findings.
3. Initially hypoflexic, later hyperreflexic with spasticity.

D. Diagnosis

1. Plain films are abnormal in 90% of patients.
2. **MRI spine survey** is the study of choice if available. Otherwise CT myelography or plain myelography.

E. Treatment

1. **Dexamethasone**, 10 mg IV
2. **Radiation therapy**
3. Decompressive laminectomy only if a tissue diagnosis is needed,
the spine is unstable or the patient has failed radiation therapy.

F. Prognosis

1. Best prognosis is with myeloma and lymphoma.
2. If ambulatory prior to treatment, 70% will remain ambulatory. If paralyzed, <10% will walk again.

IX. NEOPLASTIC CARDIAC TAMponade

A. Introduction

1. Neoplasm is the most common cause of cardiac tamponade.
2. From metastasis to the pericardium or post-irradiation.
3. Often misdiagnosed as CHF, pulmonary embolism or anxiety.

B. Pathophysiology

1. Pericardial fluid compresses the heart resulting in decreased diastolic filling and circulatory collapse.

C. Clinical Presentation

1. Symptoms - dyspnea, chest pain, cough, hoarseness, anxiety.
2. Signs - Beck’s triad of JVD, distant heart tones and hypotension. Diaphoresis, cyanosis, tachycardia and pulsus paradoxus.

D. Diagnosis

1. EKG shows low voltage, electrical alternans.
2. CXR shows a “water-bottle” heart.
3. Elevated CVP (>12-14).
4. Echocardiography is most helpful.

E. Treatment

1. Volume expansion and oxygen.
2. Pericardiocentesis if in shock.
3. Subxiphoid pericardial window with catheter placement for drainage and sclerotherapy. Possible RT/chemotherapy.

X. FEVER AND NEUTROPENIA

A. Introduction

1. Fever may develop due to infection (60%), chemotherapeutic agents, tumor necrosis, transfusions or antibiotics.
2. Incidence of infection increases with a PMN count <500/mm³.
(neutrophils and bands)

B. Clinical Presentation

1. Impaired inflammatory response from neutropenia makes it difficult to localize the source of infection.

C. Diagnosis

1. Examine for sinusitis, dental abscess, perirectal abscess (do not perform rectal exam), meningismus, cellulitis.
2. CBC, blood and urine cultures, CXR. Consider LP, viral and fungal cultures.

D. Treatment

1. **ED dose** of broad spectrum IV antibiotics. (e.g., piperacillin and an aminoglycoside, ceftazidime alone or with an aminoglycoside). (Vancomycin added if lines present)
2. Prophylactic antibiotic use
3. Reverse isolation.

XI. HYPERVIScosITY SYNDROME

A. Introduction

1. Waldenstrom’s Macroglobulinemia, Multiple Myeloma - sludging of immunoglobulins.
2. Leukemia - sludging of WBCs if > 100,000 polys, >250,000 lymphs.
3. Polycythemia - sludging of RBCs if Hct. > 60.

B. Clinical Presentation

2. **Retinopathy** with “sausage-link” or “boxcar” segmentation due to venous hemorrhage.
3. Mucosal bleeding due to abnormal platelet function.

C. Treatment

1. Plasmapheresis, leukapheresis, phlebotomy.
2. Hydration and chemotherapy.
XII. TUMOR LYSIS SYNDROME

A. Introduction
   1. Occurs 1-5 days following chemotherapy in rapidly growing tumors such as leukemia and lymphoma.

B. Pathophysiology
   1. Cell lysis results in hyperuricemia, hyperkalemia, hyperphosphatemia and subsequent hypocalcemia.

C. Clinical Presentation
   1. Hyperuricemia $\rightarrow$ renal insufficiency/failure
   2. Hyperkalemia $\rightarrow$ dysrhythmia
   3. Hypocalcemia $\rightarrow$ muscle cramping and tetany

D. Treatment
   1. Chemotherapy pretreatment with hydration and allopurinol.
   2. Urinary alkalinization is controversial as it improves uric acid diuresis, but may worsen hypocalcemic tetany.
   3. Dialysis is the treatment of choice.

XIII. COMPLICATIONS OF CHEMOTHERAPEUTIC AGENTS

A. Cyclophosphamide - BMS (bone marrow suppression), hemorrhagic cystitis

B. Methotrexate - renal toxicity, BMS

C. 5-fluorouracil - ataxia, BMS

D. Cisplatin - renal toxicity, ototoxicity

E. Bleomycin - pulmonary fibrosis

F. Adriamycin - cardiomyopathy

G. Vincristine, vinblastine- peripheral neurotoxicity
XIV. COMPLICATIONS OF RADIATION THERAPY

A. Skin - erythema, desquamation, atrophy and fibrosis

B. Lung - pneumonitis

C. Cardiac - pericarditis, myocarditis

D. GI - nausea/vomiting, bleeding, adhesions, fistulas

E. CNS - brain necrosis
HEMATOLOGY/ONCOLOGY

PEARLS

1. Hemolytic reactions are most commonly due to clerical errors, and are due to ABO incompatibility.

2. Protamine sulfate reverses the anticoagulant effect of heparin.

3. Von Willebrand’s disease is due to platelet dysfunction resulting in a prolonged bleeding time.

4. Desmopressin (DDAVP) can be used rather than cryoprecipitate in cases of minor bleeding in patients with hemophilia A and Von Willebrand’s disease.

5. Patients with sickle cell disease are prone to infections by encapsulated organisms, e.g., S. pneumonia and H. influenza.

6. Superior vena cava syndrome presents with facial plethora, dilated veins over the chest and arms, headache, visual difficulty and dyspnea.

7. Intravenous hydration is the initial treatment of hypercalcemia.

8. Hypercalcemia causes a shortening of the Q-T interval on the EKG.

9. Initial therapy of neoplastic spinal cord compression is intravenous steroids and radiation therapy.

10. Pain is the most common complaint with spinal cord compression -- weakness and sensory changes are late findings.

11. Electrical alternans on an EKG is diagnostic of pericardial tamponade.

12. A water bottle heart on X-ray is seen with pericardial effusions.

13. The incidence of infection increases in neutropenic patients when the neutrophil count drops below 500/mm3.

14. Fresh frozen plasma treats all known clotting factor defects, but with the risk of hepatitis and HIV transmission.

15. Each unit of platelets increases the platelet count by 5,000 to 10,000.
16. Febrile reactions during blood transfusion are due to sensitivity to donor WBCs and platelets. May be prevented by using washed RBCs.

17. Remember to consider autotransfusion of blood in patients with traumatic hemothoraces.
REFERENCES


15. Roy CL, et el: Does this patient with a pericardial effusion have cardiac tamponade. JAMA 2007: 297; 810


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