Oncologic Emergencies

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November 9th, 2022

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Objectives

- Explain the pathophysiology, etiology, and common causes of Tumor Lysis Syndrome
- Define the common lab findings, symptoms, pre-treatment considerations, and treatment options of Tumor Lysis Syndrome
- Describe the pathophysiology and risk factors of Disseminated Intravascular Coagulation (DIC)
- Differentiate between Acute DIC and Chronic DIC
- Identify the symptoms, common lab findings, treatment options, and supportive care of Disseminated Intravascular Coagulation (DIC)
- Identify the cancer types that are at risk for Spinal Cord Compression
- Differentiate between the symptoms of a cervical, thoracic, and lumbosacral spinal cord compression
- Explain how a spinal cord compression is diagnosed and the treatment options
- Define febrile neutropenia and the commonly seen symptoms
- Describe the assessment and management of febrile neutropenia as well as the consequences of delayed treatment and prevention tactics
- Understand the pathophysiology and risk factors of sepsis and septic shock
- Differentiate between early symptoms of sepsis, severe sepsis symptoms, and septic shock symptoms
- List the commonly seen lab results and treatment options of sepsis and septic shock

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Tumor Lysis Syndrome

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Tumor Lysis Syndrome

- What is TLS?
  - A condition in which serious electrolyte imbalances occur in the body as a result of rapid cell death and necrosis of tumor tissue
- Pathophysiology
  - As tumor cells die, their normal intracellular components, such as potassium phosphate, get released into the bloodstream
  - This can cause high concentrations in the blood that the kidneys cannot eliminate quickly enough causing electrolyte and metabolic dysfunction
  - If not treated quickly, it can cause neurologic, GI, renal, and cardiac failure, and death
  - Most commonly occurs 48-72 hours after treatment

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Tumor Lysis Syndrome

- Etiology
  - Typically associated with:
    - Leukemias with high white blood counts
    - Non-Hodgkin Lymphoma
    - Bulky, rapidly growing, treatment-responsive tumors
- Causes
  - Chemotherapy
    - Cisplatin, cytarabine, etoposide, paclitaxel, fludarabine, hydroxyurea, intrathecal methotrexate
  - Immunotherapy
    - Interferons, interleukins, rituximab, tumor necrosis factors
  - Hormonal Therapy
    - Tamoxifen
  - Corticosteroids
  - Surgery
  - Radiation

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Tumor Lysis Syndrome

- Laboratory Findings
  - Elevated:
    - Potassium >6 or an increase of 25% from baseline
    - Phosphorus >4.5 or increase of 25% from baseline
    - Uric Acid >8 or increase of 25% from baseline
  - Decreased
    - Calcium <7 or decrease of 25% from baseline

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Tumor Lysis Syndrome

- Signs and Symptoms
  - Initial
    - Nausea and vomiting
    - Abdominal pain or distension
    - Dypsnea
    - Dysrhythmias
    - Edema
    - Lethargy
    - Muscle or joint pain
    - Muscle twitching
  - Progressive
    - Increased GI symptoms
    - Oliguria, hematuria, azotemia, progressing to anuria
    - CHF, hypertension, then tachycardia, then bradycardia, progressing to ventricular arrhythmias
    - Progressive muscle weakness, paresthesias, tetany, and seizures
  - Unrecognized
    - Acute kidney failure
    - Cardiac arrest
    - DIC
    - Death

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Tumor Lysis Syndrome

- Pre-Treatment Considerations & Assessment
  - Labs
    - Electrolytes
    - Renal function
    - Liver function
  - Baseline weight
  - Baseline electrocardiogram
  - Diet considerations
    - Avoid foods high in potassium and phosphorus
  - Medication review
    - Avoid medications that may increase potassium (ACE Inhibitors, potassium sparing diuretics)

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Tumor Lysis Syndrome

- Treatment
  - Hydration
    - Aggressive hydration beginning 24-48 hours prior to the initiation of treatment and for 72 hours after treatment
    - Hydration supports renal blood flow, maintains urine output, decreased concentration of soluble acids in the urine
    - Ensure urine output is greater than 150-200mL/hour
  - Allopurinol
    - Prohibits precursors of uric acid
    - Given prophylactically, even to those with low risk
    - Begin medication 1-2 days prior to treatment and for 2-3 days post-treatment
  - Rasburicase
    - Converts circulating uric acid into water soluble metabolite, allowing plasma and urine uric acid levels to decrease rapidly

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Tumor Lysis Syndrome

- Treatment Cont.
  - Loop Diuretics
    - May help prevent fluid overload and maintain urine output
  - Oral Phosphate-Binding drugs (Albumin)
    - Treatment for hyperkalemia and hyperphosphatemia
  - Dialysis
    - If renal failure occurs

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Disseminated Intravascular Coagulation (DIC)

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DIC

- DIC is a complex system disorder that involves the activation of coagulation pathways, leading to thrombotic and hemorrhagic events
- Pathophysiology
  - DIC causes hypercoagulation, triggering the coagulation pathways to be initiated inappropriately
  - The cascade begins with the release of tissue factor, causing the release of thrombin
  - This release then causes plasminogen to convert to plasmin, causing fibrinolysis (the breakdown of fibrin within clots)
  - This then causes excessive fibrin degradation products (FDPs), which causes bleeding
  - The final result is a situation of simultaneous hemorrhage and clot formation and is a life-threatening event
  - Blood supply to vital organs is compromised

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DIC

- DIC is always associated with an underlying disorder
- Risk Factors
  - Sepsis
  - Some solid and hematologic cancers
  - Trauma, especially neurotrauma
  - Severe transfusion reaction
  - Organ destruction
  - Toxic reactions
  - Heat stroke / hyperthermia
  - Rheumatologic disorders
  - Some obstetric complications

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DIC

- Acute DIC
  - Causes
    - Infection is the most common underlying cause of acute DIC
      - Infection may produce a systemic inflammatory response, activating the cytokine system that begins the hypercoagulation cascade
    - Oncological Conditions
      - Acute promyelocytic leukemia (APL) is most often associated with acute DIC (85% of patients)
      - In APL, tissue factor is released directly from the promyelocyte blast cells into the blood stream, beginning the coagulation pathway of events
  - Symptoms
    - Bleeding that occurs simultaneously form at least 3 unrelated sites is a hallmark sign of acute DIC
- Chronic DIC
  - Causes
    - Solid metastatic mucinous adenocarcinomas and tumors of the prostate, breast, stomach, lung, and pancreas
  - Symptoms
    - Associated with minimal bleeding and diffuse thrombosis

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DIC

- Symptoms
  - Initial
    - Bleeding
      - Anywhere from occult/oozing to frank hemorrhage
    - Renal
      - Acidosis
      - Hematuria
      - Oliguria
      - Uterine hemorrhage
    - Pulmonary
      - Dypspnea
      - Hemoptysis
      - Cough
      - Tachypnea
      - Diminished breath sounds
      - Pleural friction rub

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DIC

- Symptoms Cont.
  - Initial
    - Integumentary
      - Jaundice
      - Petechiae
      - Skin necrosis of lower limbs
      - Thrombosis
      - Fever
  - Later Symptoms
    - Thrombus formation
      - Signs may be subtle but may manifest as organ dysfunction or failure occurs

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DIC

- Laboratory Findings
  - Decreased
    - Platelets
    - Fibrinogen level (severe cases, decreases slowly)
    - Antithrombin III
    - Plasminogen
    - Alpha-2 antiplasmin level
    - Protein C
  - Elevated
    - Fibrin degrading products (FDPs)
    - D-Dimer
    - Thrombin time
    - Firbinopeptide A level
  - Prolonged Results
    - Prothrombin time
    - Partial thromboplasmin time
    - International normalized ratio (INR)

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DIC

- Treatment
  - Goals
    - Early recognition and treatment of underlying cause
  - Treatment Options Based on Cause
    - APL
      - Treating with antineoplastic therapy can result in complete resolution
    - Prostate Cancer
      - Hormonal therapy
    - Infection and Sepsis
      - Antibiotic therapy
  - Correct coagulation abnormalities
  - Control and/or minimize bleeding
  - Control and/or minimize thrombotic events

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DIC

- Supportive Care
  - Hospitalization for close monitoring
    - Monitoring vitals, hemodynamic status, fluid status, weight, I&O, and oxygen
  - Anticoagulants
  - Blood products
    - Cryoprecipitates
    - Platelets
    - Plasma
    - Packed red blood cells (if active bleeding)
    - Coagulation factor concentrates

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Spinal Cord Compression

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Spinal Cord Compression

Cancer Types

- Tumors commonly metastasizing to the spinal cord
  - Lymphomas, neuroblastomas, seminomas
- Tumors commonly associated with bone metastasis that can result in SCC
  - Breast, prostate, lung, renal, myeloma, Non-Hodgkin lymphoma, Hodgkin Lymphoma
- Tumors that are primary spinal cord tumors
  - Ependymoma, glioma, astrocytoma

Location on the Spine

- Thoracic Spine – 70%
- Cervical Spine – 10%
- Lumbosacral Spine – 20%

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Spinal Cord Compression

- Cervical Symptoms
  - Early
    - Occipital headache, radiating to neck/shoulder, neck stiffness
    - Neurogenic shock (hypotension, bradycardia)
    - Paresthesia
    - Lhermitte sign (tingling sensation on back and extremities when neck is flexed or extended)
    - Hyperactive deep tendon reflexes
  - Late
    - Quadriplegia
    - Bladder, bowel, and sexual dysfunction
    - Autonomic hyperreflexia
    - Lesion above C4, may have diaphragmatic dysfunction

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Spinal Cord Compression

- Thoracic Symptoms
  - Early
    - Pain, local or radicular, or both
    - Abdominal muscle weakness
    - Lower extremity weakness
    - Paresthesia around the abdomen
    - Decreased sensation below the site of the lesion
    - Increased deep tendon reflexes distal to the lesion
  - Late
    - Lower extremity paralysis
    - Bladder, bowel, sexual dysfunction
    - Risk of autonomic hyperreflexia

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Spinal Cord Compression

- Lumbosacral Symptoms
  - Early
    - Pain, local, or radicular, or both, in groin and down legs (sciatica)
    - Pain while raising legs straight
    - Weakness in pelvic muscles & lower extremities
    - Ataxia gait
    - Paresthesia and numbness
    - Decreased reflexes
  - Late
    - Autonomic effects
    - Bowel, bladder, sexual dysfunctions

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Spinal Cord Compression

- Diagnosis
  - MRI – gold standard
- Treatment
  - Glucocorticoid therapy
    - Initial treatment
    - Reduces edema
  - Local radiation for radiosensitive tumors
  - Surgery
  - Laminectomy or kyphoplasty/vertebroplasty to stabilize vertebrae
  - Biophosphonates
  - Chemotherapy
  - Pain management

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Febrile Neutropenia

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Febrile Neutropenia

- Definition
  - A disorder characterized by an ANC < 1.0 and fever > 101.0 or a sustained temperature >100.4 for more than one hour
- Considered a medical emergency
- Prompt intervention is critical to avoid morbidity and mortality
- Symptoms
  - Hypotension (SBP <90)
  - Tachypnea (RR >24)
  - Serum Albumin - less than 3.3
  - Serum bicarbonate level – less than 21
  - Cross-reactive protein level (CRP) – greater than 20
  - High procalcitonin level – greater than 2.0

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Febrile Neutropenia

- Assessments & Management
  - Prompt intervention is essential
  - Blood and urine cultures
  - Chest X-ray
  - VRE swabs (if indicated)
  - Prompt administration of IV antibiotics
    - Cefepime is the most common first-line treatment
- Consequences of Delayed Treatment
  - Circulatory collapse
  - Acute respiratory failure
  - Sepsis and septic shock
  - Death

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Febrile Neutropenia

- Prevention
  - Educating patient and caregiver on infection prevention measures
  - Prophylactic use of colony-stimulating factors for those at high risk
    - Filgrastim and Pegfilgrastim
  - Prophylactic antibiotics, antivirals, and antifungals for patients with hematologic malignancies at high risk

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Sepsis & Septic Shock

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Sepsis & Septic Shock

- Pathophysiology
  - Gram-negative bacteremia is found in the majority of patients
  - Gram-positive bacteremia has been increasing due to the increased use of central vascular access devices and the use of cytotoxic agents
  - Endotoxins (released from gram-negative bacteremia) and exotoxins (released from gram-positive bacteremia) enter the blood stream
  - The endotoxins/exotoxins cause a release of histamine, interleukins, tumor necrosis factor-alpha, and vasoactive mediators, which in turn causes vasodilation
  - This process activates a coagulation cascade with fibrin/platelet aggregate formation resulting in microthrombin, seen in sepsis
  - The release of cytokines and increased thrombin formation continue to affect each other, leading to capillary leak syndrome, further vasodilation, increased fibrin formation, decreased blood flow, and decreased tissue perfusion

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Sepsis and Septic Shock

- Risk Factors
  - Granulocytopenia
    - Most common risk factor
    - Increased duration and severity increases the risk
  - Extreme age (>1 or <65)
  - Long intensive care hospitalizations
  - Loss of skin or mucosal injury
  - Malignancy-related immunosuppression
  - Humoral immunity modifications
  - Multiple myeloma
  - Chronic lymphocytic leukemia
  - Diabetes
  - Comorbid organ dysfunction
  - Presence of a vascular access device

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Sepsis & Septic Shock

Early Sepsis Symptoms

- High cardiac output with normal or slightly elevated blood pressure
- Capillary leak (edema develops)
- Subsequent hypotension
- Nausea

Severe Sepsis Symptoms

- Hypotension, causing hypoperfusion of organs
- Normal or elevated temperature
- Warm, flushed skin
- Bounding pulse
- Tachypnea
- Tachycardia
- Decreased gastrointestinal motility (nausea & vomiting)
- Abnormal hematologic status
- Hyperglycemia
- Lactic acidosis
- Oliguria
- Mental status changes

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Sepsis & Septic Shock

- Septic Shock Symptoms
  - Cold, clammy skin
  - Lethargy, progressing to coma
  - Hypotension
  - Tachycardia
  - Weak pulse
  - Tachypnea
  - Decreased breath sounds with pulmonary edema/rales
  - Renal failure
  - Persistent hematologic abnormalities
    - Hyperglycemia
    - Lactic acidosis
    - Hyponatremia
    - Hypokalemia
    - Hypocalcemia
    - Hypomagnesemia
    - Hypophosphatemia
    - Decreased albumin

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Sepsis & Septic Shock

- Lab Findings
  - Complete Blood Count
    - Increased or decreased white blood cells
    - Decreased hemoglobin
    - Decreased platelets
  - Metabolic panel
    - Glucose – increased with sepsis and septic shock, decreased with prolonged septic shock
    - Increased
      - BUN
      - Creatinine
    - Decreased
      - Sodium
      - Potassium
      - Calcium
      - Albumin
      - Magnesium
      - Phosphate
  - Prolonged Prothrombin time / partial prothrombin time
  - Elevated lactate
  - Elevated biochemical markers

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Sepsis & Septic Shock

Sepsis Treatment

- Fluid resuscitation
- Respiratory support
- DVT prophylaxis
- Antibiotics
- Antifungals
- Blood products
- Electrolyte replacement
- Nutritional support
- Insulin support
- Vasopressors and inotropic drugs
- Activated protein C replacement

Septic Shock Treatment

- ICU monitoring for aggressive and continuous monitoring
  - Central venous pressure monitoring
  - Oxygen support & pulse oximetry
- Aggressive fluid resuscitation
- Intubation and ventilation due to pulmonary edema, encephalopathy, and/or coma
- Supportive treatments
  - Prophylaxis for stress ulcers
  - DVT prophylaxis
  - Nutritional support
  - Assessment/intervention for delirium
  - Psychosocial support and education

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