ONCOLOGIC EMERGENCIES

Lisa Welsh, MBA, PA-C

LEARNING OBJECTIVES

Identify	Discuss	Identify	Identify
Identify common and uncommon signs and symptoms associated with oncologic emergencies	Discuss strategies for management of oncologic emergencies.	Identify patients at risk for oncologic emergencies and describe preventative measures.	Identify patients who have developed an oncologic emergency and need emergent or urgent interventions.

METABOLIC: HYPERCALCEMIA

- Common
- Up to 30% of patients with cancer
- Common associated malignancies:
  - Multiple Myeloma
  - Non-small cell lung (squamous more common)
  - Renal cell
  - Breast
  - Non-Hodgkin lymphoma
  - Leukemia
- Poor prognostic factor
- Paraneoplastic syndrome

METABOLIC: HYPERCALCEMIA

Pathophysiology:

1. **Humoral hypercalcemia of malignancy:**
   - Tumor production of parathyroid hormone-related peptide
   - Most common cause in solid tumor
   - High PTHrP levels = less response to bisphosphonates
2. **Osteolysis:**
   - Destruction and dissolution of the bone from bone metastasis
   - Breast, lung, myeloma
3. **Extrarenal calcitriol production by tumor cells:**
   - Least common
   - Hodgkin & Non-Hodgkin lymphomas, granulomatosis diseases
4. **Drugs:**
   - Supplements: calcium, vitamin D, lithium, thiazide diuretics

METABOLIC: HYPERCALCEMIA

Pathophysiology:

- Commonly associated malignancies:
  - Multiple myeloma
  - Breast
  - Squamous cell head & neck
  - Lung cancer
  - Renal
  - Cervical

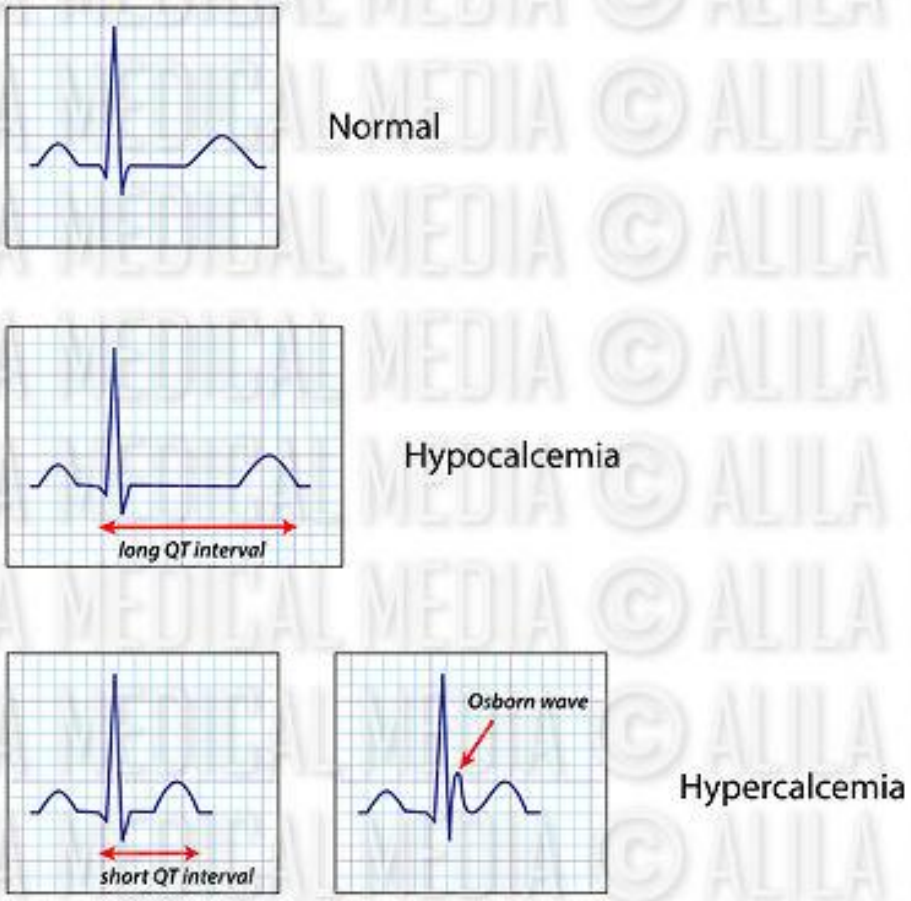
METABOLIC: HYPERCALCEMIA

Clinical Presentation

- Nonspecific complaints:
  - Anorexia
  - Nausea
  - Constipation
  - Lethargy
  - Polyuria
  - Polydipsia

Physical Exam

- Usually unremarkable
  - Volume depletion
  - Cognitive impairment
- Severe levels +/- rapid onset
  - Bradycardia
  - EKG: Short QT ± Osborn Wave
  - Cardiac arrest


Normal
Hypocalcemia
long QT interval
short QT interval
Osborn wave
Hypercalcemia
© Alila Medical Media - www.AlilaMedicalMedia.com

METABOLIC: HYPERCALCEMIA

Work Up

- CBC
- Complete metabolic panel
  - Calcium will need to be corrected for albumin
- Ionized calcium
- PTH
- EKG

METABOLIC: HYPERCALCEMIA

Treatment

- **Severe or symptomatic**
- **Calcium level >14mg/dL**
  1. **IV Fluids**
     - Volume expansion will increase renal clearance of Ca.
     - NS 0.9% preferred
     - 1000 – 2000mL in the first hour
     - 250-500mL / hr after bolus until adequate urine output / euvolemic

METABOLIC: HYPERCALCEMIA

- **Treatment Continued**
  - **Bisphosphonates**
    - Block osteoclastic bone resorption
    - Slow onset (2-3 days)
    - Pamidronate (60 – 90mg IV over 2-4 hours)
    - Zoledronic acid (4mg IV over 15mg)
    - Potentially nephrotoxic!
  - **Calcitonin**
    - Inhibits osteoclasts, enhances urinary excretion
    - Rapid onset, but patients will quickly stop responding
    - Subcutaneous injection
    - No renal adjustment

METABOLIC: HYPERCALCEMIA

Treatment Continued

- Glucocorticoids
- Inhibit conversion of calcidiol to calcitriol
- Prednisone 60mg oral daily
- Hydrocortisone 100mg IV every 6 hours

- Loop diuretics
- Should be avoided, unless patient is volume overloaded
- Exacerbates hypovolemia, impairs calcium excretion

METABOLIC: HYPERCALCEMIA

- Common
- Up to 60% of patients with cancer
- Common associated malignancies:
  - Small cell lung cancer
  - Lung cancer
  - GI
  - Lymphomas
  - Sarcomas
- Generally end of life

METABOLIC: HYPONATREMIA

Pathophysiology

1. **Secretion of antidiauretic horomone (SIADH):**
   - Malignancy – Paraneoplastic Syndrome
   - Hypovolemia
   - Salt-wasting nephropathy
2. **Drugs:**
   - Cyclophosphamide
   - Vincristine
   - Vinblastine
   - SSRIs

METABOLIC: HYPONATREMIA

Clinical Presentation

- Nonspecific complaints:
  - Headache
  - Seizures
  - Confusion
  - Lethargy
  - Nausea
  - Vomiting

Physical Exam

- Usually unremarkable
- Signs of hypovolemia
- Altered mental status

METABOLIC: HYPONATREMIA

Work Up

- CBC
- Basic metabolic panel
  - Sodium <135 mEq/L
  - BUN: (usually) <10
- Serum osmolality: <280 mOms/kg
- Urine osmolality: >100 mOms/kg
- Urine sodium: >40 mEq/L

METABOLIC: HYPONATREMIA

Treatment

- Severe or symptomatic
- Hypertonic saline (3%) at 3mL/kg over 30-60 minutes
  - Check sodium levels every 1 – 2 hours
  - SLOOOOOWLY correct (8 – 10 mEq/L in 24 hours)
- Furosemide (if risk for volume overload)
- Vaptans
  - Tolvaptan 15 – 60 mg oral daily up to 30 days
  - Conivaptan 20mg IV x1 then 20mg/24h x 2-4 days

METABOLIC: TUMOR LYSIS SYNDROME (TLS)

- Common / uncommon
- Depends on the type of malignancy
- Common malignancies - high turn over of cells:
  - Acute leukemias
  - Lymphoma (high grade)
  - Small cell
- Generally starts after starting therapy
- Can present with TLS

METABOLIC: TUMOR LYSIS SYNDROME (TLS)

Pathophysiology

- Metabolic derangement due to death of malignant cells
- Cells release intracellular components into circulation

METABOLIC: TUMOR LYSIS SYNDROME (TLS)

Clinical Presentation:

- Decrease urinary output
- Uremic symptoms
  - Fatigue
  - Cramping
  - Nausea / Vomiting
  - Hiccups
  - Confusion
  - Metallic taste
- Seizures
- Tetany

Physical Exam:

- Usually unremarkable
- May have arrythmias

METABOLIC: TUMOR LYSIS SYNDROME (TLS)

Work up

- **CBC**
  - **WBC for risk stratification**
- **CMP**
  - **Potassium: > 6mg/L (or 25% increase) -** usually the FIRST sign of impending TLS
  - Phosphate: > 4.5mg/dL (or 25% increase)
  - BUN: elevated
  - Creatinine: > 1.5 x upper limit of normal
  - Calcium: < 7 mg/dL (or 25% decrease)
- **LDH: Elevated**
- **Uric Acid: >8 (or 25% increase)**
- **Urine pH: <5**
- **EKG: Possible arrythmias due to electrolyte dysfunction**

METABOLIC: TUMOR LYSIS SYNDROME (TLS)

Table 1
Cairo and Bishop[13] definitions of tumor lysis syndrome

Laboratory TLS[a]	
Uric acid	≥476 μmol/L or 25% increase from baseline
Potassium	≥6.0 mmol/L or 25% increase from baseline
Phosphorous	≥2.1 mmol/L children, ≥1.45 mmol/L adults, or 25% increase from baseline
Calcium	≤1.75 mmol/L or 25% decrease from baseline
Clinical TLS = Laboratory TLS and 1 or more of:	
Creatinine level ≥1.5 times upper limit of normal for age and sex	
Cardiac arrhythmia or sudden death[b]	
Seizure[b]	

[a] Laboratory TLS defined as any 2 or more values that meet criteria and occur within 3 days before or 7 days after chemotherapy initiation, in the presence of adequate hydration and treatment with a hypouricemic agent.
[b] Not attributable to a therapeutic agent or other identifiable cause.

METABOLIC: TUMOR LYSIS SYNDROME (TLS)

Risk Stratification

	Risk group		
	Low	Intermediate	High
NHL	Indolent NHL	DLBCL	Burkitt's, lymphoblastic
ALL, WBC	$\leq$ 50,000/m^3	50,000-100,000/m^3	$\geq$ 100,000/m^3
AML, WBC	$\leq$ 10,000/m^3	10,000-50,000/m^3	$\geq$ 50,000/m^3
Other malignancies	UA < 7.5 mg/dL	Elevated LDH High tumor burden, rapid cell turnover or high chemosensitivity	UA $\geq$ 7.5 mg/dL Preexisting renal insufficiency

NHL: non-Hodgkin's lymphoma, ALL: acute lymphoblastic leukemia, WBC: white blood cell, AML: acute myeloid leukemia, UA: uric acid, DLBCL: diffuse large B-cell lymphoma, LDH: lactate dehydrogenase.

METABOLIC: TUMOR LYSIS SYNDROME (TLS)

Prevention & Treatment

- Hydration
- Low – Intermediate Risk
  - Allopurinol 200 – 800mg daily in 1 – 3 divided doses
    - Does NOT break down existing uric acid
    - Dose adjust for renal function
  - Febuxostat 120mg daily
    - No dose adjustment for mild – moderate renal impairment
    - Better control of serum uric acid
- High Risk - Already Developed
  - Rasburicase 3mg or 0.2mg/kg IV daily for 5 - 7 days
    - Lowers existing uric acid
  - Correct electrolytes – use caution with calcium!

METABOLIC: HYPOGLYCEMIA

- Rare
- Common malignancies:
  - Insulinomas
  - Extensive hepatic metastasis / hepatic failure
- Symptoms:
  - Confusion, palpitations, anxiety, shortness of breath, hunger
- Work up:
  - Hypoglycemia
- Treatment:
  - IV dextrose
  - Oral carbohydrate

METABOLIC: ADRENAL FAILURE

- Uncommon
- Cushing's Syndrome - Paraneoplastic Syndrome
- Common etiologies:
  - Extensive adrenal metastasis
  - Suddenly stopping prolonged glucocorticoids
  - Megestrol acetate (either on therapy or suddenly stopping)
  - Immunotherapy (ipilimumab, nivolumab, pembrolizumab)
- Presentation:
  - Weakness, hypotension, shock, hyponatremia, hyperkalemia
  - Cushingoid
- Treatment:
  - NS 0.9%
  - Glucocorticoids
    - Dexamethasone 4mg IV – preferred (no interference with assay)
    - Hydrocortisone 50 - 100mg IV

STRUCTURAL: SUPERIOR VENA CAVA SYNDROME

- Common
- Common etiologies:
  - Thoracic malignancies
  - Thrombus

STRUCTURAL: SUPERIOR VENA CAVA SYNDROME

Pathophysiology

1. **Extrinsic compression by tumor**
   - Decreased venous drainage from upper extremities, head & neck
   - Below azygous vein – more severe symptoms
   - Lung, lymphoma, germ cell
2. **Thrombus:**
   - Catheters and lines

STRUCTURAL: SUPERIOR VENA CAVA SYNDROME

Clinical Presentation

- Cough
- Shortness of breath
- Fullness
- Headache worse when bending
- Dizzy / light headed
- Orthopnea
- Chest pain
- Hoarseness

Physical Exam

- Arm swelling
- Facial swelling
- Dilated chest veins
- Stridor
- Altered mentation


7 AM

STRUCTURAL: SUPERIOR VENA CAVA SYNDROME

Work Up

- CT with IV contrast
- Chest X-ray – right hilar mass
- MRI when IV contrast contraindicated

Structural: Superior Vena Cava Syndrome

Treatment

- Most SVC cases are NOT an emergency
- Cerebral edema, impending circulatory collapse, airway edema need urgent intervention

Treatment Options

- Endovascular stent
  - Treatment of choice
- Radiation
  - Effective
  - Slow response
  - Need tissue FIRST

Supportive Care

- Oxygen
- Diuretics
- Glucocorticoids
  - If lymphoma suspected, need tissue FIRST
- Anticoagulation

STRUCTURAL: AIRWAY HEMORRHAGE

- Erosion of tumor into airway
- Proximal vs distal
- “Massive hemoptysis” 100 – 600 mL over 24 hours
- Common malignancies:
  - Lung cancer
  - Squamous cell carcinoma of head & neck
- Airway compromise from blood is the emergency

STRUCTURAL: AIRWAY HEMORRHAGE

Clinical Presentation

- Coughing blood
- Dyspnea

Exam

- Respiratory distress
- Hypoxia
- Hemoptysis

Work up

- CT angiography
- Bronchial angiography with embolization
- Rigid bronchoscopy

Management

- **Protect the airway**
- Lateral decubitus with bleeding side down
- Correct coagulopathy
- Transfusions
- IV fluids

STRUCTURAL: AIRWAY OBSTRUCTION

- Erosion or extrinsic compression of tumor into airway
- Common malignancies:
  - Lung cancer
  - Anaplastic thyroid
  - Squamous cell head & neck
  - Germ cell
  - Lymphomas

STRUCTURAL: AIRWAY OBSTRUCTION

Clinical Presentation

- Shortness of breath
- Cough
- "COPD exacerbation"

Exam

- Respiratory distress
- Inspiratory stridor
- Focal wheezing
- Hemoptysis

Work up

- CT with contrast
- Bronchoscopy

Management

- **Protect the airway**
- Oxygen
- Bronchodilators
- Stenting – but can cause infections
- Laser
- Radiation

STRUCTURAL: MASSIVE PULMONARY EMBOLI

- Second leading cause of death in cancer patients
- Malignancy and anti-tumor therapies increase risk

STRUCTURAL: MASSIVE PULMONARY EMBOLI

Clinical Presentation

- Shortness of breath
- Chest pain

Exam

- Respiratory distress
- Hypoxia
- Hemoptysis

Work up

- CT angiography
- Echo

Management

- **TPA if right ventricular strain**
- Anticoagulation

STRUCTURAL: PERICARDIAL EFFUSION / TAMPONADE

- Common, usually asymptomatic
- Metastatic, tumor invasion or drug related
- Rapid accumulation more symptomatic
- Pleural effusions can present similarly and may require drainage.

STRUCTURAL: PERICARDIAL EFFUSION / TAMPONADE

Clinical Presentation

- Shortness of breath
- Cough
- Chest pain

Exam

- Tachycardia
- Hypotension
- Distant heart sounds
- Pulsus paradoxus
- Edema

Work up

- Echo - Effusion and hemodynamics
- EKG - Low voltage, electrical alternans
- MRI – Tumor invasion

Management

- **Pericardiocentesis**
- **Pericardial window with drain**

STRUCTURAL: SPINAL CORD COMPRESSION

- Common
- Common malignancies:
  - Multiple myeloma
  - Lymphoma
  - Breast cancer
  - Lung
  - Prostate
  - Kidney
- Thoracic spine at highest risk
- High index of suspicion

STRUCTURAL: SPINAL CORD COMPRESSION

Clinical Presentation

- Back pain
  - Night
  - Worse w/ movement
  - Worse laying down
- Bowel / bladder problems

Exam

- Extremity weakness (proximal muscles)
- Inability to walk
- Hyperreflexia
- Decreased sensation

Work up

- MRI with & without contrast – entire spine
- CT with or without myelography

Management

- **Glucocorticoids**
  - **Dexamethasone 10 – 16mg x1 then 4mg q4-6**
- **Surgery**
- **Radiation**
- **Autonomic dysfunction ± Weakness requires emergency treatment**

STRUCTURAL: BRAIN METASTASIS

- Common – up to 20%
- Commonly associated cancers:
  - Non-small cell lung
  - Small cell lung
  - Breast
  - Renal
  - Melanoma
- Hematogenous spread of tumor cells

STRUCTURAL: BRAIN METASTASIS

Clinical Presentation

- Headache
- Neurological changes
- Seizures (usually multiple mets)

Exam

- Gait dysfunction
- Speech difficulty
- Cognitive difficulty

Work up

- MRI with and without contrast
- CT brain

Management

- **Impending brain herniation**
  - Intubation, avoid hypotension, 3% saline or mannitol
  - Dexamethasone 4 – 16 mg
- **Edema**
  - Dexamethasone 4 – 8mg

AUTOIMMUNE: LAMBERT-EATON SYNDROME

- Proximal muscle weakness
  - SCLC – Up to 3%
  - Caused by antibodies that target voltage gated calcium channels at NMJ
- Can be confused with myasthenia gravis
  - Starts in extremities & moves up
  - Weakness improves with activity
  - More prominent in lower extremities

Treatment:

- Immunosuppression
  - Steroids
  - IVIG
- Plasma exchange
- Anti-tumor therapy

HEMATOLOGIC: HYPER VISCOSITY

- High levels of circulating immunoglobulins coat cells, leading to increased blood viscosity, sludging and hypoperfusion.
- Commonly associated malignancies:
  - Waldenstrom macroglobulinemia - 10 – 30%
  - Leukemia
  - Multiple myeloma

HEMATOLOGIC: HYPER VISCOSITY

Clinical Presentation

- Spontaneous bleeding
- Shortness of breath
- Neurological defects
- MI

Exam

- "Sausage like" hemorrhagic retinal veins
- Bleeding

Work up

- CBC
  - Rouleaux formation
  - +/- Thrombocytosis
  - +/- Erythrocytosis
- Immunoglobulins – IgM elevated (generally >60)

Management

- **AVOID Transfusion**
- Plasmapheresis

HEMATOLOGIC: LEUKOSTASIS

- Rapid proliferation and disrupted cell adhesion resulting in large number of leukemic blasts.
- Immature leukocytes larger than mature
- Abnormal interaction between leukemic blasts and endothelium
- Most common malignancies:
  - AML
  - ALL
- Chronic leukemias less likely to cause symptoms

HEMATOLOGIC: LEUKOSTASIS

Clinical Presentation

- Bleeding
- Pain
- Fevers
- Shortness of breath
- Visual changes

Exam

- Pulmonary infiltrates
- Fever
- Neurological changes

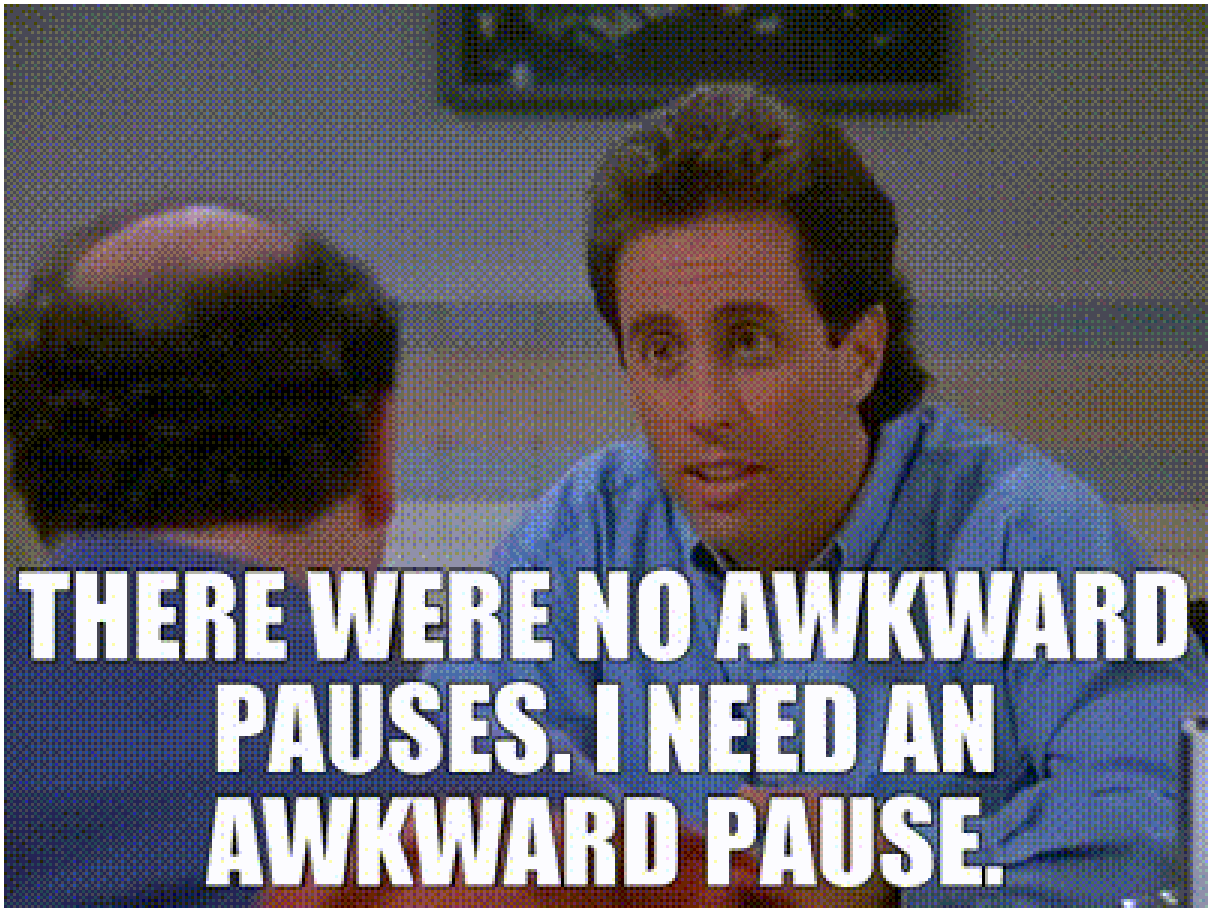
Work up

- CBC
  - Generally WBC >100

Management

- **Leukapheresis**
- **Hydroxyurea**

PAUSE: POLL



INFECTIOUS: FEBRILE NEUTROPENIA

- Common
  - Especially hematological malignancies – 80%
  - Less common solid tumor- 10 – 50%
  - Usually 5-10 days after cytotoxic chemotherapy
- Temperature – single measurement of 38.3* once or 38* for one hour
- Neutropenia – ANC <500 or expected to be <500 next 48 hours
- An organism will NOT be found in most patients

INFECTIOUS: FEBRILE NEUTROPENIA

MASCC score for febrile neutropenia

Characteristic	Points[a]
Severe symptoms or	5
Moderate symptoms	3
Hypotension	5
COPD	4
Haematological tumour and previous fungal infection	4
Inpatient status	3
Dehydration	3
Age ≥60 years	2

[a] ≤6 points predicts a low risk for complications (<5 %) and mortality (<1 %)

INFECTIOUS: FEBRILE NEUTROPENIA

Gram Positive

- Most common
- Coagulase-negative staph

Gram Negative

- E. Coli
- Klebsiella
- Pseudomonas

Fungal / Viral

- Increased incidence with prolonged or recurrent FN

INFECTIOUS: FEBRILE NEUTROPENIA

Clinical Presentation

- Fevers
- Chills
  - Chills when line flushed
- Fatigue

Exam

- Assess for erythema / tenderness
  - Oral / pharynx
    - Ulcers
  - Skin
    - Will NOT see abscess
  - Lungs
    - Diminished
    - Distress
  - Perianal
    - NO direct rectal exam
  - Abdomen
    - Typhlitis
- Lines / Ports
- CNS
  - Confusion

INFECTIOUS: FEBRILE NEUTROPENIA

Work up

- CBC with diff
- CMP
- Lactic acid
- PT / INR
- PTT
- Blood cultures x2
  - One from line or port
- Chest x-ray
- Chest CT
- Urinalysis w/ culture
- Stool cultures (C.diff)
- LP for CNS symptoms

Treatment

- Empiric broad spectrum
  - Cefepime
  - Carbapenem
  - Piperacillin/tazobactam
- Gram positive suspected
  - Vancomycin
- CGSF
  - May play a role in profoundly ill or prolonged neutropenia

TREATMENT SIDE EFFECTS

Gastrointestinal

- **Bowel Perforation**
  - VEGF inhibitors (bevacizumab)
- **Liver Failure**

Pulmonary

- **Pneumonitis**
  - mTOR inhibitors (everolimus, temsirolimus)
  - Kinase inhibitors (erlotinib, gefitinib, crizotinib, idelalisib**)**
  - Monoclonals (rituximab)

Cardiovascular

- **Heart Failure**
  - HER2 (tratuzumab, pertuzumab)
  - Immunotherapy (ipilimumab, nivolumab, pembrolizumab)
- **Arterial thrombosis**
  - VEGF inhibitors (bevacizumab, aflibercept, ramucirumab)
  - Kinase inhibitors (ponatinib, pazopanib)
- **Arrythmias**
  - Kinase inhibitors (dasatinib, vandetanib, ibrutinib, lenvatinib)
  - Antiemetics (ondansetron, metoclopramide)
  - Proteasome inhibitors (bortezomib, carfilzomib)