Oncologic Emergencies

Lisa Welsh, MBA, PA-C
Inpatient Hematology / Oncology
No relevant financial relationship(s) exist
Learning Objectives

- Identify common and uncommon signs and symptoms associated with 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.
- Discuss strategies for management of oncologic emergencies.
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
**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
    - Cardiac arrest
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

2. 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!

3. Calcitonin
   - Inhibits osteoclasts, enhances urinary excretion
   - Rapid onset, but patients will quickly stop responding
   - Subcutaneous injection
   - No renal adjustment
3. **Glucocorticoids**
   - Inhibit conversion of calcidiol to calcitriol
   - Prednisone 60mg oral daily
   - Hydrocortisone 100mg IV every 6 hours

4. **Loop diuretics**
   - Should be avoided, unless patient is volume overloaded
   - Exacerbates hypovolemia, impairs calcium excretion
Metabolic: Hyponatremia

- 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 antidiuretic hormone (SIADH):**
   - Malignancy
   - 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
  - SLOOOOOOWLY 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
- Up to ______ of patients with cancer

- Common malignancies - high turn over of cells:
  - Acute leukemias
  - Lymphoma (high grade)
  - Small cell
- Generally starts after starting therapy
- Can present with TLS
Pathophysicsology

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

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

**Physical Exam:**
- Usually unremarkable
- May have arrhythmias
Metabolic: TLS

Work up

- CBC
  - WBC for risk stratification

- CMP
  - Potassium: > 6mg/L (or 25% increase)
  - 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
### Table 1
Cairo and Bishop\textsuperscript{13} definitions of tumor lysis syndrome

<table>
<thead>
<tr>
<th>Laboratory TLS\textsuperscript{a}</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Uric acid</td>
<td>( \geq 476 \ \mu\text{mol}/L ) or 25% increase from baseline</td>
</tr>
<tr>
<td>Potassium</td>
<td>( \geq 6.0 \ \text{mmol}/L ) or 25% increase from baseline</td>
</tr>
<tr>
<td>Phosphorous</td>
<td>( \geq 2.1 \ \text{mmol}/L ) children, ( \geq 1.45 \ \text{mmol}/L ) adults, or 25% increase from baseline</td>
</tr>
<tr>
<td>Calcium</td>
<td>( \leq 1.75 \ \text{mmol}/L ) or 25% decrease from baseline</td>
</tr>
</tbody>
</table>

**Clinical TLS = Laboratory TLS and 1 or more of:**

- Creatinine level \( \geq 1.5 \) times upper limit of normal for age and sex
- Cardiac arrhythmia or sudden death\textsuperscript{b}
- Seizure\textsuperscript{b}

\textsuperscript{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.

\textsuperscript{b} Not attributable to a therapeutic agent or other identifiable cause.
# Risk Stratification

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

**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

- Rare

- 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

- 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
Pathophysiology

1. **Extrinsic compression by tumor**
   - Decreased venous drainage from upper extremities, head & neck
   - Below azygous vein – more severe symptoms

2. **Thrombus:**
   - Catheters and lines
# 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
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: 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
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
  - Breast cancer
  - Lung

- Thoracic spine at highest risk
Clinical Presentation
• Back pain
  • Night
  • Worse w/ movement
• Bowel / bladder problems

Exam
• Extremity weakness
• Inability to walk

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
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
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

<table>
<thead>
<tr>
<th>Clinical Presentation</th>
<th>Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Spontaneous bleeding</td>
<td>- “Sausage like” hemorrhagic retinal veins</td>
</tr>
<tr>
<td>- Shortness of breath</td>
<td>- Bleeding</td>
</tr>
<tr>
<td>- Neurological defects</td>
<td></td>
</tr>
<tr>
<td>- MI</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Work up</th>
</tr>
</thead>
<tbody>
<tr>
<td>- CBC</td>
</tr>
<tr>
<td>- Rouleaux formation</td>
</tr>
<tr>
<td>- +/- Thrombocytosis</td>
</tr>
<tr>
<td>- +/- Erythrocytosis</td>
</tr>
<tr>
<td>- Immunoglobulins – IgM elevated (generally &gt;60)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>- AVOID Transfusion</td>
</tr>
<tr>
<td>- Plasmapheresis</td>
</tr>
</tbody>
</table>
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
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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Points&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe symptoms or</td>
<td>5</td>
</tr>
<tr>
<td>Moderate symptoms</td>
<td>3</td>
</tr>
<tr>
<td>Hypotension</td>
<td>5</td>
</tr>
<tr>
<td>COPD</td>
<td>4</td>
</tr>
<tr>
<td>Haematological tumour and previous fungal infection</td>
<td>4</td>
</tr>
<tr>
<td>Inpatient status</td>
<td>3</td>
</tr>
<tr>
<td>Dehydration</td>
<td>3</td>
</tr>
<tr>
<td>Age ≥60 years</td>
<td>2</td>
</tr>
</tbody>
</table>

<sup>a</sup> ≤6 points predicts a low risk for complications (<5 %) and mortality (<1 %)
# Infectious: Febrile Neutropenia

<table>
<thead>
<tr>
<th>Gram Positive</th>
<th>Gram Negative</th>
<th>Fungal / Viral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most common</td>
<td>E. Coli</td>
<td>Increased incidence with prolonged or recurrent FN</td>
</tr>
<tr>
<td>Coagulase-negative staph</td>
<td>Klebsiella</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pseudomonas</td>
<td></td>
</tr>
</tbody>
</table>
### 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 DRE
- Abdomen
  - **Typhlitis**
- Lines / Ports
- CNS
  - Confusion
## Infectious: Febrile Neutropenia

<table>
<thead>
<tr>
<th><strong>Work up</strong></th>
<th><strong>Treatment</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• CBC with diff</td>
<td>• Empiric broad spectrum</td>
</tr>
<tr>
<td>• CMP</td>
<td>• Cefepime</td>
</tr>
<tr>
<td>• Lactic acid</td>
<td>• Carbapenem</td>
</tr>
<tr>
<td>• PT / INR</td>
<td>• Piperacillin/tazobactam</td>
</tr>
<tr>
<td>• PTT</td>
<td>• Gram positive suspected</td>
</tr>
<tr>
<td>• Blood cultures x2</td>
<td>• Vancomycin</td>
</tr>
<tr>
<td>• One from line or port</td>
<td>• CGSF</td>
</tr>
<tr>
<td>• Chest x-ray</td>
<td>• May play a role in profoundly ill or prolonged neutropenia</td>
</tr>
<tr>
<td>• Chest CT</td>
<td></td>
</tr>
<tr>
<td>• Urinalysis w/ culture</td>
<td></td>
</tr>
<tr>
<td>• Stool cultures (C.diff)</td>
<td></td>
</tr>
<tr>
<td>• LP for CNS symptoms</td>
<td></td>
</tr>
</tbody>
</table>
Treatment Side Effects

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

**Cardiovascular**
- Heart Failure
  - HER2 (tratuzumab, pertuzumab)
  - Immunotherapy (ipilimumab, nivolumab, pembrolizumab)
- Arterial thrombosis
  - VEGF inhibitors (bevacizumab, aflibercept, ramucirumab)
  - Kinase inhibitors (ponatinib, pazopanib)

**Arrhythmias**
- Kinase inhibitors (dasatinib, vandetanib, ibrutinib, lenvatinib)
- Antiemetics (ondansetron, metoclopramide)
- Proteosome inhibitors (bortezomib, carfilzomib)

**Pulmonary**
- Pneumoniits
  - mTOR inhibitors (everolimus, temsirolimus)
  - Kinase inhibitors (erlotinib, gefitinib, crizotinib, idelalisib)