Oncologic Emergencies

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Prevalence of cancer: American Cancer Society

• 13.7 million Americans are living with cancer or history of the disease
• American Cancer Society projects 1.6 million new diagnoses this year
• Cancer is the 2\textsuperscript{nd} leading cause of death in the US (Heart disease #1)
• Cancer accounts for more than 500,000 deaths per year
### Prevalence of cancer

New therapies have led to longer survival
- New drugs
- Radiation
- Bone marrow transplants
- Immunotherapy - most recent and area of growth at OSU

### Cancer-related ED visits

- Patients with high acuity
- Admission rate of 60-70%
- Often (~5%) a new diagnosis made in the ED
- Frequently the more acute patients with lower survival rates present to the ED
- Also older patients and those with limited healthcare access present to the ED
Cancer-related ED visits

Resisting labels is critical for appropriate treatment
- Cancer does not mean terminal
- Cancer does not assume DNR
- Treatment is indicated
  - Pain
  - Dehydration
  - Vomiting
  - Infection
  - Palliative

Why a specific Emergency Department?
- Provide specialized care in the emergency setting for cancer patients
- Improve access to unique treatment and research opportunities for patients with cancer
- Establish hospital based guidelines for emergency department care
- Evaluation of patient outcome
  - Admissions
  - Inpatient length of stay
  - Infection rates
  - Patient Satisfaction
### Classification of Oncologic Emergencies

Can be broken down into 3 main areas
- Structural
- Metabolic/endocrine
- Hematologic

### Structural Oncologic Emergencies

- Spinal Cord Compression
- Malignant pericardial effusion
- Brain metastases
- Superior Vena Cava Syndrome
# Spinal Cord Compression

- Major emergency requiring radiation treatment
- Most are due to metastatic lesions
- Most common in the thoracic spine (70%) and lumbrosacral (20%)
- Most common early symptom is pain (95%)
- Pain is positional and usually worse when supine
- Occurs in approximately 5% of all cancer patients
- Most common in breast, lung and prostate cancer, renal, lymphoma
- Life threatening if above C3

## Spinal Cord Compression - Exam findings

- Tenderness to palpation
- Weakness
- Spasticity
- Abnormal reflexes
- Sensory deficits
  - Good indicator of location of lesion
- Palpable bladder
- Decreased rectal tone
**Spinal Cord Compression**

- Early recognition is key. Early MRI imaging
- Prognosis is closely related to pretreatment level of function
- Late Signs
  - Autonomic dysfunction
  - Urinary retention
  - Constipation
- Transport for rapid evaluation of emergent radiation therapy and steroids
- Surgery for tissue diagnosis and stabilization
- Treatment delays may result in loss of bowel or bladder function

**Malignant pericardial effusion**

- Due to neoplastic infiltration or radiation treatment
- Can lead to cardiac tamponade
- Difficult diagnosis to make and often misdiagnosed as CHF, PE or anxiety
- Beat to beat alteration of the QRS
- Symptoms
  - Dyspnea
  - Orthopnea
  - Cough
  - Chest pain
  - Weakness
### Malignant pericardial effusion

- **Physical exam findings:**
  - “muffled” heart sounds
  - Increased JVP
  - Decreased systolic blood pressure

- **Echocardiogram (Most Helpful Tool):**
  - Diastolic collapse of RA and RV
  - Dilated IVC

### Malignant pericardial effusion

**Cardiac tamponade**
- Initial treatment is temporizing
  - Oxygen, IVF, vasopressors
- May require pericardiocentesis, pericardial window
- 60% of malignant effusions reaccumulate
- Treat underlying malignancy
Brain Metastases

- Most common form of malignant CNS involvement
- Common associated cancers:
  - Lung (most common)
  - Breast
  - Melanoma
  - Leukemia/lymphoma
- Causes symptoms via compression and edema
  - Headache
  - Seizures
  - Focal weakness
  - Exam may be normal

Brain Metastases

- Diagnosis: Find the primary tumor
- CT scan of the chest, abdomen, and pelvis
- If negative, then consider mammogram or other imaging study
- In 30% of patients no primary tumor is identified
Brain Metastases

- Alleviate Symptoms – ie palliation
- Radiation is the primary treatment for brain metastases
- If single brain lesion, then surgery may be reasonable with or without radiation
- Corticosteroids
  - Especially if signs of edema
- Chemotherapy
- Anti-seizure medications – tend to improve quality of life

Superior Vena Cava Syndrome

- Obstruction of the SVC which carries blood back into the heart
- Approximately 90% caused by cancer
- Lung cancer is the most common (65%)
- Clinical features:
  - Edema of the face and arms
  - Swollen collateral veins on the chest
  - Shortness of breath
  - Coughing
  - Difficulty swallowing
  - Headache
Superior Vena Cava Syndrome

- Lung cancer patients account for 65% of all SVCS cases
  - 3 – 15% of patients with Lung CA
  - Four times more likely in right vs left sided tumors
- Lymphoma - 8%
  - Usually in the anterior mediastinum
- Breast and other mediastinal tumors 10%
- Non-malignant conditions account for remainder

Superior Vena Cava Syndrome

- Supportive care and transport
- Elevate the head of the bed and provide oxygen if hypoxic
- Immediate radiation therapy consultation
- Consider anticoagulation (50% will have clot present)
- Radiation is the definitive treatment
- Surgery and chemotherapy in selected cases
- Intravenous stents, balloon angioplasty and surgical bypass are becoming more common
Oncologic Emergencies

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Overview

• General Considerations
• Hypercalcemia of malignancy
• Tumor Lysis Syndrome
• Septic Shock
General Considerations

- Oncologic Emergencies Have Increased
- Rapid Recognition Required
- Aggressive Treatment is Indicated
- If due to underlying cancer, then treat the cancer
- Palliation in Advanced Malignancies
  - Must Consider Doing Nothing

Case # 1

- A 60 y/o white female is brought to the ER by her family for new onset worsening confusion
  - The patient notes only vague abdominal pain and constipation
  - PE:
    - HR 115, BP 88/40, RR 10, T 100.2
    - Elderly appearing female
    - Dry mucous membranes
    - Tachycardia, no murmurs
    - Lungs are clear
    - Abdomen w/ decreased bowel sounds
Hypercalcemia of Malignancy

- Most Common Metabolic Emergency in Cancer
- Occurs in about 10%-20% of Cancer Patients
- Most Often Seen with Lung, Breast Hematologic Malignancies
BLT with a Kosher Pickle and Mayonnaise

Cancers that go to bone

• Breast
• Lung / Lymphoma
• Thyroid
• Kidney
• Prostate
• Myeloma

Hypercalcemia

Etiology

• Syndrome Mediated by Production of PTHrP
  • Parathyroid hormone-related peptide which binds to parathyroid hormone receptors, mobilizing calcium from bones, and increasing renal reabsorption of calcium.
  • This Activates Osteoclast Activity
  • Level of Boney Metastasis Does Not Necessarily Correlate with Level of Calcium

• Direct Tumor Invasion into Bony Structures
  • Individual tumor cells secrete a variety of mediators that up-regulate local osteoclastic activity, causing calcium to be released into the serum.

* Immobility May Contribute to Hypercalcemia
# Hypercalcemia

## Acute Symptoms

<table>
<thead>
<tr>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nausea</td>
<td>• Oliguria</td>
</tr>
<tr>
<td>• Vomiting</td>
<td>• Renal failure</td>
</tr>
<tr>
<td>• Constipation</td>
<td>• Stupor, coma</td>
</tr>
<tr>
<td>• Muscle Weakness</td>
<td>• Ileus</td>
</tr>
<tr>
<td>• Mental Status Changes</td>
<td>• Heart block</td>
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<tr>
<td>• Acute Renal Insufficiency</td>
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</table>
# Hypercalcemia Symptoms

<table>
<thead>
<tr>
<th>CNS</th>
<th>Cardia</th>
<th>GI</th>
<th>Renal</th>
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<tbody>
<tr>
<td>Weakness</td>
<td>Bradycardia</td>
<td>Nausea / Vomiting</td>
<td>Polyuria</td>
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<tr>
<td>Hypotonia</td>
<td>Decreased QT</td>
<td>Constipation</td>
<td>Calcinosis</td>
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<tr>
<td>Proximal Myopathy</td>
<td>Prolonged PR Interval</td>
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<tr>
<td>Mental Status Changes</td>
<td>Widened T wave</td>
<td>Pancreatitis</td>
<td></td>
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<tr>
<td>Seizure /Coma</td>
<td>Arrhythmias</td>
<td>Dyspepsia</td>
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Adapted from Escalante et al, Cancer Management, May 2014

## Hypercalcemia Diagnosis

- History and Physical
- Serum calcium (>11 mg/dL)
- Phosphorus is low or normal
## Treatment General Approach

- If Ca++ < 12 and Asymptomatic can be Treated as Outpatient
- Reduce or Eliminate Causative Malignancy
- Hydration with IVF (200 – 300ml/Hr based on UOP)
  - Usually Doesn’t Normalize Calcium Alone
- Diuresis With Loop Diuretic after Hydration
- Biphosphonates – inhibit osteoclastic activity and calcium resorption from bone
- Denosumab

## Hypercalcemia Treatment

**Bisphosphonates**
- Bind to hydroxyapatite crystals
- Onset around 48 hours
- Duration 2-4 weeks
- Pamidronate 60 – 90mg IV
- Zoledronic Acide 4 – 8 mg

**Corticosteroids**
- Limited Value Outside Hematological Malignancies
- Onset 1 to 5 days
- Duration 2-4 weeks
- Dose: Varied

**Calcitonin**
- Binds directly to osteoclasts
- Onset: 2 – 6 hours
- Duration: 6 - 12 hours
- Dose: 4 IU/Kg SQ q12hr

**Gallium**
- Onset: 24 – 48 hours
- Duration: 2 – 3 weeks
- Dose: 200mg/m2 CIV for 5 days
Hypercalcemia Treatment

Volume Expansion
- Loop Diuretic
  - Maintain Urine output ~ 200ml per hour
- Bisphosphonate
  - Consider Corticosteroids
  - Denosumab

Chronic / Prevention
- Supportive Measures / Bisphosphonate
- Cancer Directed Therapy
  - Dialysis

Denosumab
- Potent inhibitor of osteoclast-mediated bone resorption
- Fully humanized monoclonal antibody
- Binds RANKL (receptor activator of nuclear factor kB ligand) to inhibit the formation, function, and survival of osteoclasts
- Reduces serum calcium in patients with bisphosphonate-refractory hypercalcemia of malignancy
Case #2

- 59-year-old woman who was diagnosed with non-Hodgkins Lymphoma
- Presented to Hematology 1 day post treatment and was found to have worsening urinary output.
- Physical examination notable for diffuse lymphadenopathy
  - Otherwise Normal

<table>
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<th>Time</th>
<th>BUN (mg/dL)</th>
<th>Calcium (mg/dL)</th>
<th>Creatinine (mg/dL)</th>
<th>Phosphorous, Inorganic (mg/dL)</th>
<th>LD (UL)</th>
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Tumor Lysis Syndrome (TLS)

- Result of a high rate of cell turnover.
  - Results in the release of intracellular products into the circulation.
  - Overwhelms normal homeostatic mechanisms that control potassium, calcium, phosphorus and uric acid.
- Hyperkalemia, Hypocalcemia, Hyperphosphatemia and Hyperuricemia may occur alone or in combination with one another.

Tumor Lysis Syndrome (con’t)

- Can occur with a variety of tumors
  - Most commonly with hematological malignancies
  - Poorly differentiated lymphomas
  - Post Treatment
  - Myeloproliferative disorders
  - Leukemias
    - Acute myelogenous & acute lymphocytic Leukemia
    - Chronic myelogenous leukemia
    - Chronic Lymphocytic leukemia
## Tumor Lysis Syndrome

### Features of TLS

- Hyperkalemia
  - Most Life-threatening Component of TLS
  - Sudden Increase Can Cause Cardiac Arrhythmias and Death
- Must Rule Out Other Causes
- Treatment is Based on the Underlying Cause

### Additional symptoms

- Paresthesias
- Altered level of consciousness
- Seizure
- Nausea/vomiting
- Anorexia
- Flank pain
- Oliguria, hematuria
- edema
Tumor Lysis Syndrome Diagnosis

- Labs:
  - Serum potassium
  - Calcium
  - Phosphorus
  - Uric acid
  - Creatinine

Cairo-Bishop Classification of TLS

- Uric Acid > 8 mg/dl (> 476 umol/L) or 25% increase from baseline
- Potassium > 6 mEq/L (>6 mmol/L) or 25% increase from baseline
- Phosphorus > 6.5 mg/dl (>2.1 mmol/L) or 25% increase from baseline
- Calcium < 7 mg/dl (< 1.75 mmol/L) or 25% decrease from baseline
- Creatinine > 1.5 times the ULN
- Cardiac Arrhythmia or Sudden Death
- Seizure
- Two or More Laboratory Changes Must be Observed within 3 Days Before or 7 Days After Cytotoxic Therapy
- The same criteria do not apply to spontaneous TLS

Lewis et al CA CANCER J CLIN 2011;61:287–314
# Tumor Lysis Syndrome Hyperuricemia

- **Prophylactic Measures Prior to the Initiation of Chemotherapy.**
- **Avoid Drugs That Increase Serum Urate or Produce Acidic Urine**
  - Thiazides Diuretics and Salicylates
- **Alkalization of the Urine Should be Initiated to Maintain a Urine pH > 7.0.**
  - Sodium Bicarbonate Solution (50-100 mmol/L)
  - Adjusted so that an Alkaline Urinary pH is Maintained.
  - Carbonic Anhydrase Inhibitor, Acetazolamide May be Used to Increase the Effects of Alkalization.

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## Tumor Lysis Syndrome Hyperuricemia

- **Prior to Era of Allopurinol Use**
  - Acute uric acid nephropathy developed in as many as 10 percent of patients treated with acute lymphoblastic leukemias
- **Gouty Arthritis May Be Seen**
  - Biggest Risk – ARF
- **Treat with Allopurinol**
  - Start 1 – 2 days Prior to Chemotherapy
  - 10mg/kg/d q 8 hrs
  - Careful in Renal Disease
- **Rasburicase: 0.05 – 0.2 mg/kg**
- **Dialysis May Be Required**
## Tumor Lysis Syndrome
### Hyperphosphatemia and hypocalcemia

- Phosphate Levels May Reach Four Times Normal
- As Concentration of Phosphate Increases, it Combines with Calcium and Precipitates in the Renal Tubule and in Soft Tissues: “Malignant Calcemia”
- Result is Renal Failure
- Symptoms Include Agitation, Tetany and Bone Pain
- Aluminum Hydroxide: 50 – 150 mg/kg/d divided q 4 – 6 hours
- Dialysis
- Hypocalcemia: Treat with Calcium Gluconate if Symptomatic

## Tumor Lysis Syndrome
### Treatment of Hyperkalemia

- Sodium Polystyrene 15 – 30 gm
- Normal Saline
- Regular Insulin: 10 U IV
  - Follow BG
  - Dextrose 50% with Insulin
- Sodium Bicarbonate: 50 mEq IV
- Calcium Chloride 100 – 200 mg IV
- Albuterol nebulized
- Dialysis
# Case # 3

- Patient is a 85 year old white female who resides in an ECF who experienced worsening abdominal pain over days was transferred to your facility with dizziness and fevers to 102.5°F
- BP 78/38, pulse 133, pulse ox 92% RA
- Pulmonary: crackles bilateral bases
- Abdomen: soft, tender to palpation in the hypogastrum
- Patient minimally responsive
- Start Dopamine to 10mcg / hr
- Blood pressure 100/50, pulse 120

## Septic Shock

- A response to overwhelming infection
- Marked by:
  - Hemodynamic instability
  - Altered metabolism
  - Abnormal coagulation
- 75% of cancer patients who get septic shock die if not treated immediately.
- Most common cause - gram-negative bacteria.
Septic Shock (con’t)

• Early
  • Warm, flushed, skin
  • May be febrile/have chills
  • Tachypnea
  • Anxiety
  • Altered mental status
  • Progressive hypotension
  • Decreased urine output

• Late
  • Cold, clammy skin
  • Temperature probably sub-normal
  • Vasoconstriction
  • Systemic vascular resistance
  • Decreased cardiac output
  • Rapid, thready pulse
  • Low/unobtainable B/P
  • Lips/nailbeds cyanotic
  • Decreased urine output
  • Altered level of consciousness

Septic Shock Diagnosis

• Laboratory findings
  • Blood Cultures Positive
  • WBC Increased or Decreased, with left shift (increased segs and bands)
  • Increased PT/PTT
  • Decreased Platelets/Fibrinogen levels
  • Increased BUN/creatinine
  • ABGs Reveal Respiratory Alkalosis
    • Progresses to Metabolic Acidosis
<table>
<thead>
<tr>
<th>Septic Shock</th>
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</thead>
<tbody>
<tr>
<td>Treatment</td>
</tr>
<tr>
<td>• Fluid resuscitation</td>
</tr>
<tr>
<td>• Raise B/P, Improve Perfusion</td>
</tr>
<tr>
<td>• Dopamine</td>
</tr>
<tr>
<td>• Improve Renal Perfusion</td>
</tr>
<tr>
<td>• Increase Peripheral Vascular Resistance</td>
</tr>
<tr>
<td>• Broad Spectrum Antibiotics</td>
</tr>
<tr>
<td>• Immediately After Cultures</td>
</tr>
<tr>
<td>• Supportive Electrolyte Replacement</td>
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