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 2nd 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%)
- 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

### 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

- **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
Laboratory

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

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

BLT with a Kosher Pickle and Mayonaisse

Cancers that go to bone

• Breast
• Lung / Lymphoma
• Thyroid
• Kidney
• Prostate
• Myeloma
**Hypercalcemia Acute Symptoms**

- **Early**
  - Nausea
  - Vomiting
  - Constipation
  - Muscle Weakness
  - Mental Status Changes
  - Acute Renal Insufficiency

- **Late**
  - Oliguria
  - Renal failure
  - Stupor, coma
  - Ileus
  - Heart block
  - Acute Renal Insufficiency

**Hypercalcemia Symptoms**

<table>
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<th>CNS</th>
<th>Cardia</th>
<th>GI</th>
<th>Renal</th>
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<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>Calciumosis</td>
</tr>
<tr>
<td>Proximal Myopathy</td>
<td>Prolonged PR</td>
<td>Ileus</td>
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<tr>
<td>Interval</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental Status</td>
<td>Widened T wave</td>
<td>Pancreatitis</td>
<td></td>
</tr>
<tr>
<td>Changes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seizure / Coma</td>
<td>Arrhythmias</td>
<td>Dyspepsia</td>
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**Hypercalcemia Diagnosis**

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

Adapted from Escalante et al, Cancer Management, May 2014
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
• Bisphosphonates – 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

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

Chronic / Prevention
Supportive Measures / Bisphosphonate
Cancer Directed Therapy

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

**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

**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 Alkalinization.

### 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
# Septic Shock

## Treatment

- Fluid resuscitation
  - Raise B/P, Improve Perfusion
- Dopamine
  - Improve Renal Perfusion
  - Increase Peripheral Vascular Resistance
- Broad Spectrum Antibiotics
  - Immediately After Cultures
- Supportive Electrolyte Replacement