

## 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<sup>nd</sup> 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

# Laboratory

Albumin (3.4-7) g/L	ALT (7-20) U/L	AST (7-24) U/L	BUN (6.2-20) mg/dL	Calcium (8.8-10.2) mg/dL	Creatinine (0.6-1.2) mg/dL	Phosphorus (2.4-4.1) mg/dL	Magnesium (1.6-2.2) mg/dL	Potassium (3.5-5.1) mmol/L	Calcium Ionized (1.0-1.3) mmol/L
28.16						2.8 L			
36.11						Specimen not received in laboratory			
15.79						Specimen not received in laboratory			
95.00			8	8.7 L	0.96	3.3 L	1.8	3.9	
95.00			11	8.2 L	0.81	2.8 L	1.6	3.9	
95.00			17	8.9 L	0.83	2.1 L	1.8	3.8	
95.00			19 H	8.2 L	0.86	2.4 L	2.0	4.1	
95.00			12 H	8.2 L	0.70	2.1 L	2.2	3.4 L	
Albumin (3.4-7) g/L	ALT (7-20) U/L	AST (7-24) U/L	BUN (6.2-20) mg/dL	Calcium (8.8-10.2) mg/dL	Creatinine (0.6-1.2) mg/dL	Phosphorus (2.4-4.1) mg/dL	Magnesium (1.6-2.2) mg/dL	Potassium (3.5-5.1) mmol/L	Calcium Ionized (1.0-1.3) mmol/L
95.00			49 H	8.9 L	0.84	2.5 L	2.3	3.2 L	
95.00			56 H	8.9 L	0.96	3.9	2.5	3.4 L	
95.24			66 H	7.9 L	1.63 H	5.8 H	2.5	4.1	
84.19			Specimen not received in laboratory	Specimen not received in laboratory	Specimen not received in laboratory	Specimen not received in laboratory	Specimen not received in laboratory	Specimen not received in laboratory	Specimen not received in laboratory
21.48			53 H	8.2 L	1.65 H	5.8 H	2.3	4.1	
15.00			33 H	8.7	1.63 H	5.4 H	2.2	3.9	
95.00			17 H	9.0	1.22 H	4.8 H	2.3	3.7	5.58 H
21.83			27 H	9.0	0.90	4.9 H	2.1	3.8	
Albumin (3.4-7) g/L	ALT (7-20) U/L	AST (7-24) U/L	BUN (6.2-20) mg/dL	Calcium (8.8-10.2) mg/dL	Creatinine (0.6-1.2) mg/dL	Phosphorus (2.4-4.1) mg/dL	Magnesium (1.6-2.2) mg/dL	Potassium (3.5-5.1) mmol/L	Calcium Ionized (1.0-1.3) mmol/L
95.00			19	11.3 H	0.90	5.8 H	1.9	3.9	
13.50	Specimen not received in laboratory	Specimen not received in laboratory	Specimen not received in laboratory			Specimen not received in laboratory	Specimen not received in laboratory		
13.49	4.2 L	16	20	11.9 H	0.88	5.8 H	1.9	4.2	
16.38	2.4 L	13	16	7	0.85			3.6	
16.38			Specimen not received in laboratory		Specimen not received in laboratory			Specimen not received in laboratory	
35.58			7		0.74			3.5	

# 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 Bony 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

- |   |  |
|---|--|
| <ul style="list-style-type: none"> <li>• <b>Early</b></li> <li>• Nausea</li> <li>• Vomiting</li> <li>• Constipation</li> <li>• Muscle Weakness</li> <li>• Mental Status Changes</li> <li>• Acute Renal Insufficiency</li> </ul> | <ul style="list-style-type: none"> <li>• <b>Late</b></li> <li>• Oliguria</li> <li>• Renal failure</li> <li>• Stupor, coma</li> <li>• Ileus</li> <li>• Heart block</li> </ul> |
|---|--|

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|--|--|

### Hypercalcemia Symptoms

CNS	Cardia	GI	Renal
Weakness	Bradycardia	Nausea / Vomiting	Polyuria
Hypotonia	Decreased QT	Constipation	Calcinosis
Proximal Myopathy	Prolonged PR Interval	Ileus	
Mental Status Changes	Widened T wave	Pancreatitis	
Seizure /Coma	Arrhythmias	Dyspepsia	

Adapted from Escalante et al, Cancer Management, May 2014

### Hypercalcemia Diagnosis

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



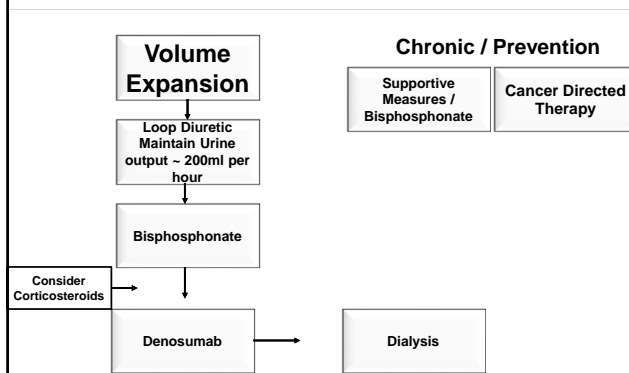
## Treatment General Approach

- 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
- **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/m<sup>2</sup> CIV for 5 days
- **Corticosteroids**
  - Limited Value Outside Hematological Malignancies
  - Onset 1 to 5 days
  - Duration 2-4 weeks
  - Dose: Varied

## Hypercalcemia Treatment



## Denosumab

- Potent inhibitor of osteoclast-mediated bone resorption
- Fully humanized monoclonal antibody
- Binds RANKL (receptor activator of nuclear factor  $\kappa$ B 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

	BUN (0.0-20.0) mg/dL	Calcium (8.6-10.0) mg/dL	Creatinine (0.6-1.1) mg/dL	Phosphorus, Inorganic (2.7-4.5) mg/dL	LD (100-190) U/L
21:59	64 H	5.9 LL ⊗	3.24 H	9.9 H	4508 H
15:06	57 H	6.4 L	2.71 H	9.8 H	5914 H
05:37	89 H	5.6 LL ⊗	2.96 H	14.6 HH ⊗	6134 H ⊗ Repeated and verified
23:44	83 H	6.2 L	2.83 H	14.3 HH ⊗	7313 H ⊗
17:55	72 H	6.5 L	2.34 H	12.4 HH ⊗	8133 H ⊗
11:40	64 H	7.1 L	1.97 H	12.1 HH ⊗	8776 H ⊗
04:50	50 H	7.5 L	1.63 H	10.6 HH ⊗	6637 H ⊗
20:03	25 H	6.7 L	1.18 H	7.6 H	1900 H
	BUN (0.0-20.0) mg/dL	Calcium (8.6-10.0) mg/dL	Creatinine (0.6-1.1) mg/dL	Phosphorus, Inorganic (2.7-4.5) mg/dL	LD (100-190) U/L
18:38					
17:51	23 H	8.6	1.33 H	10.2 HH ⊗	1473 H
17:46	Duplicate order, tests credited SEE W78558	Duplicate order, tests credited SEE W78558	Duplicate order, tests credited SEE W78558	Duplicate order, tests credited SEE W78558	Duplicate order, tests credited SEE W78558
17:29					
16:53					
16:14					
14:54	13	10.2 H	1.12 H	6.6 H ⊗	447 H
14:53	Duplicate order, tests credited SEE ACCESSION NUMBER W77573	Duplicate order, tests credited SEE ACCESSION NUMBER W77573	Duplicate order, tests credited SEE ACCESSION NUMBER W77573	Duplicate order, tests credited SEE ACCESSION NUMBER W77573	
	BUN (0.0-20.0) mg/dL	Calcium (8.6-10.0) mg/dL	Creatinine (0.6-1.1) mg/dL	Phosphorus, Inorganic (2.7-4.5) mg/dL	LD (100-190) U/L

## 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

## Tumor Lysis Syndrome

- 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  $\geq 8$  mg/dl ( $\geq 476$   $\mu\text{mol/L}$ ) or 25% increase from baseline
- Potassium  $\geq 6$  mEq/L ( $\geq 6$  mmol/L) or 25% increase from baseline
- Phosphorus  $\geq 6.5$  mg/dl ( $\geq 2.1$  mmol/L) or 25% increase from baseline
- Calcium  $\leq 7$  mg/dl ( $\leq 1.75$  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
- **Alkalinization 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 102.5F
- 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**