

Oncologic Emergencies



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Disclosures



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 $>14\text{mg/dL}$
 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

Metabolic: Hypercalcemia



Treatment Continued

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 mOsm/kg
- Urine osmolality: >100 mOsm/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
- 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

Metabolic: TLS



Pathophysiology

- 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 arrhythmias due to electrolyte dysfunction**

Metabolic: TLS



Table 1
Cairo and Bishop¹³ definitions of tumor lysis syndrome

Laboratory TLS^a

Uric acid	$\geq 476 \mu\text{mol/L}$ or 25% increase from baseline
Potassium	$\geq 6.0 \text{ mmol/L}$ or 25% increase from baseline
Phosphorous	$\geq 2.1 \text{ mmol/L}$ children, $\geq 1.45 \text{ mmol/L}$ adults, or 25% increase from baseline
Calcium	$\leq 1.75 \text{ mmol/L}$ 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: 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 ≥ 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.



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

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

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**

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**

Structural: Spinal Cord Compression



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



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

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 DRE
- 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

Cardiovascular

- Heart Failure
 - HER2 (trastuzumab, 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)
 - Proteasome inhibitors (bortezomib, carfilzomib)

Pulmonary

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