Oncologic Emergencies

Overview: Defining an Oncology Emergency
• Any significant clinical condition which is related to a malignancy or from sequelae of cancer-related therapy that requires immediate evaluation and treatment
• Clinical conditions include: metabolic, hematologic, neurologic, infectious or cardiovascular

Objectives
• Identify Clinical Conditions that represent major categories of oncologic emergencies
• Review the key approaches to management of the major oncologic emergencies

Overview of Major Classifications of Oncologic Emergencies

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<th>Emergency</th>
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<td>Neurologic</td>
<td>Spinal Cord compression</td>
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<td>Increased ICP</td>
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<td>Metabolic</td>
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<td>Infectious</td>
<td>Febrile Neutropenia</td>
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Hypercalcemia of Malignancy

Most common metabolic emergency in cancer patients

Case: Hypercalcemia
• 75 yo F with Stage IV breast cancer with metastases to the bones, comes to Emergency Department with several days of generalized weakness, decreased appetite and po intake, also constipation. VS: HR 130, BP 100/90 other VSS. There is a non-focal Neuro exam and Imaging confirms osteolytic metastases along T and L spine, both hips and 4th and 5th R ribs; Labs: Ca 14 mg/dL (corrected), K 2.9 meq/L, Phos 2.4 g/dL, Ser Cr 1.5 (from 1.1)
• Management: IVF resuscitation, followed by bisphosphonate (zometa 4 mg IV x 1)
HYPERCALCEMIA

**DEFINITION**
- Serum Calcium > 10.5 mg/dL
- Lower albumin levels = higher calcium level
- Actual Serum Calcium (mg/dL) + 0.8 (4.0 – Serum Albumin (g/dL))
- Patient with: Serum Calcium-11.5, serum albumin-2.1 → Corrected serum Calcium=13 mg/dL

**ASSOCIATED FINDINGS**
- Decreased levels: Serum intact Parathyroid hormone (iPTH), phosphorus, 1,25-dihydroxyl vitamin D

**Hypercalcemia Mechanisms**
- **Osteolytic Metastases**
  - Breast cancer, multiple myeloma
- **Humoral Mediators**
  - Releasing Parathyroid hormone-Like hormone, prostaglandins, osteoclast activating factor
  - Breast, Squamous cell, lymphoma, bladder cancer, ovarian cancer
- **Ectopic PTH Secretion**
  - Ovarian, lung, papillary thyroid, rhabdomyosarcoma
- **1,25-dihydroxvitamin D**
  - Lymphoma, ovarian dysgerminomas

**Hypercalcemia: Clinical Manifestations**
- **Neurologic**
  - Confusion/restless state
  - Lethargy
  - Hypotonia
- **Cardiovascular**
  - Bradycardia
  - Q-T shortened
  - P-R prolonged
  - QRS widened
- **Constitutional**
  - Anorexia
  - Weight decrease
- **Gastrointestinal**
  - Nausea, vomiting
  - Constipation
- **Renal**
  - Polyuria
  - Increased Serum Creat
  - Pruritis
  - Polynephrocalcinosis

**Hypercalcemia: Clinical Manifestations**

**Primary Treatment**
- Volume Resuscitation
- Bisphosphonates
- Loop Diuretics

**Additional Therapies**
- Steroids
- Calcitonin

**Hypercalcemia Case**
55 y/o with a new diagnosis of multiple myeloma presents to clinic.
- Calcium =10-12 mg/dL for several months
- 2 small lytic lesions in the pelvis
- Denies any symptoms related to hypercalcemia
- What is the next step in management?
  A. Admission for stat fluids + bisphosphonates
  B. Outpatient fluids + bisphosphonates
  C. Outpatient Lasix + bisphosphonates
  D. Initiate multiagent myeloma therapy + bisphosphonates
- Answer: D. Initiate multiagent myeloma therapy + bisphosphonates
- Since the hypercalcemia is chronic and the patient is asymptomatic, treat the underlying process
Tumor Lysis Syndrome

- High turnover cancers
- Chemo-induced rapid cell death
- Cell death related release of intracellular contents into the bloodstream

- Critical Labs:
  - Ca (low),
  - K (high),
  - Phosphorus (high),
  - Mg (low),
  - Uric acid (high)
  - BUN/ Creat (high)
  - Fibrinogen (low)
  - (LDH (high))

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Tumor Lysis Syndrome

TLS: Clinical Manifestations

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<tr>
<th>Overview</th>
<th>Definition</th>
<th>Signs/Symp toms</th>
<th>Management</th>
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<tr>
<td>Hyperkalemia</td>
<td>K&gt;5</td>
<td>Parasthesias, muscle cramping/muscle weakness, nausea/vomiting</td>
<td>Frequent electrolyte monitoring (e.g. K, Ca, Mg, Phos, Cr)</td>
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<tr>
<td>Hyperphosphatemia</td>
<td>Phos &gt;10</td>
<td>Oliguria, azotemia</td>
<td>Hydration with NS, NS with Sodium Bicarbonate (urine alkalization)</td>
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<tr>
<td>Hypocalcemia</td>
<td>Ca &lt;4.5</td>
<td>Arrhythmias, seizures</td>
<td>telemetry</td>
</tr>
<tr>
<td>Hyperuricemia</td>
<td>Uric Acid &gt;10</td>
<td>n/v, diarrhea, oliguria, azotemia</td>
<td>Rasburicase for U/A&gt;10; Prophylactically: Allopurinol 100-200 mg bid</td>
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Prophylaxis/Treatment:
- Hydration with NS
- Alkalize the urine with D5 and bicarb (pH>7)
- Allopurinol 200-400mg po 24-48 hours before chemo
- Q6-8 hour labs including U/A
- Frank hyperuricemia:
  - Rasburicase 0.15-0.2 mg/kg/day
  - Metabolizes uric acid, prevents formation of uric acid
  - Recombinant urate oxidase
  - Toxicity: anaphylaxis, methemoglobinemia
- Dialysis

Tumor Lysis Syndrome Case

- 35 y/o male with no significant past medical history is diagnosed with diffuse large B cell lymphoma with multiple nodal stations involved above and below the diaphragm.
  - Started on R-CHOP in the infusion center (outpatient)
  - Pt experiences cardiac arrest that evening at home
  - He is resuscitated in the field and brought to the ER

- What is the most likely cause of the cardiac arrest?
  - A. Reaction to chemotherapy
  - B. Hyperkalemia
  - C. Underlying coronary artery disease
  - D. Underlying undiagnosed cardiac conduction disease

- Answer: B. Hyperkalemia

- Answer: A. Reaction to chemotherapy

Sequela of tumor lysis:
- Hyperkalemia causing lethal cardiac arrhythmias
- Hyper-phosphatemia causing ARF
- Hypo-calcemia causing tetany, ARF, arrhythmias
- Prophylaxis and prevention is the key
  - Aggressive pre-chemo hydration
  - Allopurinol or rasburicase for markedly elevated uric acid
  - Alkalize the urine

Tumor Lysis Syndrome Case

- Answer: B. Hyperkalemia
  - Reaction to chemotherapy
  - B. Hyperkalemia
  - C. Underlying coronary artery disease
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Tumor Lysis Syndrome
Spinal Cord Compression

- 1-4% of cancer patients
- Presents as extradural metastatic disease
- T spine (70%) > LS spine (20%) > C spine (10%)

High risk of cord compression in cancers that metastasize to bone
- 50% breast, lung, prostate
- 50% renal cell carcinoma, sarcoma, melanoma, lymphoma, myeloma

Pediatric cancers: sarcoma, neuroblastoma, lymphoma

Early signs: back pain, radicular pain
  - Weeks to months before neuro symptoms
Intermediate signs: weakness, sensory loss
Late signs: autonomic dysfunction, urinary retention, constipation

Spinal Cord Compression: Diagnosis

- MRI: Gold Standard
  - Tumor related cord compression vs. epidural abscess
  - Tumor: decreased enhancement on T1 sequences, increased enhancement (bright) on T2 series
- CT Myelography
- X-Ray/Plain film
  - 66% of patients will have a bone related abnormality

Early signs: back pain, radicular pain
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Prognosis
- Outcome = degree and duration of neuro impairment prior to therapy
- Maranzano et al:
  - 209 patients
    - Ambulatory - 98% remained ambulatory after rx
    - Non-ambulatory - 60% were ambulatory after rx
    - Paraplegic - 11% were ambulatory after rx
- Outcome better in radiosensitive tumors (NHL > RCC)
Spinal Cord Compression

• Treatment goals:
  – Preserve or recover neurologic function
  – Spine stabilization
  – Local tumor control
  – Pain control

• Prognosis:
  – Severity, Duration of neurologic impairment prior to intervention determines early and long term outcome

• XRT:
  – Most common treatment for SCC
  – Multi-focal sites
  – Non-invasive
  – Appropriate if anticipate limited life expectancy

• Surgery
  – Spinal stabilization
  – Solitary-oligo sites
  – Superior outcomes
  – But risk of surgical complications

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Prospective Randomized Trial of 101 patients with malignant spinal cord compression:
  – Arm 1 - Surgery → XRT (n=50)
  – Arm 2 - XRT (n=51)
  – Primary endpoint: recovery/preservation of ambulation
  – Trial terminated after Early Interim analysis

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Spinal Cord Compression: Evidence Analysis

• Prospective study of 209 patients with cord compression:
  – Ambulatory prior to Rx for SCC: 98% continued ambulation
  – Non-Ambulatory prior to Rx for SCC: 60% regained ambulation
  – Paraplegia prior to Rx for SCC: 10% regained ambulation
  – NHL (radio-sensitive) > RCC

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Patchell et al Lancet 2005

Take-home message: Patients should be evaluated for surgery.

Patchell et al Lancet 2005

Superior Vena Cava Syndrome (SVCS)

• Historically, was associated with aortic aneurysms (TB or syphilis).
• Since the 1990s: Malignancy accounts for nearly 70% of SVCS

Spinal Cord Compression Case

• 65 y/o male with known prostate cancer presents with a 6 week history of progressive urinary retention, severe low back pain, paraplegic in the ER
  – Given stat steroids
  – MRI shows frank T10 cord compression with a large vertebral body lesion
  – What are the chances the patient will be ambulatory after steroids and XRT?

A. 75%
B. 50%
C. 25%
D. 10%

Answer: D. 10%.

* Paraplegic patients who present with >48 hours of symptoms rarely regain neurologic function

Spinal Cord Compression: Evidence Analysis

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Answer: D. 10%.

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Superior Vena Cava Syndrome: Mechanisms for Superior Vena Cava Obstruction

- Neoplastic invasion of the venous wall associated with intravascular thrombosis
- Extrinsic pressure of a tumor mass against a relatively fixed thin-walled superior vena cava
- Complete obstruction: intravascular thrombosis and extrinsic pressure.
- Incomplete obstruction: secondary to extrinsic compression without thrombosis.
- Other causes include compression by intravascular arterial devices.

SVC Syndrome

- Symptoms:
  - Neck swelling
  - Arm swelling
  - Dysphagia, cough
  - Orthopnea
  - SOB worse with change of position
  - Facial Erythema

- PE Findings:
  - Neck/facial edema
  - Vein dilation
  - Plethora/cyanosis
  - Laryngeal/glossal edema
  - MS changes
  - R pleural effusion

SVC Syndrome: Treatment

- Treatment Options:
  - Radiation
  - Chemotherapy
  - Thrombolytics/anticoagulation
  - Stent placement
  - Bypass surgery

- Prognosis
  - Etiology of the underlying obstruction
  - Schraufnagal, et al:
    - Median OS=10 months (+/- 25 months)
    - Thoracic malignancy OS < 5 months

SVC Syndrome Case

56 y/o male smoker presents with 1 week of facial flushing, SOB, and headache.

- CT chest shows 3-cm central mass in the RUL with vessel collateralization, mediastinal lymphadenopathy

- What is the next step in management?
  A. Steroids
  B. Tissue diagnosis
  C. Rad Onc consult
  D. Chemotherapy

- Answer: A. Steroids
  - Treat the obstructive symptoms first then obtain tissue as soon as possible

SVC Syndrome: Non malignant causes

- Metastatic Disease (10%)
  - Breast Cancer
  - Testicular/Germ Cell Tumors

- Other causes include compression by intravascular arterial devices.

SVC Syndrome: Malignant Causes:

- Primary intrathoracic tumor (90%)
  - Lung Cancer
  - Lymphoma

- Metastatic Disease (10%)
  - Breast Cancer
  - Testicular/Germ Cell Tumors

- Other causes include compression by intravascular arterial devices.

SVC Syndrome: Radiation:

- Rx of choice for NSCLC
- Combine with chemo for NHL and SCLC
- 2 – 4 Gy in 1 – 4 weeks

SVC Syndrome: Anticoagulation:

- Catheter-Associated
- Use of urokinase/streptokinase
- No data on long term anticoagulation

SVC Syndrome: Stenting

- Expandable wire stent in the SVC
- Difficult with intraluminal thrombosis
- 52 pts with lung cancer and SVC syndrome
  - 100% had resolution of the obstruction
  - 80% had symptom resolution
  - 17% re-obstruction due to disease progression

SVC Syndrome: SVC Syndrome Case

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SVC Syndrome: Summary Recommendations

- If symptomatic: start steroids and/or diuretics
- Get imaging to evaluate extent of obstruction, whether there are collaterals, identify thrombus
- If SVC compression related to a mass is asymptomatic (incidental finding)-try to obtain tissue diagnosis prior to therapy
- Consider Thrombolysis and/or Stenting (based on nature of the obstruction)
- Tumor/histology-driven chemotherapy or RT

Hyperleukocytosis

- **WBC > 100,000K with >75% immature/blast ("unidentified ") cells**
- Most commonly seen in acute leukemia
  - AML, ALL, CML Blast phase >CLL
- Hyper-viscosity related state:
  - Dypsnea
  - Altered mentation
  - Bleeding
  - Infiltrates on CXR

Hyperleukocytosis Case

- **40 y/o previously healthy female brought to the ER by family with 2 week h/o gum bleeding, rash on BLE, fatigue, occasional confusion**
  - Pt is obtunded but moving all extremities, unable to answer questions
  - Oozing at IV site
  - BP 60/40, HR 120s, RR30s, T39
  - WBC=120,000, 90% unidentified cells
  - Hg = 6 g/dL
  - Platelets = 10,000
  - Review of peripheral smear confirms acute leukemia

Hyperleukocytosis

- **Special situations:**
  - **CLL**
    - Can have WBC in the several 100,000 range without symptoms of increased viscosity
    - Mature lymphocytes are not as “sticky” as immature myelocytes
    - Treat the CLL
  - **Waldenstrom’s macroglobulinemia**
    - High level of clonal IgM paraprotein
    - Lymphadenopathy like a lymphoma
    - Can have markedly increased serum viscosity
    - If patient is symptomatic = acute apheresis to remove the large IgM protein

Hyperleukocytosis

- **Treatment:**
  - Aggressive volume resuscitation
  - Leukapheresis to remove the blasts mechanically
  - Allopurinol to decrease uric acid
  - Hydroxyurea to reduce blast count
  - Alkalinize the urine
  - Chemotherapy
Hyperleukocytosis Case

- What is the most appropriate next step in management?
  A. Place apheresis catheter and start Leukapheresis
  B. Chemotherapy
  C. Admission to the ICU, intubation if necessary, aggressive hydration, stabilization of vital signs
  D. Blood and platelet transfusion

- Answer: A
  - ABCs always come first!
  - After pt is stabilized, she will need Leukapheresis, continued volume resuscitation (transfusions), Hydroxyurea

Infectious Complications

Febrile Neutropenia

- Single temp > 38.3
- Sustained temp > 38 for 1 hour or more
- ANC < 500 or ANC < 1000 with anticipated further drop
- ANC nadir 7-10 days after chemotherapy
- 50% of patients with neutropenic fever will have an established or occult infection
- Fever may be suppressed by steroids, pain relievers with Tylenol, NSAIDS

Febrile Neutropenia: Treatment

- Cefepime 1 gm IV q8h
- Or Ceftazidime 1 gm IV q8h
  - Does not cover MRSA, enterococcus, coagulase negative staphylococcus, many anaerobes
- Vancomycin
  - Indwelling catheters
  - Patients with mucositis
  - Patients with cellulitis

Febrile Neutropenia

- Work up
  - CBC with diff and chemistries
  - Blood cultures x 2
  - At least one culture from indwelling catheter site
  - UA with micro, C+5
  - Stool for O&P, c. diff, cultures
  - CXR
  - H&P is crucial—several sites are often missed
    • Oropharynx (pharyngitis)
    • Perirectal area (abscess)
    • Sites of indwelling catheters (cellulitis)
    • Skin exam (rashes, viral infections, HZV)

Febrile Neutropenia

- Treatment
  - Continue broad spectrum antibiotics until a source is found, then can taper according to organism
  - If no organism is found and source is not obvious, continue broad spectrum antibiotics until pt is no longer neutropenic
  - Fever after 48 hours of Ceftazidime/Vancomycin with no obvious source:
    • Broaden Ceftazidime to Cefepime or Meropenem
    • Consider fungal coverage especially with hematologic malignancies
Febrile Neutropenia
• Growth Factors
  – Neulasta: Pegylated G-CSF (long acting)
    • 1 dose given 24-48/72 hours after chemotherapy
  – Neupogen: short acting G-CSF
    • Daily doses for 7-10 days after chemotherapy
    • Cheaper than Neulasta

• Indications for G-CSF in neutropenic fever:
  – Sustained ANC < 500 for several days with fever
  – Hemodynamic instability
  – Severe infection (e.g. bowel perforation)
  – Avoid giving G-CSF in hematologic malignancies

Febrile Neutropenia Case
• 26 y/o female with AML s/p induction chemotherapy 14 days ago presents with fever to 39 degrees x 1 day.
  – Has been on prophylactic antibiotics for 5 days: Levaquin, acyclovir, and diflucan
  – Does not appear acutely ill
  – CXR with RLL infiltrate
  – Has a productive cough but clear to auscultation
  – Pancytopenia with ANC = 100
  – Port site is clear
  – Did not receive any growth factors

Febrile Neutropenia Case
• In addition to starting broad spectrum antibiotics, what is the next most reasonable medication to start?
  A. Growth Factors
  B. High dose acyclovir
  C. Steroids
  D. Voriconazole

Answer: D. Voriconazole
  – Patients with heme malignancies are placed on prophylactic antibiotics during neutropenic period
  – Often develop infections resistant to standard antibiotics, most commonly fungal infections
  – Voriconazole and posaconazole will cover aspergillosis (resistant to diflucan)

Clinical Pearls
• Read the question carefully!
  – Is the patient inpatient or outpatient?
  – Is the patient sick or not sick?
  – Does the patient have a heme malignancy?
  – How old is the patient?
  – Is the patient symptomatic?
  – Are the symptoms acute or chronic?

ABCs and symptom management always come first, then treatment of underlying disease.