Oncologic Emergencies

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T32 in Cancer Health Disparities

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Overview/Objectives

- Review most important clinical emergencies in oncology
- Case based format
- Key points in diagnosis and management
- No disclosures

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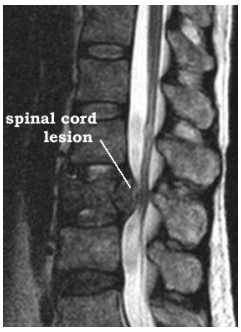

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SPINAL CORD COMPRESSION

- Occurs in up to 5% of cancer patients
- Most common: breast, lung, prostate
- Also seen in NHL, renal cell, multiple myeloma
- Associated with poor prognosis
- CRITICAL to diagnose and treat in timely fashion
  - Neurological status at presentation and rapidity of onset predict functional outcome

Lawton, et al, 2019, JCO Assessment and Management of Patients With Metastatic Spinal Cord Compression: A Multidisciplinary Review

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Etiology

- Usually due to direct extension from spinal bony mets
- Less commonly extends through neural foramina
- Can occur from destruction of cortical bone causing vertebral collapse and displacement into spinal canal
- Inflammatory response contributes to pain/neurologic compromise
- Most common in thoracic spine (70%) due to smaller available free space within thoracic canal
  - Lumbosacral spine (20%)
  - Cervical spine (10%)

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Symptoms of SCC

- Back pain (~90%) -> often first presenting symptom
- **This is why back pain in a cancer patient is a “red flag” and merits prompt imaging**
- Weakness (35-75%)
- Sensory loss
- Bowel, bladder dysfunction (late finding)
- Gait ataxia

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Diagnosis

- Early recognition is essential
- **MRI is imaging modality of choice**
- Recommendation is to image the entire spine as many patients have multiple sites of disease
- Often sensory level affected does not correspond to area of suspected cord compression

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Treatment

- Immediate dexamethasone
  - Increases likelihood of ambulation post treatment, improves pain scores
  - Typical dosing: 10mg IV x1 followed by 16mg daily in divided doses (ie, 4mg q6hrs)
- Opiate analgesics
- Prompt neurosurgery and rad-onc consultation (even in the middle of the night!)
  - Surgery + XRT improved outcomes (ability to ambulate) over XRT alone

Landmark studies: Patchell 2005 Lancet, Vecht, Neurology 1989, Sorenson, Eur J Cancer 1994

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SVC SYNDROME

- Caused by occlusion of SVC due to either external compression or internal obstruction
- Low pressure vessel with thin walls surrounded by lymph nodes, trachea, right bronchus, thymus, great vessels
- Symptoms are due to venous distension and pressure behind the obstruction

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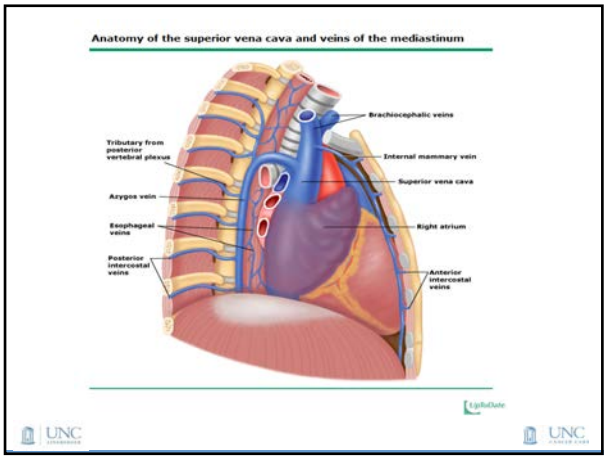

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Etiology

- Non-malignant causes
  - Catheter related
  - Pacemaker leads
  - Infectious (TB, syphilis, fibrosing mediastinitis)
- Malignancy-related SVC
  - NSCLC: 50%, portends poor prognosis
  - SCLC: 25%
  - NHL: 10%

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Presentation

- Can be subacute or quite rapid, depending on degree of collateralization
- Facial, neck, and upper extremity swelling
- Dilated chest veins
- Dyspnea, cough, hoarseness
- Headache, confusion, or lethargy

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Pemberton's Sign

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Diagnosis

- **CT chest with contrast** is imaging of choice
- MR venography is a potential alternative
- Prompt Mediastinoscopy vs CT guided biopsy
- **Usually can delay treatment while obtaining tissue diagnosis since treatment guided by tumor type** (ie R-CHOP vs platinum based chemotherapy)

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Treatment

- **Emergent if stridor/respiratory compromise or lethargy/coma**
- Endovascular stent placement or thrombolysis are emergent therapy options (VIR consult)
- Radiotherapy: benefit in 72 hours
- Chemotherapy: benefit in 1-2 weeks
- Steroids: Only if laryngeal edema or known steroid responsive cancer
- Diuretics: Unclear benefit

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HYPERCALCEMIA

- Most common cause among inpatients is cancer
  - Malignancy diagnosed in >1/3 of all patients with hypercalcemia who present to ED
- Affects ~20% of cancer patients
  - ~50% of these patients die within 1 month

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Pathophysiology

- Tumor secretion of PTHrP (Humoral hypercalcemia of malignancy) (~80%)
  - PTHrP increases osteoclastic bone resorption and enhances calcium resorption through renal tubules
- Local bone destruction (ie, bone mets) -> local release of cytokines, osteoclast activating factors (~20%)
- 1,25-dihydroxy vitamin D production (<1%)
  - Increases calcium absorption in gut and osteoclast activity
- Ectopic secretion of PTH (<1%)

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Malignancies associated with hypercalcemia

Osteolytic metastases:
Breast cancer
Multiple myeloma
Lymphoma
Leukemia
Humoral hypercalcemia (PTHrP):
Squamous cell carcinomas
Renal carcinomas
Bladder carcinoma
Breast cancer
Ovarian carcinoma
Non-Hodgkin lymphoma
CML
Leukemia
Lymphoma
1,25-dihydroxyvitamin D:
Lymphoma (Non-Hodgkin, Hodgkin, lymphomatosis/granulomatosis)
Ovarian dysgerminomas
Ectopic PTH secretion:
Ovarian carcinoma
Lung carcinomas
Neuroectodermal tumor
Thyroid papillary carcinoma
Rhabdomyosarcoma
Pancreatic cancer

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Symptoms

- Weakness, fatigue
- Polyuria, polydipsia (nephrogenic DI)
- GI symptoms (abdominal pain, nausea, vomiting, constipation)
- Psychiatric symptoms (memory loss, apathy)
- Bone pain
- "Stones, bones, groans, psychiatric overtones"

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Diagnosis

- Serum lab value does not necessarily account for acuity or degree of symptoms
  - Mild < 12 mg/dl
  - Moderate 12-14 mg/dl
  - Severe > 14 mg/dl
- Remember to use ionized or corrected calcium

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ECG Findings

- Shortened QT interval
- Osborn or J wave (if severe)

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Treatment

- **Fluids**: NS at initial rate of 200-300 cc/h
  - Loop diuretics only if fluid overload, CHF, or renal failure
- **Bisphosphonates**
  - Block osteoclastic bone resorption, delayed onset (24-48h)
  - Zoledronic acid 4 mg over 15 min or pamidronate
- **Calcitonin** (SubQ or IM)
  - Early onset of action: hours, but short duration (48h)
  - Can help temporize while bisphosphonates take effect
- Consider steroids if increased calcitriol production
- Consider HD for patients w/ neurological symptoms, calcium >18, renal failure, CHF

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TUMOR LYSIS SYNDROME

- Most common in aggressive heme malignancies
  - High grade lymphoma, AML– usually after treatment but can present spontaneously, especially if large tumor burden
  - Occasionally seen after treatment of solid tumors
- Massive release of intracellular contents from malignant cells -> leads to metabolic derangements

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Laboratory Abnormalities

- Hyperkalemia
  - Life-threatening arrhythmias
- Hyperuricemia
  - Crystallize in renal tubules -> obstructive uropathy
  - Can lead to acute renal failure
- Hyperphosphatemia
  - Leads to hypocalcemia, tetany, seizures, arrhythmias

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Risk Factors for TLS

- *High grade lymphoma
  - Burkitt's lymphoma
- *ALL with WBC ≥ 100,000
- *AML with WBC ≥ 50,000
- High tumor cell proliferation rate
- Chemosensitivity
- Large tumor burden: Bulky disease, WBC ≥50,000, or pre-tx LDH > 2x ULN
- Dehydration
- Pre-existing CKD

Landmark Study: Coiffier, B. Journal of Clinical Oncology, 2008

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Management

- Prevention: If high or intermediate risk
  - Allopurinol: Decreases uric acid formation
  - IVF
  - Consider rasburicase
- Treatment: FLUIDS
- Rasburicase: Degrades uric acid to allantoin
  - Consider if pre-existing hyperuricemia
  - Relative contraindication: G6PD deficiency -> can lead to hemolysis and methemoglobinemia
- Treat electrolyte abnormalities
- HD in severe cases

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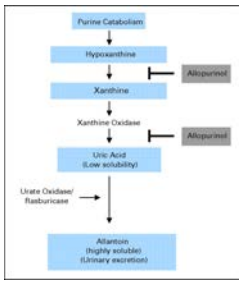
Fig 1. Purine catabolism pathway



Coiffier, B. et al. J Clin Oncol; 26:2767-2778 2008 – Landmark Study

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Symptoms of Leukostasis

- Pulmonary: dyspnea, hypoxia, infiltrates
- Neurologic: AMS, vision changes, headache, tinnitus
- Fever in up to 80%
- Spontaneous TLS and DIC

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Hyperleukocytosis/Leukostasis

- Hyperleukocytosis = WBC >100k
- Leukostasis = increased viscosity, white cell plugs in the microvasculature due to blasts being less deformable, endothelial activity
- Most common with AML
- Can also see in ALL, CML in blast crisis
- Rare in CLL and CML in chronic phase

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Treatment

- One week mortality of 20-40% if untreated
- Treatment:
  - Hydroxyurea for cytoreduction (in asymptomatic patients) or induction chemotherapy
  - Leukapheresis if symptomatic -> involves MICU admission, line placement, transfusion med input
  - IV hydration and allopurinol for TLS prophylaxis
  - **Avoid PRBC transfusions prior to leukoreduction, if possible**

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What is Neutropenic Fever?

- Fever: single oral temperature >/= 38.4 C or temperature >/= 38.0 C sustained over 1 hour
- Neutropenia: ANC <500 or expected to decrease to <500 during next 48 hours
- Neutropenic fever is an oncologic emergency
  - Important to evaluate patient with fever and start antibiotics as soon as possible

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Neutropenia

- Risk of neutropenic fever depends on depth and duration of neutropenia and comorbidities
- Generally due to myelosuppressive chemotherapy
  - Solid tumors: duration of neutropenia < 5 days
  - Heme malignancies: can last >14 days
  - BMT: can be months
  - Highest risk usually 5-10 days after chemo
- Can also occur w/o chemo or at presentation in heme malignancy or if marrow involvement
- New AML is functionally neutropenic
- Remember to check diff

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Approach to Patient with Neutropenic Fever

- Thorough physical exam
  - Skin, oral cavity, line sites
  - Abdomen (typhlitis), perianal area (not DRE)
- Labs
  - CBC diff, CMP
  - UA and culture
  - Blood cultures (if CVC, at least 1 from line)
  - COVID-19 PCR
  - "Sepsis Bundle"
- CXR
- Further workup guided by symptoms/exam

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Neutropenic Fever Treatment

- Rapid treatment CRITICAL!
- Anti-pseudomonal coverage (**cefepime**) for all patients
- Vancomycin
  - Suspected catheter-related infection
  - Skin or soft tissue infection
  - Hemodynamic instability
- Use zosyn if c/f anaerobes, carbapenem if c/f ESBLs
- Consider adding antifungal if persistent fever after 4-7 days of broad spectrum coverage without clear source

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Hyperviscosity Syndrome

- Elevated WBC count or excess protein levels causing increased viscosity and impeding blood flow
- Occurs in MM, **Waldenstrom's (high IgM)**, leukemia, polycythemia
- Stasis of blood flow -> ischemia, hemorrhages
- Serum viscosity does not always correlate with symptoms (but generally >4 centipoise; nl 1.5)

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Symptoms

- Neuro symptoms: HA, confusion, dizziness => ataxia, coma, stroke
- Blurry vision, retinal hemorrhages, papilledema
- Bleeding: typically mucosal (epistaxis, gums)
- Cardiopulmonary: new/worsening heart failure

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Treatment

- Hydration (often dehydrated)
- Plasmapheresis (ie, line placement, ICU admission, transfusion medicine consult)
- Avoid transfusion support if able
  - Especially for pRBCs
  - Increases already high viscosity
- Treatment of underlying condition (chemotherapy)
- Rituximab can cause "IgM flare" in WM, thus may want to hold for 1st cycle (or pheresis first)

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Thank you!

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