ONCOLOGIC EMERGENCIES

FOR THE NON-ONCOLOGY PROVIDER

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Disclosures

- Member of Merck Speaker Bureau

Learning Objectives

Identify	Recognize	Determine
Clinical signs and symptoms of common oncologic emergencies	Oncologic emergencies with appropriate urgency	Appropriate initial intervention for common oncologic emergencies

Types of Emergencies By System

- Hematologic
  - Neutropenic Fever
- Cardiopulmonary
  - SVC syndrome
  - Pneumonitis
- Neurologic
  - Spinal cord compression
  - CNS disease
- Metabolic
  - Tumor Lysis Syndrome
  - Hypercalcemia

Case Study

- 64-year Caucasian female
- h/o breast ca on adjuvant chemotherapy, C3D9
  - dd cyclophosphamide/doxorubicin
- Tmax 102.4 at home
- Fatigue, constipation
- Port in place, last accessed 9 days ago
- Using OTC laxatives and suppository; successful
- Remaining ROS negative

Case Study

- Vitals
  - BP 104/68 HR 106, Temp 102.1 oral, SpO2 99% RA
- Physical Exam
  - Appears fatigued, NAD. Rigors
  - CV Exam with mild tachycardia, regular
  - Abd exam unremarkable
  - Port site well healed, no drainage
  - Skin without erythema, lesions or breakdown
- Labs
  - WBC 1.2, ANC 0.2

Febrile Neutropenia

- Definition
  - ANC <500 (ANC= Total WBC x % neut + % bands)
  - Single temp > 101.3 or 100.4 sustained > 1hr
- Timing
  - Often occurs during nadir
  - Nadir typically 5-14 days after administration of chemotherapy
    - Can last variable amounts of time
- Symptoms
  - May only be the fever!

Febrile Neutropenia

- Common Causes
  - Bacterial
    - Gram negative → E. Coli, Pseudomonas, Klebsiella
    - Gram positive → coag neg staph, S. aureus, Strep sp.
    - Common sites include GI, GU, respiratory, skin
  - Fungal infections
    - Candida
    - Aspirgillosis
  - Viral infections
    - Herpes simplex virus (HSV)
    - Varicella zoster

Febrile Neutropenia

- Labs
  - Blood cultures x2
    - 1 set from indwelling line
  - Urine culture
  - Symptom dependent
    - Sputum culture
    - Stool culture
- Imaging
  - CXR

Febrile Neutropenia - Treatment

Risk Stratification

- **MASCC (Multinational Association for Supportive Care in Cancer) Scoring**

MASCC Score

Characteristic	Score
Burden of illness:[1] • No or mild symptoms • Moderate symptoms • Severe symptoms	 5 3 0
No hypotension	5
No chronic obstructive pulmonary disease	4
Solid tumour or haematological malignancy with no previous fungal infection	4
No dehydration requiring parenteral fluids	3
Outpatient at presentation	3
Age <60 years	2

[1]Only one score for this characteristic (5, 3 or 0 – points are not cumulative).
A score of 21 or more points is predictive of low-risk febrile neutropenia.

Febrile Neutropenia - Treatment

- Antibiotics
  - Low Risk (MASCC >21)
    - IV antibiotics: Cefepime
    - Oral:
      - Ciprofloxacin + amoxicillin/clavulanate
      - Levaquin
      - Moxifloxacin
  - Potentially can be managed outpatient if:
    - Able to return to clinic in 24hrs
    - Able to give first dose of abx IV in clinic

Febrile Neutropenia - Treatment

- Antibiotics
  - High Risk (MASCC <21)
    - Cefepime
    - Add:
      - Piperacillin/Tazobactam (anaerobe coverage)
      - Meropenem (if hx of ESBL)
    - PCN Allergic:
      - Meropenem + amikacin or ciprofloxacin + amikacin +tigecycline

- If/When a source is identified adjust antibiotics to treat known infection

Febrile Neutropenia

- Antifungal & Antiviral Agents
  - Empiric treatment IF neutropenic expected to last >7 days AND persistent/recurrent fever AND no focal source
  - Consider adding earlier in unstable patients
  - Fluconazole, Amphotericin B, caspofungin, voriconazole are all reasonable options
  - Antiviral medications are often targeted to CMV treatment
- Myeloid Growth Factor
  - Granulocyte Colony-Stimulating Factor (GCSF)
  - Daily injection to help correct neutropenia and reduce morbidity
  - Often reserved for severe neutropenia <500
  - Stop when ANC >1000

Febrile Neutropenia

- Important considerations
  - Treat as an emergency
  - NO digital rectal exams or medication administration
  - Check lines/ports
  - Check the oral cavity
  - Pan culture for source

Patient Outcome

- Admitted and started on broad spectrum antibiotics
- Given filgrastim x 4 days until ANC recovery
- Urine culture positive for E.coli
  - Antibiotics changed to levofloxacin
- Fever resolved on hospital day 3
- Discharged home on hospital day 5 with completion of 10 day course of oral Levaquin
- Cycle 4 completed, delayed by 2 weeks

Case Study

- In ED
  - 58-year-old M with PMH HTN, HL, former remote smoker
  - New complaints of progressive mid to low back pain, in past 3 days feeling “like a belt”
  - No inciting injury or trauma
  - Last 3 days has been using the walls for balance when walking
    - Daughter has observed him as “unsteady”
  - Baseline activity level - walks 2-3 miles 3x/week
  - Remaining ROS neg

Case Study

- In ED
  - VS are within normal limits
  - CBC, CMP within normal limits
  - Ataxic gait, patellar DTR 3+ bilaterally
- Imaging
  - MRI – Lytic lesion consistent at L1 body, L1-L2 with edema and thecal sac impingement at this level
  - CT head – no acute abnormalities
  - CXR – Left hilar mass with adenopathy

Spinal Cord Compression

- Definition
  - Any indentation of the thecal sac
  - Can be with or without symptoms
- Spinal cord begins at base of brain and continues to approximately L1-2
- Distal nerve roots regenerate, spinal cord does not

Spinal Cord Compression

- Symptomatic cord compression is an emergency

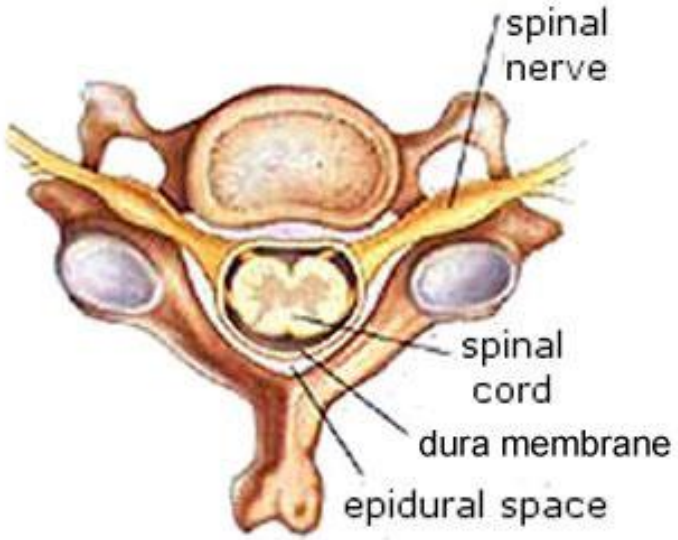
- Can cause irreversible neurologic damage
- In most cases it is not immediately life threatening
  - Requires urgency due to neurologic compromise
- Can be the result of malignancy
- Goals of treatment
  - Functional preservation
  - Pain control

Spinal Cord Compression

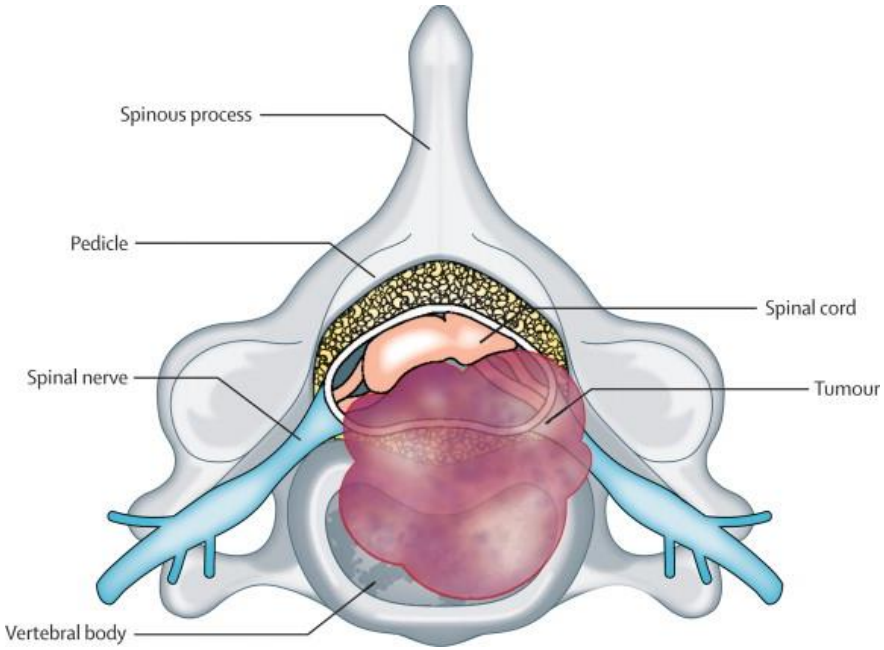
- Common Presentation
  - Back pain
  - Gait disturbance or falls
- Neurologic Deficits
  - Focal weakness and/or sensory changes
  - Urinary or bowel retention
  - These are LATE findings
- Outcome Predictors
  - Rapid course with poor outcomes vs insidious onset with improved outcomes

Spinal Cord Compression

Normal Anatomy



Spinal Cord Compression



Spinal Cord Compression

- Diagnostic Imaging Considerations
  - Plain films generally not adequate
  - MRI is the best imaging tool
  - CT good alternative if MRI not feasible, more useful if able to do CT myelogram

  - Patients with known malignancy with isolated, non radiating midline back pain, consider this diagnosis EARLY, especially if any presence of GU/GI symptoms that are new

Spinal Cord Compression

Examination Pearls

- Pain
  - Usually initial symptom
  - Increasing intensity, often unresponsive to meds
- Motor dysfunction/Weakness
  - Test both upper and lower extremities
  - Evaluate gait
  - DTR testing to evaluate for myelopathy
- Sensory
  - Less common finding, has slower recovery
- Bowel/Bladder dysfunction
  - LATE finding
  - May be retention or constipation
  - Rarely will be the only symptom

Spinal Cord Compression - Treatment

- Steroids
- Surgery
- Radiation

Spinal Cord Compression - Treatment

- Steroids
  - Dexamethasone is medication of choice
  - Given as an initial bolus dose then interval dosing
  - Tapering once patient stabilizes
  - Dosing considerations
    - Hyperglycemia
    - PUD

Spinal Cord Compression

- Surgery
  - Best overall outcomes
  - Often followed by radiation (XRT) to treatment site
  - Preferred treatment if:
    - Patient with limited or isolated tumor burden
    - Patient with good performance status
      - ECOG PS 0-2

Spinal Cord Compression

- Radiation Therapy
  - External Beam Radiation (XRT)
    - Used in patients with more extensive tumor burden or poorer performance status
    - Takes places in daily doses over a series of treatments
  - Stereotactic Radiation (SRS)
    - Useful tool for tumors less chemo sensitive
    - Targeted high dose therapy that limits exposure of adjacent tissues to radiation beam

Patient Outcome

- Admitted for workup of new cord compression and pulmonary mass
- Noted to have adenocarcinoma of the lung with lumbar metastatic disease; diagnosis by lumbar biopsy
- Underwent resection of L1 mass with subsequent XRT
- Post surgical recovery began systemic chemotherapy with carboplatin/pemetrexed

Case Study

- 78-year-old male patient metastatic NSCLC
- On maintenance pemetrexed therapy for 1.5 years
- In past 4-6 weeks more fatigue and generalized malaise
- New nausea/vomiting and anorexia
- New myalgias/arthralgias in extremities; generalized weakness
- New R flank pain, no other GU complaints
- Family reports recent confusion
  - Baseline cognition AAO x3

Case Study

- Vital Signs
  - BP 102/48 HR 110 RR 18 Temp 98.4 oral
- Exam
  - Frail. AAOx person only. Somnolent during visit
  - +R CVA tenderness
  - Mild tenderness on palpation of long bones
  - Abdominal exam benign
- Labs
  - WBC 9.7
  - HgB 10.8
  - Ca2+ 13.7
  - BUN/Cre 31/1.4
  - Albumin 2.8

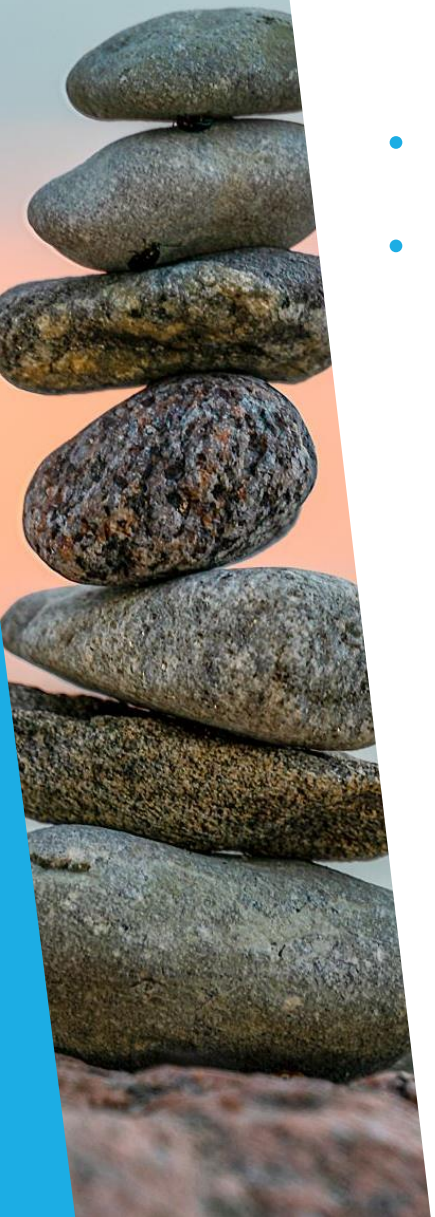
Hypercalcemia

- Definition
  - Total serum calcium concentration > 10.4 mg/dL or ionized serum calcium > 5.2 mg/dL

  - Mild: Corrected Ca > 10.5 to <12mg/dl
  - Moderate: Corrected Ca 12 to 14mg/dl
  - Severe: Corrected Ca >14mg/dl

- Corrected Calcium = (4.0mg/dl – [serum albumin]) x 0.8 + [observed calcium]

Hypercalcemia



- Clinical Presentation
- **Stones, Bones, Groans, & Psychic Moans**
  - Pain, weakness, fatigue
  - Renal calculi, thirst, polyuria, dehydration
  - Nausea/vomiting, anorexia, abdominal pain, constipation
  - Bone pain, myopathy, hypertonia
  - Depression, confusion, ataxia, stupor, coma

Hypercalcemia - Treatment

- Volume expansion with isotonic saline
  - Starting rate 200-300ml/hr then adjusted to maintain UOP of 100-150cc/hr
  - Watch for fluid overload
- Bisphosphonate infusion
  - Zoledronic Acid 4mgIV over 15 minutes is drug of choice
  - Results seen in 12-48 hours
  - With chronic use can cause renal impairment, generally less so in the acute setting, however caution with CKD and myeloma patients

Patient Outcome

- Admitted for treatment of hypercalcemia and new mental status changes
- Calcium normalized at 48 hours
- Renal function back to baseline in 24 hours
- CT head negative
- Seen by PT/OT and discharged with home health
- Was able to resume maintenance pemetrexed in outpatient setting

Case Study

- 68 y/o female
- Stage IV NSCLC on nivolumab (s/p 4 cycles)
- 3 days of progressive dyspnea both at rest and on exertion
- New nonproductive cough
- Uses inhaled steroids for her COPD & rescue inhalers
  - No improvement
- Not oxygen dependent at baseline.

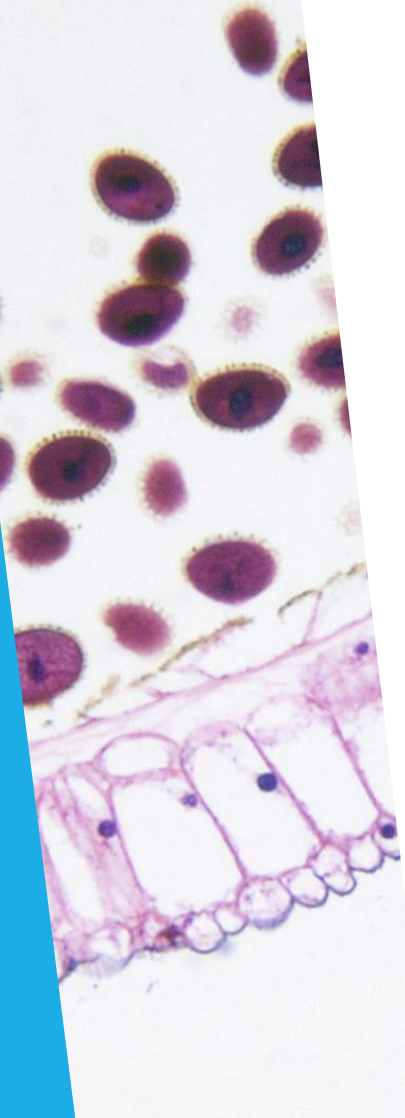
Case Study

Vitals:

- SpO2 84% on RA at rest
- BP 148/88, HR 96, RR 22

Exam:

- Weak and frail. Dyspneic with conversation
- RRR
- Scattered dry crackles throughout



Immunotherapy Related Pneumonitis

- Rare adverse effect with immune modulated therapies
- 4 types
  - Organizing pneumonia (OP)
  - Nonspecific interstitial pneumonia (NSIP)
  - Hypersensitivity pneumonitis (HP)
  - Diffuse alveolar damage (DAD)

Organizing Pna

Non-specific interstitial pna

Diffuse alveolar damage

Immunotherapy Related Pneumonitis

Common Agents

- PD-1 inhibitors such as pembrolizumab and nivolumab among most common
- PDL-1 and CTLA-1 inhibitors (atezolizumab, avelumab, durvlaumab, ipilumumab)

Pre-disposing factors

- Smoking related malignancies & underlying pulmonary disease
- Prior thoracic XRT
- Concurrent tx with conventional chemotherapy or dual immunotherapy tx

Evaluation

- CT chest
- Pulmonary function testing
- Pulmonology referral

Immunotherapy Related Pneumonitis

Treatment

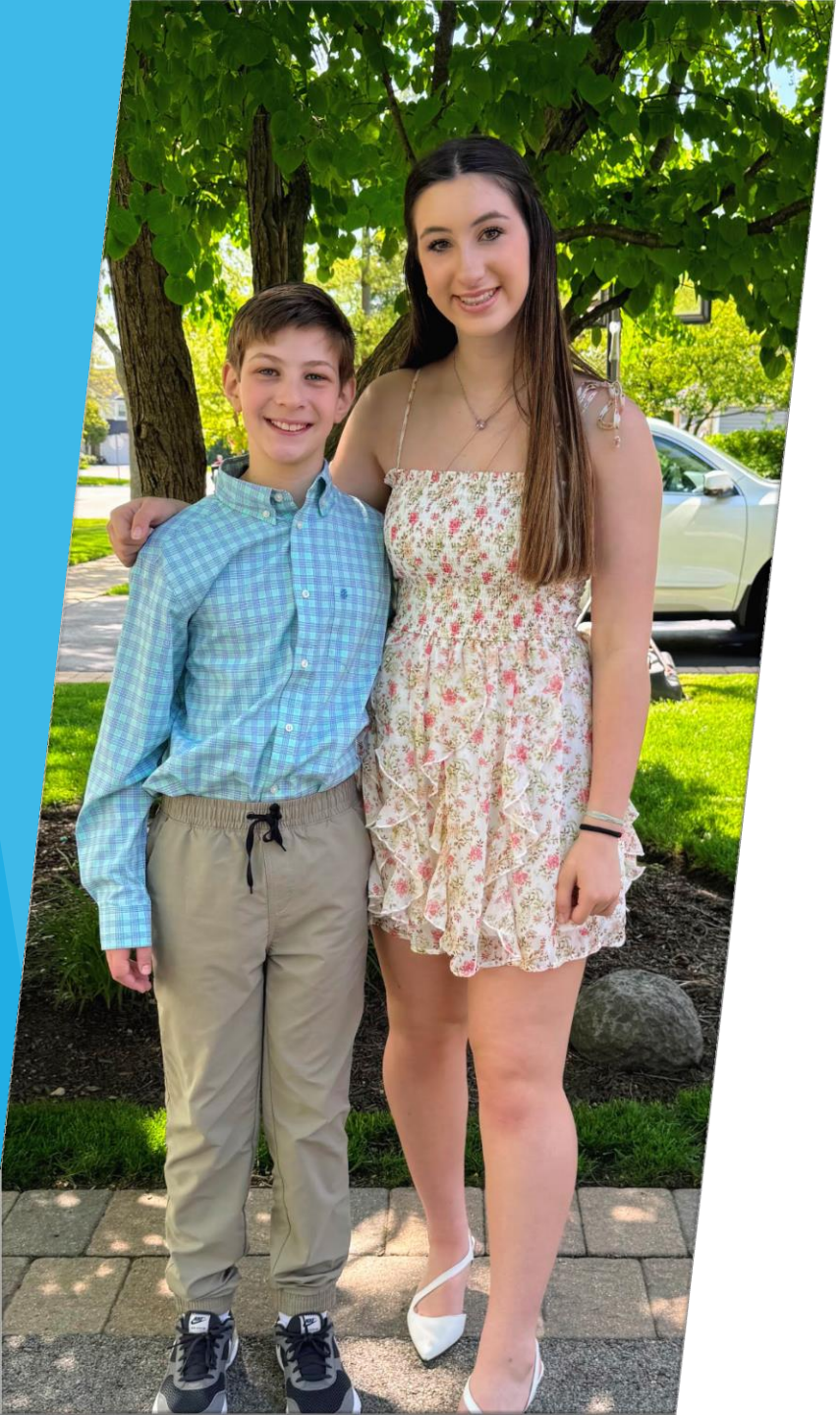
- Mild symptoms
  - Monitoring only
- Moderate symptoms
  - Prednisone at 0.5-1mg/kg/day for 3-6 months
  - Evaluation by pulmonology
  - May require supplemental oxygen
- Severe symptoms
  - Admission
  - Ventilatory support
  - High dose IV steroids with methylprednisolone

Patient Outcome

- Admitted for hypoxemia
- Started on oral steroids and oxygen
- Evaluated by pulmonology
  - Inhaled steroid medications adjusted
- Nivolumab discontinued
  - Consideration of traditional chemotherapy ongoing
- Discharged home on portable oxygen and prolonged oral steroid course

Take Aways

- Oncology patients don't always look sick or sicker during an emergency
- Always investigate new neurologic symptoms
- New abrupt-onset symptoms and clinical findings merit a workup
- Listen to your gut



QUESTIONS?

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