Oncologic Emergencies and Paraneoplastic Syndromes

Internal Medicine Board Review

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Oncologic Emergencies

Why should I learn this?

- Cancer therapy is largely outpatient, so these patients are likely to walk into your office.
- Treatment should not be delayed while attempting to contact the oncologist.
- May be the presenting symptom
- Board Exams
Oncologic Emergencies

Definition: Acute condition caused by cancer or the treatment of cancer where early recognition and intervention would result in the avoidance of mortality or permanent morbidity.
Oncologic Emergencies

- **Initial Evaluation:**
  - Brief focused history
  - Focused Exam
  - Lab/radiograph review
  - Initial Intervention and Additional Studies
  - Then comprehensive history and exam
Oncologic Emergencies

Categories:
- Metabolic
- Hematologic
- Structural
- Treatment related
Metabolic: **Tumor Lysis Syndrome**

- **Definition:** acute lysis of tumor cells as a result of chemotheraphy or radiation therapy, usually within 72 hours of therapy

- **Tumor Types:**
  - Leukemia
  - High-grade lymphoma
  - SCLC
Metabolic: Tumor Lysis Syndrome

**Features:**
- azotemia
- acidosis
- hyperphosphatemia
- hyperkalemia
- hypocalcemia
- hyperuricemia
- ARF

**Symptoms:**
- Nausea
- Vomiting
- Weakness
- Fatigue
- Neuromuscular irritability
- Arrhythmia
Metabolic: **Tumor Lysis Syndrome**

**Tx/Prevention:**
- fluids
- allopurinol
- rasburicase
- urine alkalinization
- HD
- kayexalate
- phos-lo
Metabolic: Hypercalcemia

- Seen in 20 to 30% of cancer patients
- Rate of calcium mobilization from bone exceeds renal calcium excretion

Tumor Types:
- Multiple myeloma
- Squamous Cell: lung, H&N, esophagus
- Breast
- Kidney
Metabolic: Hypercalcemia

- **Mechanisms:**
  - Bone Mets - osteoclast activity
  - Parathyroid hormone-related peptide (binds PTH receptors)
  - Calcitriol production - lymphoma
  - Co-existing Primary Hyperparathyroidism
  - Osteoclast activating factor (OAF) - Multiple Myeloma
Metabolic: **Hypercalcemia**

- **Treatment:**
  - **Calcitonin** — increases renal calcium excretion and by decreasing bone reabsorption
  - **Bisphosphonates** — inhibit calcium release from bone by interfering with the metabolic activity of osteoclasts, and is cytotoxic to osteoclasts. (Pamidronate, zoledronic acid, ibandronate and etidronate)
Metabolic: **Hypercalcemia**

- **Treatment**
  - **Glucocorticoids** (eg, prednisone in a dose of 20 to 40 mg/day) will usually reduce serum calcium concentrations within two to five days by decreasing calcitriol production and OAF.
  - **Volume expansion** with isotonic saline.
  - **Loop diuretic** will also contribute to increased calcium excretion by inhibiting calcium reabsorption in the loop of Henle.
  - **Hemodialysis**.
**Metabolic: SIADH**

- **Definition**: An inappropriate elevation in ADH release that produces hyponatremia by interfering with urinary dilution/excretion of water.

- **Tumor Types**:
  - small cell carcinoma of the lung
  - other lung tumors
  - duodenum
  - pancreas
  - olfactory neuroblastoma
Metabolic: SIADH

- **Symptoms:**
  - Anorexia
  - Nausea
  - Myalgia
  - Headaches
  - Seizures
  - Coma

- **Lab:**
  - Low sodium
  - Low serum osmolarity
  - Concentrated urine
Metabolic: **SIADH**

**Treatment:**

- **Water restriction** is the mainstay of therapy in asymptomatic hyponatremia
- **Hypertonic saline** (or salt tablets)
- **Loop Diuretic** - lowers the urine osmolality and increases water excretion by impairing the renal responsiveness to ADH
- **Demeclocycline** and **lithium** act on the collecting tubule cell to diminish its responsiveness to ADH
Metabolic: SIADH

- Remember to exclude other causes of hyponatremia
  - Medications: vincristine, cyclophosphamide
  - Adrenal insufficiency
  - Brain mets
Hematologic: Febrile Neutropenia

- Neutropenia and Risk:
  - Risk of an occult infection increases with an ANC <1,000 cells/microL
  - It is substantially higher for those with an ANC <500 cells/microL
  - And is highest for those with an ANC <100 cells/microL
  - A rapid decline in ANC
  - Prolonged duration of neutropenia (>7 to 10 days)
Hematologic: **Febrile Neutropenia**

- Defined as a **single temperature** of $>38.3^\circ C$ ($101.3^\circ F$), or a **sustained temperature** $>38^\circ C$ ($100.4^\circ F$) for more than one hour

- Patients may present with hypothermia, hypotension, or clinical deterioration as the initial signs of occult infection.

- Consequently there should be a **low threshold** for starting empiric antibiotics
Hematologic: Febrile Neutropenia

- Most common pathogens:
  - *S. aureus*
  - *S. epi*
  - Streptococcal species
  - Others: Candida albicans, aspergillus, Fusarium, viral
  - Most often the source goes unidentified
Hematologic: **Febrile Neutropenia**

- **Work Up:**
  - Blood Cultures: peripheral and line
  - Urine Cultures
  - CXR - may not see infiltrate
  - CT chest if fever persist after 4-7 days
  - LP if clinically indicated
Hematologic: Febrile Neutropenia

- **Monotherapy**
  - Beta-lactam carbapenem- meropenem, imipenem, piperacillin tazobactam
  - 4th generation cephalosporin-ceftazidime, cefepime

- **Dual Therapy**
  - Aminoglycoside Plus Beta-lactam
  - Fluoroquinolone Plus Beta-lactam
Hematologic:  **Febrile Neutropenia**

- **Vancomycin** - if line associated, cellulitis, severe mucositis, hypotension, history of MRSA colonization, or recent quinolone prophylaxis, patients with clinical deterioration or persistent fever despite empiric antibiotics.

- **Anti-fungal** - fever persists after 4-7 days
Hematologic: Febrile Neutropenia

- 70% mortality rate if initiation of antibiotics is delayed.
Hematologic: **Hyperviscosity Syndrome**

- Results from high levels of serum proteins
- Classically, the syndrome is a result of increased amounts of IgM, as seen in Waldenstrom's macroglobulinemia
- Multiple myeloma in which abnormal polymers of IgA, IgG, or kappa light chains are produced
Hematologic: **Hyperviscosity Syndrome**

- Impairment in the microcirculation of the CNS
- Headache
- Dizziness
- Vertigo
- Nystagmus
- Hearing loss
- Visual impairment
- Somnolence
- Coma
- Seizures
- Mucosal hemorrhage
- Heart failure
- Renal failure
- Sausage-like beading in the retinal veins
Hematologic: **Hyperviscosity Syndrome**
Hematologic: **Hyperviscosity Syndrome**

- Severe neurologic impairment, such as stupor or coma, should be treated with plasma exchange on an emergency basis
- Chemotherapy for the underlying cause
- **AVOID pRBC TRANSFUSIONS**
Structural: **SVC Syndrome**

- **Definition:** Partial or complete obstruction of blood flow through the SVC to the Right atrium

- **Causes:**
  - compression
  - invasion
  - thrombosis
  - fibrosis
Structural: **SVC Syndrome**

- **Tumor Types:**
  - Lung
  - NHL
  - Thymoma
  - Germ cell
  - Breast
Structural: **SVC Syndrome**

- **Signs:**
  - JVD
  - Venous dilation of chest wall
  - Facial edema
  - Upper extremity edema
  - Papilledema if onset is rapid

- **Symptoms**
  - Head fullness or pressure
  - Cough
  - Dyspnea
  - Chest pain
  - dysphagia
**Structural: SVC Syndrome**

- **Treatment:**
  - SVC stent
  - XRT
  - Chemotherapy
  - Anti-coagulants or thrombolytics

- **Pearls:**
  - Secure an accurate diagnosis with biopsy
  - Oxygen
  - Elevate HOB
  - Diuretics sparingly if at all
Structural: **Cord Compression**
**Structural: Cord Compression**

- Occurs in 1-5% of cancer patients
- 95% are caused by extradural metastases involving the vertebral column
  - T-Spine: 70% (spinal canal is narrowest here)
  - L-Spine: 20%
  - C-Spine: 10%
Structural: **Cord Compression**

- **Tumor Types:**
  - Lung
  - Breast
  - Unknown primary
  - Prostate
  - Renal
Structural: **Cord Compression**

- **Symptoms:**
  - Pain, Pain, Pain - localized or radicular, worse with movement, cough, sneeze
  - Urinary retention/incontinence (late)
  - Constipation (late)
  - Poor prognostic features: paralysis or urinary retention
Structural: **Cord Compression**

- **Dx:** MRI

- **Treatment:**
  - Narcotics
  - Dexamethasone: dose is controversial
    - Initial: 20-100mg IV bolus
    - Maintenance: 6-16mg q 6 hours
  - XRT
  - Neurosurgery- spine stabilization
Structural: **Cord Compression**

- Permanent neurologic impairment can result if treatment is delayed by only a few hours.
- Major quality of life issue that might be preventable.
Paraneoplastic Syndromes

- Paraneoplastic neurologic syndromes are a heterogeneous group of neurologic disorders caused by mechanisms other than metastases, metabolic and nutritional deficits, infections, coagulopathy or side effects of cancer treatment.

- These syndromes may affect any part of the nervous system from cerebral cortex to neuromuscular junction and muscle.
Paraneoplastic Syndromes

The more common syndromes

- Lambert-Eaton myasthenic syndrome affects 3% of patients with small-cell lung cancer
- Myasthenia Gravis affects 15% of all patients with thymoma
- <1% incidence for other solid tumors
Paraneoplastic Syndromes

- Review Article: “Paraneoplastic neurological syndromes” in Orphanet Journal of Rare Diseases May 2007, 2:22
- Occur in < 0.01% of cancer patients
Paraneoplastic Syndromes

Pathogenesis:

- **Onconeural antibodies**: antibodies directed at tumor antigens that cross-react with components of the nervous system
- 50% of patients with PNS do not have detectable antibodies
- Antibodies may be present in the absence of a PNS
Paraneoplastic Syndromes

- **Definite PNS Criteria:**
  - Classical neuro syndrome and cancer develops within 5 years of the neuro disorder
  - Non-classical neuro syndrome improves after treatment of underlying cancer
  - Non-classical neuro syndrome with onconeural antibodies AND cancer develops within 5 years
  - Neuro syndrome with well-characterized onconeural antibodies (Hu, Yo, CV2, Ri, Ma2, anphiphysin) AND no cancer
Paraneoplastic Syndromes

- Possible Criteria:
  - Classic neuro syndrome, No Ab, No cancer, but is at high risk for an underlying tumor
  - Neuro syndrome, partially characterized Ab, No cancer
  - Non-classical neuro syndrome, No Ab, cancer diagnosis within 2 years
Paraneoplastic Syndromes

- **Anti-Hu**: (antineuronal nuclear antibody ANNA-1)
  - Encephalomyelitis- asymmetric paresthesias SCLC
  - Limbic encephalitis- memory and mood

- **Anti-Yo**: Cerebellar degeneration- dysarthria and ataxia

- **Anti-Tr**: Cerebellar degeneration (Hodgkin’s)
Paraneoplastic Syndromes

- **Anti-Ta**: Limbic encephalitis (testicular/breast)

- **Anti-amphiphysin**: Stiff-person syndrome

- **Anti-GAD**: Stiff-person syndrome (breast)

- **LEMS Ab**: Lambert-Eaton, SCLC
PNS: Lambert-Eaton myasthenic syndrome

- Disorder of reduced acetylcholine (ACh) release from the presynaptic nerve terminals

- Antibodies directed against the voltage-gated calcium channel (VGCC) interfere with the normal calcium flux required for the release of acetylcholine
**PNS: Lambert-Eaton myasthenic syndrome**

- **Symptoms**
  - slowly progressive
  - proximal muscle weakness, particularly involving the legs
  - Deep tendon reflexes are typically depressed or absent

- Ptosis and diplopia
- Dry mouth
- Erectile Dysfunction
- Respiratory failure may occur late in the course.

**Hallmark:** Recovery of lost deep tendon reflexes or improvement in muscle strength with vigorous, brief muscle activation
PNS: Lambert-Eaton myasthenic syndrome

- **Diagnosis:**
  - **Post-exercise facilitation:** Maximal isometric contraction the limb for 10 to 15 seconds may lead to temporary reappearance of previously depressed or absent DTR’s, and temporary improvement of muscle weakness.
  - **Ab to voltage-gated calcium channel (VGCC)**
  - **Electrodiagnostic studies-EMG**
PNS: Lambert-Eaton myasthenic syndrome

- Occurs much less frequently than myasthenia gravis
- Approximately one-half of LEMS cases are associated with a malignancy, usually SCLC
PNS: Myasthenia gravis

- Mediated by autoantibodies against the acetylcholine receptor (AChR-Ab)
- The majority of patients AChR-Ab positive myasthenia gravis have thymic abnormalities: hyperplasia in 60 to 70% and thymoma in 10 to 12%
**PNS: Myasthenia gravis**

- **Symptoms**
  - Fluctuating skeletal muscle weakness, worse later in the day or evening
  - Fatigue - meaning worsening contractile force of the muscle
  - 50% of patients present with ocular symptoms of ptosis and/or diplopia
  - 15% present with bulbar symptoms (dysarthria, dysphagia, and fatigable chewing)
  - Less than 5% present with proximal limb weakness alone
  - Respiratory insufficiency
PNS: Myasthenia gravis

Diagnosis

- **Tensilon test**- Edrophonium chloride is an acetylcholinesterase inhibitor prolongs the presence of Ach in the neuromuscular junction and results in an immediate increase in muscle strength

- Serologic tests for autoantibodies

- Electrophysiological studies
PNS: Myasthenia gravis

- **Treatments:**
  - Symptomatic treatments (anticholinesterase agents)
  - Chronic immunomodulating treatments (corticosteroids and other immunosuppressive drugs)
  - Rapid immunomodulating treatments (plasma exchange and intravenous immune globulin)
  - Surgical treatment (thymectomy)
Others

- **Carcinoid Syndrome**
  - Carcinoid tumors of foregut derivatives (small intestine, stomach, bronchus, pancreas, thyroid)
  - Overproduce 5-HT (5-hydroxytryptamine) serotonin, histamine, tachykinins, kallikrein and prostaglandins
  - Urine excretion of 5-HIAA
Carcinoid Syndrome

**Symptoms:**
- Episodic flushing
- Fall in blood pressure and rise in pulse rate
- Secretory diarrhea
- Wheezing and dyspnea
- Carcinoid heart disease - right side
Carcinoid Syndrome

- **Treatment:**
  - Somatostatin analog octreotide
  - Cyproheptadine, a serotonin antagonist
  - Chemotherapy effectiveness is questionable
  - Isolated lesions: cryo, RFA (treat with octreotide prior to anesthesia to prevent crisis)
Others

- **Zollinger-Ellison Syndrome** - excessive gastrin secretion from a gastrinoma
- Develop peptic ulcers, most are in the first portion of the duodenum
- Diarrhea can also be a prominent feature
ZES

- **Diagnosis:**
  - Fasting serum gastrin concentration
  - Secretin stimulation test
  - Gastric acid secretion studies
50 yo female, presents to ER c/o falling, difficulty arising from a chair. Weakness improved during the day. Also c/o dyspnea on exertion. 45 pack years.

Proximal muscle weakness on exam

What is the most appropriate management?

A. Follow up with PCP
B. Physical Therapy
C. Admit for EMG and possible treatment
D. Smoking cessation classes
56yo female presents to ER c/o epistaxis, blurry vision, confusion.
PMHx: HTN

Vs all normal, blood at nares and gums, bibasilar crackles, no edema

Labs: Hgb-8, plts-350, WBC-8.0, normal diff., T. ptn 10.2, albumin 3.0, lytes all normal

What is the most likely diagnosis?

- A. Essential thrombocythemia
- B. CML
- C. AML
- D. Hyperviscosity
What is the most appropriate therapy?

A. Platelet transfusion
B. pRBC transfusion
C. Plasmapheresis
D. Prednisone

What tests or physical exam findings will assist in finding the diagnosis in the ER?

A. CT brain
B. Serum viscosity
C. Fundoscopic exam
D. B and C

Questions obtained from The John Hopkins Internal Medicine Board Review 2004
65yo man presents to the ER with confusion, increased thirst, and increased urination. PMHx: HTN

Vs normal, dry mm, skin tenting

Labs: Cr=5.4, BUN=46, K=5, Ca=12.5, Alb=3.0, T. protein=9

What is the most appropriate initial therapy?

A. Normal saline
B. Dialysis
C. Pamidronate
D. Diuretics

Questions obtained from The John Hopkins Internal Medicine Board Review 2004
Thank You and Best of Luck!