

Oncologic Emergencies

Vesicant Extravasation Necrosis

- Certain chemotherapy agents when extravasated from a peripheral IV can cause severe local skin and soft tissue necrosis and need to be managed emergently
- Distinguished from irritants which cause local inflammatory reaction, tenderness along vein with burning and erythema but do not lead to tissue injury or necrosis
- The severe vesicants include: **Doxorubicin, Daunorubicin, Mechlorethamine, Mitomycin C, Dactinomycin and Vinca alkaloids**
- The mild to moderate vesicants include: 5-FU, etoposide, bleomycin, cisplatin, irinotecan, mitoxantrone, paclitaxel, streptozocin, oxaliplatin, docetaxel, and doxil
- Necrotic tissue reactions can continue for weeks despite withdrawal of the offending agent
- **In all cases prompt recognition is key – infusion should be terminated immediately if the patient complains of pain, burning, or stinging at the infusion site or if local swelling is observed. Elevate the affected extremity, apply ice pack (except if vesicant is a Vinca alkaloid) and contact the oncologist.**
- Surgical consultation should be made for persistent pain, erythema and swelling even in the absence of blister formation

Agent specific therapies

Mechlorethamine and Mitomycin C	0.17 M sodium thiosulfate IV and 50-90% DMSO topically
Vinca alkaloids	apply local heat 150 U hyaluronidase IV
Doxorubicin and Daunorubicin	59-90% DMSO topically

Neutropenic Fevers

Definition:

Neutropenia (ANC <500-1000) with associated fever (oral temp >101.3 or >100.4 for >1hr)

General Concepts:

- Myelosuppressive chemotherapy should never be given without a CBC within 48 hours of treatment
- Neutrophil nadir generally occurs 5-10 days after last chemo dose with recovery of leukocytes count 5 days after nadir. However there is tremendous variation with chemo agents, with particularly delayed nadirs in chemo for hematologic malignancies, mitomycin C and nitrosoureas
- See chemotherapy tables for nadirs of specific drugs

Work up and Management

- Complete history and physical focusing on localizing sources of infection including oral cavity, catheters, and visual inspection of perianal region without DRE
- Blood and urine culture in all, sputum, stool and CSF if symptomatic, CXR and other radiologic studies as pertinent to clinical presentation
- Keep in mind, because of neutropenia common infections may present with underwhelming symptoms or even asymptotically
- Consider whether patient low or high risk based on age, ANC, expected nadir of chemotherapy agent, presence of SIRS physiology or sepsis, co-morbidities including diabetes, cardiopulmonary disease, or concurrent steroid or immunosuppressant use
- Initiate empiric antibiotics after cultures drawn, with or without growth factors

Low Risk:

Consider outpatient management with PO Cipro 500mg q8 and Augmentin 500mg q8 and daily f/u until afebrile 4-5 days
In hospitalized, Ceftazidime 2g IV q8 or Primaxin 500mg IV q6

High Risk:

Neupogen 5mcg/kg SC daily
Consider Zosyn 4.5g IV q6 or Ceftazidime 2g IV q8 + Aminoglycoside
Add Vanco for documented MRSA colonization, indwelling catheters, severe mucositis, or hemodynamic compromise
Consider coverage for Clostridium septicum (Clinda, pen G) for "typhlitis" (neutropenic enterocolitis) classically presents with RLQ pain
Transfuse platelets when <20,000 if febrile and <10,000 if afebrile

- If persistently febrile after 3 days empiric therapy without source, consider antifungal therapy

Malignant Spinal Cord Compression

General Concepts:

- True neurologic emergency that requires prompt recognition and treatment
- Back or radicular pain with neurologic symptoms is MSCC until proven otherwise
- Incidence increasing because of improving survival
- Occurs in 2.5-6% of cancer patients, most common solid tumor - lung, breast and prostate, most common hematologic - myeloma and lymphoma
- Neurologic status at diagnosis and time to development of symptoms are important prognostic factors for outcome¹ (the better going into treatment, the better upon completion)
- Usual mechanism is spread of tumor to thoracic (> lumbar > cervical) vertebral bodies that subsequently encroach on spinal canal causing vascular compromise

Presentation and Work Up:

- 90-95% of patients with MSCC have back pain

¹ Int J Radiation Oncology Biol Phys. 2002;53:975

- 30% of patients with more than 1 site of involvement
- In 20% of patients with MSCC it is the presenting sign of cancer
- Can also present with radicular pain, motor weakness, gait disturbance and bowel or bladder dysfunction
- Plain radiographs may help, but **emergent MRI of entire spine is the study of choice given high chance of more than 1 site of disease**

Treatment:

- Initiate steroids upon suspicion – Decadron 40mg IV then 10mg IV q6
- Rapid consultation with neurosurgeon and radiation oncologist if lesion found
- Emergent radiation therapy remains traditional standard of care, radical tumor resection prior to radiation is under further investigation and currently not available outside of specialized centers^{2,3}

Radioresponsive tumors

Lymphoma
Myeloma

Radioresistant tumors

Renal Cell
Melanoma
Sarcoma

- Surgery in highly selected cases, including gross instability of spine, previous radiation therapy to site, progressive symptoms on radiation therapy, need for tissue diagnosis, and radioresistant tumors

Altered Mental Status in Cancer Patient

General Concepts:

- Always consider metabolic i.e. hypercalcemia or medication related causes
- Lung cancer, breast cancer and melanoma most common cancer with metastasis to brain
- 90% of brain metastasis are supratentorial

Presentation and Work up:

- Complete history to extent possible, including corroborative information from family members, care providers including extent of cancer, history of treatment, known sites of metastasis, recent medication changes particularly opiates, benzodiazepines, anti-nausea medications, recent imaging studies, presence or absence of seizures, localizing neurologic symptoms
- Physical examination focusing on general and neurologic exam, with focused exam as pertinent
- Consider contrast CT scan of brain if suspicious of CNS metastasis, MRI is the most sensitive and specific diagnostic modality

Hypercalcemia of malignancy

General Concepts:

- More common in advanced malignancy
- Most common malignancies – breast, lung and multiple myeloma
- 3 subtypes

² Mayo Clin Proc. 2005; 80:1177

³ Lancet. 2005;366:643

1. Humoral hypercalcemia of malignancy – mediated by malignant cell release of PTHrP (ParaThyroid Hormone related Peptide) that stimulates osteoclastic bone resorption and distal tubular calcium reabsorption. Most common subtype
 2. Local bone destruction by tumor with release of cytokines, including osteoclast activating factors
 3. Tumor production of vitamin D analogues i.e. calcitriol, seen in lymphomas, myelomas
- Bisphosphonates block osteoclastic bone resorption – use intravenous forms, oral formulations not effective in hypercalcemia of malignancy

Presentation and Work up:

- Classic symptoms include lethargy, confusion, anorexia, nausea, constipation, polyuria and polydipsia
- Check renal function, albumin level (for corrected calcium), alkaline phosphatase, electrolytes including phosphate
- Low serum chloride suggestive of diagnosis (<100 mEq/L)
- Intact PTH expected to be low
- Usually have associated moderate to severe dehydration

Treatment:

- Treat the underlying cancer
- Initiate intravenous hydration with normal saline titrated to extent of hypovolemia
- For symptomatic hypercalcemia, give a bisphosphonate (caution with renal insufficiency, monitor creatinine) need to wait 3-4 weeks for repeat
 - Zoledronic acid 4mg IV over ≥ 15 minutes
 - Pamidronate 60-90mg IV over 2-4 hours
- Consider calcitonin 6-8 units/kg SC or IM for rapid, short lived response
- Consider steroids if vitamin D analogues suspected as cause or in lymphoma or myeloma
- Maintain calcium x phosphorous product of less than 70
- Consider monthly administration of IV bisphosphonate with metastatic bone disease

Tumor Lysis Syndrome

Basic Concepts:

- Usually seen after therapy for aggressive hematologic malignancies, large bulky solid tumors and chemo-sensitive tumors
- Caused by release of intracellular contents after tumor cell death including nucleic acids converted to uric acid, potassium, and phosphorous (leading to hypocalcemia)
- Untreated will lead to renal failure through crystallization of uric acid in renal tubules and life-threatening hyperkalemia
- Prevention based on adequate hydration and administration of Allopurinol 600mg/day, 2-3 days prior to chemotherapy in those at highest risk

Presentation and Work up:

- Thorough history including timing of last chemotherapy, mental status changes, urine output, palpitations, or seizures
- Check LDH as surrogate for cell turnover

- Consider EKG to evaluate electrolyte abnormalities
- Consider admission for cardiac monitoring

Treatment:

- Aggressive intravenous fluid management for goal urine output >100mL/hr
- Management of hyperkalemia (i.e. calcium, insulin, dextrose, Kayexalate)
- Management of hyperphosphatemia (i.e. Phoslo or Renagel depending on calcium x phosphate product)
- Consider IV recombinant urate oxidase (rasburicase) for severe cases
- Alkalinization of urine is controversial and not routine
- Hemodialysis reserved for refractory cases and those with renal or cardiac compromise

Superior Vena Cava Syndrome

Basic Concepts:

- Occlusion or compression of SVC
- Most common malignancies associated are lung cancer (75%) and lymphoma
- Indwelling central lines may lead to thrombosis, giving unilateral symptoms
- Symptoms minimized if occlusion occurs gradually and collaterals form

Presentation and Work up:

- Dyspnea (75%), facial swelling, head fullness and cough exacerbated by leaning forward or lying flat
- Distended neck and chest wall veins (collaterals), facial edema, plethora and edema of upper extremities
- CXR and consider CT scan chest if high clinical suspicion

Treatment:

- Surgical biopsy if no previous tissue diagnosis (It is safe despite elevated venous pressure)
- Multimodality treatment including radiation, chemotherapy and sometimes stenting of SVC depending on tumor type
- Consider thrombolysis for catheter related thrombosis if < 5 days old with subsequent anticoagulationⁱ
- Stent placed by interventional radiology may relieve symptoms

ⁱPrimary texts: Oncologic Emergencies: Diagnosis and Treatment. Mayo Clin Proc. June 2006;81(6): 835
Clinical Oncology. 3rd edition. Elsevier Inc. 2004