Oncology Emergencies

Gerald Hsu, MD, PhD
Asst Clinical Professor of Medicine

Workshop outline

- Five case scenarios that cover:
  - Cord compression
  - Hypercalcemia
  - Tumor lysis syndrome
  - Fever and Neutropenia
  - Thrombocytopenia
- Discussion of your cases and questions
Case #1

- 60 year old man with established metastatic prostate cancer to bone
- PSA 166 ng/mL at diagnosis 18 mos prior to admission
- Prostate bx Gleason score 5+5
- Bone scan positive diffusely
- PSA fell to 2.2 with LHRH analog therapy

- 14 mos after dx, PSA rising
- Multiple painful bony areas
- Now presents with 5 days of gait difficulty, progressing to left foot drop and inability to walk
- Admitted to the hospitalist service
Physical exam

- Thin but not cachectic
- Diffuse abd tenderness but no invol guarding
- No spinal tenderness
- 3/5 strength in lower extrem flexors bilaterally; 5/5 strength in extensors.
- Sensory exam normal
- Reflexes normal
- Diminished but present rectal tone

Which of the following is the most common early manifestation of epidural spinal cord compression?

A. Motor weakness.
B. Numbness or paresthesias.
C. Localized back pain.
D. Urinary incontinence.
Lab tests

- Creatinine, lytes, calcium, lft’s nl
- CBC okay x mild anemia (hgb 11 g/dL)
- PSA last 52 at outside facility, pending here

Which of the following imaging studies should be pursued

A. CT myelogram
B. Bone scan (Technetium 99)
C. FDG PET scan
D. MRI lumbar spine
E. MRI whole spine
What is the right dose of dexamethasone in suspected spinal cord compression?

A. 8 mg IV/PO BID
B. 4 mg IV/PO Q6H
C. 100 mg IV now; 24 mg IV/PO Q6H until either radiation therapy or surgery
D. Either a or b
Which of the following therapeutic options should be pursued?

A. Radiation therapy  
B. Surgical decompression  
C. Surgical decompression followed by radiation therapy

**Surgery + radiation vs. Radiation alone**


- Population: Good surgical candidate with life expectancy >3 mos, paraplegia <48 hours
- Outcomes:
  - 1º: Function. **Ability to walk** 84% of surg+xrt arm vs. 57% in xrt alone arm.
  - 2º: **Survival benefit.** 126 days vs. 100 days.

**Caveats:**
- Single site of compression
- Radiation within 2 weeks of surgery
- Excluded pts with radiosensitive tumors
- 18 patients with spinal instability were assigned to radiation alone arm
- There was no difference in outcome between arms for patients >65
Case 1: Outcome

- Patient taken to Anterior Corpectomy for acute cord decompression by Neurosurgical and CT surgery teams
- Slow recovery of motor function occurred
- Eventually completed radiation therapy

Key points: cord compression

- Back pain precedes motor symptoms
- Avoid high dose steroids.
- Surgery + radiation is likely to benefit a specific population:
  - obtaining path for diagnosis
  - spinal instability
  - under 65, life expectancy >3 mos, disease that is not radiosensitive, paraplegia <48 hrs
Case #2

51 year old man without PMHx presents with:
- Acute onset of both right-sided rib and back pain
- Cough
- Weight loss
- Confusion

Baseline evaluation shows
- WBC 6.3 x 10^3/mm^3, Hgb 16.9 g/dL, plt 340 x 10^3/mm^3
- Na 125 mmol/L, K 4.2 mmol/L, Cr 1.0 mg/dL, Ca 12 mg/dL, albumin 1.8 g/dL, Phos 4.4 mg/dL
- Tender ribs, no fracture on CXR
- Blood smear with rouleaux
- Total serum protein 10.5 g/dL
- Dx: symptomatic hypercalcemia, likely from multiple myeloma
Hypercalcemia manifestations

- Progressive mental impairment and renal failure.
- A poor prognostic sign.
- Treatment is indicated if hypercalcemia is severe.

<table>
<thead>
<tr>
<th>Ca²⁺ mg/dL</th>
<th>Ionized Ca²⁺ mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.0</td>
<td>1.4</td>
</tr>
<tr>
<td>12.0</td>
<td>2.0</td>
</tr>
<tr>
<td>14.0</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Mild

Moderate

Severe

Hypercalcemia of Malignancy

What are the mechanisms of hypercalcemia in malignancy?

What are the main components of therapy for hypercalcemia of malignancy?
### Type

<table>
<thead>
<tr>
<th>Type</th>
<th>Mechanism</th>
<th>Associated cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humoral</td>
<td>PTHrP</td>
<td>• Squamous cancers (most commonly lung)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Breast cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Renal cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Ovarian or endometrial cancer</td>
</tr>
<tr>
<td>Osteolytic</td>
<td>Cytokine mediated and PTHrP</td>
<td>• Multiple Myeloma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Breast cancer</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Lymphoma</td>
</tr>
</tbody>
</table>

Primary hyperparathyroidism in setting of malignancy is not uncommon... so check PTH

Much less common:

• 1,25(OH)₂D secreting tumors (lymphomas)
• PTH secreting tumors
Hypercalcemia of Malignancy

What are the mechanisms of hypercalcemia in malignancy?
Most commonly, PTHrP mediated. Not necessarily indicative of bone metastases.

What are the main components of therapy for hypercalcemia of malignancy?

Treating Hypercalcemia: Which of the following is not an initial component of management?

A. 80 mg IV furosemide
B. 2L Normal Saline
C. IV pamidronate
D. IV calcitonin
Treating Hypercalcemia of Malignancy

**Volume repletion and supportive care**
- NS 200-300 cc/hr
- Oral phos repletion (goal 2.5-3 mg/dL)

**Bring down the calcium**
- Bisphosphonate +/- calcitonin
  - Either pamidronate or zoledronate
  - Response time: hours for calcitonin; about a day with bisphophonate
  - Duration: up to 3 weeks

**Treat underlying cause**

Options for treating severe hypercalcemia in AKI (Cr >4.5)

- Full dose bisphosphonate
- Reduced dose bisphosphonate with slower infusion rate
  - (eg. 4 mg zolendronic acid over 1 hour or 30 mg pamidronate over 4 hours)
- Calcitonin until kidney function improves
- RANK ligand inhibitor (ie. denosumab) that is not renally cleared.
bisphosphonate

denosumab

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Hypercalcemia of Malignancy

What are the mechanisms of hypercalcemia in malignancy?

- Most commonly, PTHrP mediated.
- Not necessarily indicative of bone metastases.

What are the main components of therapy for hypercalcemia of malignancy?

- Volume repletion.
- Bisphosphonate +/- calcitonin.
- Treatment of underlying cause.

Case #3

- 64 year old man with CLL (+deletion 17p, bulky adenopathy) is admitted to the hospitalist service with nausea, vomiting, lethargy, and muscle cramps.
- He was started on venetoclax (Bcl-2 inhibitor) two days prior by his oncologist.
- Labs were notable for:
  - pre-venetoclax wbc of 105 x 10^3/mm^3 (90% lymph) and uric acid of 9 mg/dL
  - Cr 3.4 mg/dL, K 6.0 mEq/L, Ca 7.8 mg/dL, Phos 5.5 mg/dL, uric acid 10 mg/dL
  - ECG: sinus tach, CXR: mild increased interstitium
Which of the following is true about the diagnosis and management in this case?

A. This patient is at high risk for complications of tumor lysis syndrome.
B. He should have received allopurinol prior to initiation of therapy.
C. CBC and lytes should be checked QD.
D. Renal replacement should be initiated.

Tumor Lysis Syndrome

Definition: A syndrome resulting from “the metabolic derangements that occur with tumour breakdown following the initiation of cytotoxic therapy.”

— Cairo & Bishop

Laboratory tumor lysis = 2 or more electrolyte abnl
- K > 6 mEq/L
- Phos > 4.5 mg/dL
- UA > 8 mg/dL
- Ca < 7 mg/dL

or 25% change from baseline

Clinical tumor lysis = laboratory tumor lysis +
- Cr 1.5x ULN or
- cardiac arrhythmia/sudden death or
- seizure
### TLS risk stratification (simplified)

<table>
<thead>
<tr>
<th>HIGH</th>
<th>MEDIUM</th>
<th>LOW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burkitt lymphoma/leukemia</td>
<td>CLL</td>
<td>Multiple Myeloma</td>
</tr>
<tr>
<td>High grade DLBCL</td>
<td>NHL with elevated LDH</td>
<td>CML</td>
</tr>
<tr>
<td>ALL (wbc &gt;100K)</td>
<td>ALL (wbc &lt;100K)</td>
<td>Other solid tumors</td>
</tr>
<tr>
<td>AML (wbc &gt;100K)</td>
<td>AML (wbc &lt;100K)</td>
<td></td>
</tr>
<tr>
<td>CLL with high burden disease + venetoclax</td>
<td>small cell lung cancer</td>
<td></td>
</tr>
<tr>
<td></td>
<td>germ cell tumors</td>
<td></td>
</tr>
</tbody>
</table>

**TLS risk stratification (simplified)**

- Occurs in tumors with high body burden and high chemosensitivity
- Usually high-grade lymphomas or leukemias
- Usually due to therapy, so you know the diagnosis already
- May occur at onset of therapy, or after a day or two
- Generally, only an issue for *first chemo*
**TLS management:**

- **Fluids**
  - 2-3 L/m2/day. (D5 1/4 NS preferable)

- **Hypouricemic agents**
  - allopurinol if uric acid is wnl
    - exception is patients of Asian descent (due to inheritance of HLA allele that predisposes to severe cutaneous rxns)
  - febuxostat (alternative to allopurinol)
  - rasburicase if high-risk or elevated uric acid in intermediate-risk patients
    - exception is patients with G6PD deficiency
    - In practice, 3 mg dose is commonly used

- **Monitoring**
  - For patients at high-risk, serum K, Cr, Ca, Phos, uric acid, LDH q4-8H (in addition to 4 hours after first rasburicase dose)
  - Urine output (2 ml/kg/hr)

**TLS: Indications for RRT**

- Persistent hyperkalemia
- Symptomatic hypocalcemia secondary to hyperphosphatemia
- Elevated calcium-phosphate product (70 mg²/dL²)
- Oliguria or anuria
Key points: TLS

- Patients at highest risk are those with aggressive heme malignancies and large burden disease. Novel therapies are making this more common.

- Risk stratify. If high risk, rasburicase.

- Management: fluids, hypouricemics, and TLS labs (frequency dependent on risk).

Case #4

- 77 year old woman with Chronic Lymphocytic Leukemia, intermittently receiving chemotherapy for the last 3 years for symptoms

- Admitted with dehydration, fatigue, mild renal insufficiency, and anemia for fluids and transfusion (WBC = 18 x 10^3/mm^3; hgb = 7.1 g/dL; plts = 88 x 10^3/mm^3; Cr = 2.7 mg/dL)

- On hospital day #2, lab calls with panic value neutrophil count of 400/mm^3 just as ward calls with patient temperature of 100.8F
Which of the following antibiotics is most appropriate?

A. levofloxacin
B. cefipime
C. vancomycin
D. fluconazole

Context: When was chemo given?
- What was given?
- Type of cancer?
- Risk factors?

Evaluation: What to obtain and why?

Management: Which antibiotic(s)?

-10-7 chemo

day 0

Evaluation: PE/catheter inspection
- Blood, urine cultures
- CXR (if respiratory sx)

Management: WITHIN 60 MIN
- cefipime, pip/tazo, carbapenem
- +/- vancomycin
Oral chemo causing neutropenia

- 6-mercaptopurine
- Altretamine
- Busulfan
- Capecitabine
- Carmustine
- Chlorambucil
- Crizotinib
- Cyclophosphamide
- Dasatinib
- Etoposide
- Everolimus
- Hydroxyurea
- Imatinib
- Lenalidomide
- Lomustine
- Melphalan
- Methotrexate
- Pazopanib
- Procarbazine
- Sorafenib
- Sunitinib
- Temozolomide
- Thalidomide
- Topotecan
- Vandetanib
- Vemurafenib

If the patient has a central venous catheter, under what conditions should it be removed?

A. Persistent fever despite antibiotic therapy for more than 48 hours.
B. Central line associated blood stream infection caused by coag-negative staph.
C. *S. Aureus* bacteremia from non-catheter related etiology.
D. Blood stream infection from any source that persists for more than 72 hours despite adequate antibiotic therapy.
Context: Persistent neutropenia?  
Culture data?  
Management: Broaden coverage?  
Catheter removal?

-10-7 chemo  
day 0  day 2

Evaluation:  
* consider additional imaging  
Management:  
* consider d/c vanc  
* consider removal of catheter if CLABSI

If fever persists for more than four days, which of the following should be considered?

A. Initiation of antifungal therapy.  
B. Initiation of granulocyte colony stimulating factor (GCSF).  
C. Continuation of empiric antibiotics until neutropenia resolves to 500 cells/mm³.  
D. 1 and 2  
E. 1 and 3
Context: Persistent fever?
Still neutropenic?
No actionable data from cx?

Management: GCSF?
Antifungal?
Duration of antibiotics?

-10-7
day 2
day 4-7

chemo

Management:
GCSF is generally not indicated
If persistent F&N, initiate anti-fungal
For documented infxn, complete abx course
Otherwise, abx until neutropenia resolves

Key points: F&N

- Antibiotics ASAP = mortality benefit.
- Likely causative organism depends on duration of neutropenia:
  - short term: bacterial
  - long term (weeks): fungi, viruses, opportunistic
- Cefipime, pip/tazo, or carbapenem. Vanc in certain circumstances.
- Consider antifungal therapy if fever persists beyond 4 days.
- Duration of therapy depends on organism and site.
  If unexplained fever, continue antibiotics until neutropenia resolves.
Case #5

- You have just received signout on a 61 year old female patient admitted for community-acquired pneumonia 2 days ago
- Clinically she has yet to ‘turn the corner’ despite several days of antibiotics
- Before she is seen, you get the stat page from the lab that her morning CBC shows a platelet count of 14,000 / mm³

What do you want to know right now?

A. PT/PTT/fibrinogen to rule out DIC
B. Yesterday’s platelet count to see how far it’s fallen
C. Is the patient bleeding?
D. Has this patient received heparin in any form in the last week?
E. LDH to rule out TTP
**Thrombocytopenic bleeding**

- Petechiae and mucosal bleeding (the image below) are common but by themselves don’t require systemic treatment
- **Active bleeding with a platelet count under 50,000/mm³ requires platelet transfusion regardless of etiology**

**Platelet vs. factor bleeding**

<table>
<thead>
<tr>
<th>CLINICAL CHARACTERISTIC</th>
<th>PLATELET DEFECT</th>
<th>CLOTTING FACTOR DEFICIENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of bleeding</td>
<td>Skin, mucous membranes</td>
<td>Deep in soft tissue</td>
</tr>
<tr>
<td>Bleeding after minor cuts</td>
<td>Yes</td>
<td>Not usually</td>
</tr>
<tr>
<td>Petechiae</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Ecchymoses</td>
<td>Small, superficial</td>
<td>Large, palpable</td>
</tr>
<tr>
<td>Hemarthrosis, muscle hematomas</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Bleeding after Surgery</td>
<td>Immediate, mild</td>
<td>Delayed, severe</td>
</tr>
</tbody>
</table>
Which of the following is true about differentiating between different causes of acute thrombocytopenia?

A. DIC is not associated with thromboembolic complications.
B. Unlike DIC, TTP is usually associated with normal fibrinogen levels, D-dimers, and PT/PTT.
C. Only TTP is characterized by thrombocytopenia associated with microangiopathic hemolytic anemia.
D. HIT is usually associated with abnormal PT/PTT
E. HIT is usually associated with abnormal D-dimer levels
Acute Thrombocytopenia in Inpatients

<table>
<thead>
<tr>
<th>Cause</th>
<th>Severity</th>
<th>Treatment Keys</th>
</tr>
</thead>
<tbody>
<tr>
<td>DIC</td>
<td>Variable, can be severe (&lt;20Kplts/mm³)</td>
<td>Treat the underlying disorder; Support with platelets and factors</td>
</tr>
<tr>
<td>HIT</td>
<td>Moderate (typically 50-120K)</td>
<td>Stop all heparin products; Anticoagulate with direct thrombin inhibitor</td>
</tr>
<tr>
<td>Other drug-induced</td>
<td>Variable, can be severe</td>
<td>Stop offending drug/drug class</td>
</tr>
<tr>
<td>TTP</td>
<td>Moderate, rarely severe</td>
<td>Plasma exchange required +/- corticosteroids</td>
</tr>
<tr>
<td>HELLP</td>
<td>Variable, can be severe</td>
<td>Delivery</td>
</tr>
<tr>
<td>ITP</td>
<td>Variable, can be severe</td>
<td>Diagnosis of exclusion, very unlikely to develop in inpatient</td>
</tr>
</tbody>
</table>

Acute Thrombocytopenia in Inpatients - Medication induced (beyond heparin)

Most common:
- Antibiotics:
  - vancomycin
  - penicillin
  - ceftriaxone
  - TMP/SMX
  - rifampin
- Gp IIb/IIIa inhibitors
- ibuprofen
- quinine

Abciximab > Tirofiban > Ebtifibitide
- Rapid plt drop (minutes to hours)
- Incidence: ~1-4%
- Eval: r/o pseudo-thrombocytopenia
- Management:
  - discontinue IIb/IIIA inhibitor, asa, heparin
  - plt transfusion
  - consider IVIG/steroids
Acute Thrombocytopenia in Inpatients - Medication induced (beyond heparin)

Most common:
- Antibiotics:
  - vancomycin
  - penicillin
  - ceftriaxone
  - TMP/SMX
  - rifampin
- Gp IIb/IIIa inhibitors
- ibuprofen
- quinine

• Timecourse: Within first day vs. 5-10 days
• Nadir can be severe (ie. <20K)
• Evaluate other etiologies (including pseudo), CBC, smear review, consider antibody testing
• Management:
  - consider med d/c
  - consider plt tx, IVIG, steroids

Back to the Case
- INR 1.7  PTT 60 seconds
- Fibrinogen is normal
- D-dimer is elevated
- Smear is notable for occasional schistocyte
Which of the following is the most likely diagnosis?

A. DIC
B. TTP
C. ITP
D. HIT
E. Other medication related

Clinical pearls: DIC

- Search for the underlying cause
- Check PT, PTT, Fibrinogen, D-dimers BID
- When to give platelets?
  - Plt < 10K
  - Plt < 50K if bleeding, peri-procedure/op
- If bleeding,
  - cryo to maintain fibrinogen above 100
  - FFP if PT/PTT are elevated
- There is little evidence to support prophylactic anticoagulation
Clinical pearls: HIT

- Assess pre-test probability (4 T’s)
- Check anti-PF4. If result available within a day, wait until negative before sending SRA if suspicion remains high.
- Look for DVT.
- Start a direct thrombin inhibitor (argatroban or bivalirudin).
- Platelet count improves within days.

How long should patients with likely HIT be anticoagulated with warfarin after their platelet counts are normal?

A. If no clot, stop; If clot, 6 months
B. If no clot, 2-3 months; If clot, 6 months
C. If no clot, 2-3 months; If clot, indefinite
Clinical pearls: TTP

- Access: Quinton or equivalent high-volume central catheter
- Plasma exchange is generally done daily
- Prednisone 1 mg/kg daily
- Improvement observed within 5 days.
- Plasma exchange usually continued every other or every third day after full platelet recovery 2-4 more times, steroids tapered

Key points: Thrombocytopenia

- If bleeding, transfuse platelets regardless of etiology
- Distinguishing between DIC, TTP, and HIT
  - DIC: abnormal coags, D-dimer
  - TTP: MAHA+thrombocytopenia, normal coags
  - HIT: normal coags, presence of anti-PF4
- Medication induced thrombocytopenia — it isn’t just heparin
- Management pearls:
  - DIC: address underlying disorders and coags if bleeding
  - TTP: plasma exchange + steroids
  - HIT: direct thrombin inhibitor; warfarin after platelet count returns to normal with 5 day bridge
**SUMMARY**

- **Cord compression**
  - Dexamethasone 16 mg daily. Radiation +/- surgery.

- **Hypercalcemia**
  - Fluids, bisphosphonate, calcitonin

- **Tumor lysis syndrome**
  - Rasburicase for patients at high-risk.

- **Fever and Neutropenia**
  - Cefipime, pip/tazo, carbapenem. Consider vanc.
  - Freifeld et al., CID (2011) 52:e56.

- **Acute thrombocytopenia**
  - Platelet transfusion.
  - Let clinical context, coags, fibrinogen, smear guide mgmt.

**Suggested Real-Time References**

- **Internet Free:**
  - Emedicine.medscape.com (reference section)
  - www.merckmedicus.com (includes Harrison’s online & Hospital Medicine online)

- **Internet Cost:**
  - UpToDate (www.utdol.com)
  - MDConsult (www.mdconsult.com)

- **Mobile Device Applications (Free):**
  - Medscape (Diseases & Conditions)
  - Clinical Care Options Oncology inPractice (Freter & Haddadin Oncologic Emergencies section)