Oncologic Emergencies

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“Listen, pal, they’re all emergencies.”

Mike Twohy, New Yorker, May 8 2006
Which of the following is true regarding hypercalcemia of malignancy?

1. All patients should receive bisphosphonate therapy
2. The most common cause is bone metastasis
3. EKG findings can mimic those seen during a myocardial infarction
4. Prognosis is related to severity of the calcium elevation, not the underlying malignancy
5. This talk is super boring

Answer: 3
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Tumor Lysis Syndrome:
1. Usually occurs in the setting of solid malignancies
2. Is now often more complicated by Xanthine Stones as opposed to Uric Acid stones
3. Should be treated only once it occurs because prophylaxis is costly and toxic
4. Is favorable because it indicates treatment response

Answer: 2
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Brain Metastasis

This is an MRI of a patient with an oncologic emergency and the patient should receive whole brain radiation immediately.
1. True
2. False

Answer: 2
Brain Metastasis

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- True
- False

1/20/15 T1 post-gad MRI
The following patient should undergo emergent surgical resection of brain metastasis:

1. 75 y.o. male with locally advanced esophageal cancer. Screening MRI showed 6 small brain metastases.

2. 55 y.o. male with known renal cell cancer and new onset confusion and unilateral weakness. Ct head shows single, large hemorrhagic brain metastasis with mass effect. MRI shows no additional intracranial metastases.

3. 67 y.o. female with extensive stage small cell lung cancer and increasing headache and morning nausea. MRI brain shows a small metastases in the left temporal lobe.

4. All of the above.

5. None of the above.

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In a patient with newly diagnosed epidural spinal cord compression the optimal dexamethasone dose is:

1. 100mg IV x 1, then 10mg TID
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Definition?

- Possible life threatening complication either from malignancy itself or its treatment
Overview

• Oncologic Emergencies
  o Definition
  o Broad Overview

• Case 1: Hypercalcemia

• Case 2: Tumor Lysis Syndrome

• Case 3: Brain Metastases

• Case 4: Spinal Cord Compression
Structural

- Cord Compression
- Brain Metastasis
- Tamponade
- Biliary Obstruction
- SVC Syndrome
- Airway Obstruction
- Pain
Hematologic

- Hyperleukocytosis
- DIC
- Transfusion Reactions
- Bleeding
- Thrombosis
Infectious

- Neutropenia
- Immune Compromise
- Catheter Related Infections
- Post Obstructive Pneumonia
- Cholangitis
Metabolic

- Hypercalcemia
- Tumor Lysis Syndrome
- Hyponatremia
- Hyperkalemia
- Myeloma Kidney
- Infusion Reactions
Case 1

59 year old woman
• 6 weeks of malaise, decreased appetite
• Progressive weakness
• Back pain

Initial laboratory workup
• Total protein 12
• albumin 2.2
• Calcium 12.5
• Hb 7, Cr 1.7
• IgG paraprotein 8g/dl
• EKG diffuse ST and T wave changes
Case 1

Initial CT

Marrow

ASH Slide Bank, 2002
Hypercalcemia of Malignancy

Background

• Present in 20% of malignancies (?)

• Most common cause is malignancy inpatient setting

• Seen in both solid and blood cancers
  o Most commonly breast, lung, myeloma

• Associated with poor prognosis
  o 80% dead at one year
  o Median survival 3-4 months
Mechanism: Osteolytic Metastasis (20%)

83 year old man with prostate cancer

74 year old woman with breast cancer
Mechanism: PTHrP 75%

- Solid tumors (even without mets)
- NHL, CML blast phase
- Does not stimulate Vit D production
- Uncoupling bone formation and resorption
- Large Flux into circulation and inhibited kidney excretion
Physical Exam...not much
Stones, Bones, Groans, Psychiatric overtones

**Kidney (stones)**
- Polyuria
  - Most common sign
  - Poorly understood
- Nephrolithiasis
- Thirst
- Bones (more due to malignancy)
  - Pain
  - Weakness

**Gastrointestinal (groans)**
- Constipation
- Nausea vomiting
- Peptic ulcer disease
- Pancreatitis

**Psychiatric Overtones**
- Concentration
- Confusion
- Fatigue
- Depression (30-40%)
EKG Changes
Management

Based upon Clinical Severity

• Mild (Ca <12, ionized <1.4)

• Moderate (Ca 12-14)

• No immediate rx

• Avoid aggravators
  o Thiazides, lithium
  o Volume depletion
  o Inactivity
  o High calcium diet

• Increase hydration
  o 6-8 glasses water per day
  o (good luck)

• No loop diuretics
  o Inhibit effectiveness of drugs that inhibit bone resorption
Management

Severe (Ca>14, ionized >3.5)
• Should be treated regardless of symptoms

• Volume (NS 2-300/h, UO 1-150/h)
  o Goals: Increases urine excretion and corrects dehydration
  o Onset minutes to hours

• Calcitonin (PTH antagonist)
  o Goal: inhibit bone resorption
  o Symptomatic patients
  o Onset 1-4 hours
  o Tachyphylaxis

• Bisphosphonates
  o Inhibits osteoclast resorption
  o Zometa > pamidronate
  o Onset 2-4 days

• Rarely
  Dialysis (AKI, CHF)
  Gallium (5 day infusion)
• Denosumab
  o RANKL inhibitor
  o May be effective in refractory cases
Case 1

59 year old woman with myeloma

- Malaise, appetite, weakness, pain all could have been attributed to myeloma
- Non specific EKG changes
- Corrected calcium 14

- Initially treated with fluids with Cr
- Normalization, bisphosphonates responded within 48h
- Initial therapy poorly tolerated
- Responded nicely to second line oral therapy
- Decided to stop therapy… she felt better because of lifestyle changes
- Rise in calcium, worsening anemia,
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Case 2

16 year old male

- Lethargy, bruising, dry cough, and neck swelling
- Fever led to antibiotics
- Exam: Bulky adenopathy throughout, mild organomegaly, petechiae
- WBC 98k, Hb 9, PT 24.5 (nl 13-17)
- Cr 0.9, LDH 6200
- Diagnosis of acute leukemia by blood film
- Marrow T cell ALL

Maslak, ASH Slide Bank, 2003
Case 2

Management

• Day 1
  o allopurinol 300 qd
  o 6L fluid/24h with good UO

• Day 2
  o Standard chemotherapy
  o 12h breathless, ABG pH 7.21, PCO2 31, K 7.2, LDH 13,000, Calcium 1.8, phos 4.4, uric acid normal
  o Bicarbonate, calcium, kayexalate

• Day 4
  o Fevers, acidosis, decreased urine output
  o DIC, high Uric acid, low Calcium, high phosphorous

• Day 6
  o Dialysis
  o LDH 40,000, Ca 1.3, phos 6.3
  o Cerebral edema, grand mal seizure
Tumor Lysis Syndrome

- Definition: Occurs when tumor cells release their contents (K+, Phos, DNA) into the bloodstream.

- May lead to acute kidney injury, arrhythmias, seizures, even death.

NEJM, 364; 19. May 12, 2011
TLS: Diagnosis

- Laboratory Criteria
  - -3 to +10 days chemotherapy
  - Typically 1-3 days post treatment
  - Elevated
    - Uric Acid >8 mg/dL
    - PO4 > 4.5
  - Depressed
    - Calcium < 7 mg/dL

- Clinical Criteria
  - Laboratory Criteria PLUS
    - Increased creatinine >1.5 ULN (not thought due to chemo)
    - Cardiac Arrhythmia
    - Neuromuscular Irritability
    - Seizure
Show and Tell

NEJM, 364; 19. May 12, 2011
TLS

- **Tumor Types**
  - **High Risk (>5%)**
    - Acute leukemias
    - Burkitt’s Lymphoma
    - Diffuse large B cell lymphoma with impaired kidneys or high K, UA, PO4
  - **Intermediate Risk (1-5%)**
    - CLL on certain therapies (FR or revlimid) + WBC50k
    - Rare bulky Solid Tumors
      - Small Cell lung
      - Germ Cell
  - **Low Risk**
    - Myeloma, CML
16 year old male with ALL

- **Day 10**
  - Cardiopulmonary Arrest on HD
  - Successful resuscitation, but no recovery of respiratory effort
  - CT brain multiple intracerebral hemorrhages
  - Subsequently died

- **Autopsy**
  - Hemorrhages brain
  - Lungs edema and hemorrhage
  - Kidneys eosinophilic material consistent with ATN
  - Spleen and marrow no evidence of leukemia

Lupescu et al, Bucharest, DOI: 10.1594/ecr2012/C-2548
Tumor Lysis Syndrome:

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TLS: Treatment

Prevention

- **Hydration**
  - 3L/m2/day
  - Furosemide
    - Controversial, ok to maintain urine output
  - Bicarbonate
    - Not recommended

- **Allopurinol**

- **Rasburicase**

Pession et al, Oncologia Ematologia Pediatrica 2008
“If we pull this off, we’ll eat like kings.”

Brain Metastasis

- 55 Male known, but asymptomatic metastatic renal cell carcinoma
- Observation Jan 2014 - Oct 2014
- On Sutent (tyrosine kinase inhibitor) x 1 month after documented progression
- Presents to clinic on 12/22/14 with right sided weakness and altered mental status
- Non-contrast CT head shows hemorrhage with edema and left to right shift
Hemorrhagic Brain Metastasis

- 12/22 Craniotomy w/ evacuation of hematoma and tumor resection
- Path – Adenocarcinoma c/w Renal Cell Carcinoma
- Post-op Right-sided weakness – resolved with in patient rehab
- Pt d/c from hospital on Keppra 500mg BID without steroids.
- Rad Onc Clinic 1/15 with normal strength and no neurologic deficit
Work Up

• CT, typically leading to MRI

• Search for the primary – typically CT – Chest/Abdomen/Pelvis

• Biopsy of primary or, other metastatic site once identified

• If solitary lesion, consider biopsy or resection
Brain Metastasis

- Most common intracranial tumor ~170,000 cases/yr.
- 20-40% of all cancer patients develop brain metastasis
- “Solitary” = one brain metastasis, only site of disease
- “Single” = one brain metastasis, other sites of disease
- Most common primary sites – lung, breast, melanoma, renal cell carcinoma
The following patient should undergo emergent surgical resection of brain metastasis:

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B. 55 y.o. male with known renal cell cancer and new onset confusion and unilateral weakness. CT head shows single, large hemorrhagic brain metastasis with mass effect increased ICP. MRI shows no additional intracranial metastases.

C. 67 y.o. female with extensive stage small cell lung cancer and increasing headache and morning nausea. MRI brain shows a small metastases in the left temporal lobe.

D. All of the above.

E. None of the above.
Management

- Steroids – typically dexamethasone
  - I like to start 10mg IV or orally, then 4mg QID and taper once radiation has started.  **This will stabilize most patients until a treatment plan can be made.**
  - GI prophylaxis is important for patients on high dose steroids  (Proton Pump Inhibitor or Ranitidine 150mg BID
  - Steroids are generally not needed in asymptomatic patients.
  - Survival Steroids only ~ 1-2 months

- Anti Seizure Medications
  - i.e. Keppra (levitiracetam) - typically only needed if patient has had a seizure

- Surgery
  - Particularly for large, symptomatic lesions with increased ICP/hydrocephalus or evidence of herniation or brain stem compression
    - Consider for all solitary lesions or many single lesions in patients with good performance status/systemic control

- Radiation
  - Whole Brain XRT – Survival typically 4-12 months
  - Post-op XRT – variable
  - Stereotactic Radiation Therapy
Post Operative Radiation

- Surgery used to provide rapid relief of symptoms in patients with large symptomatic metastases
- Provides Histologic Diagnosis
- Also often the treatment of choice for larger solitary or single brain metastases
- Local recurrence ~50% so most patients get post op whole or partial brain radiation
- Post-op RT improves survival 10 with vs 6 months without.
Brain Metastasis

This in an MRI of a patient with an oncologic emergency and the patient should receive whole brain radiation immediately.

- True
- False
Whole Brain Radiotherapy

- 75 Male, screening MRI obtained during routine work up of esophageal cancer
- 40# weight loss, dysphagia
- No neurologic symptoms, headache or nausea
- MRI shows at least 5 small brain metastases without edema
- Pt opted for WBRT and was treated as an outpatient 4 days after the MRI
- Pt did not require steroids or keppra

1/20/15 T1 post-gad MRI
Prognosis – RPA Classification

• Class 1 – KPS ≥ 70, Age ≤ 65, Primary tumor controlled without extra-cranial metastases - Median Survival 7.1 months

• Class 2 – KPS , Age >65, Uncontrolled primary or extra-cranial metastases - Median Survival 4.2 months

• Class 3 – KPS <70 – Median Survival 2.3 months
Spinal Cord Compression

- 48 y.o. Male. Multiple medical problems including sclerosing cholangitis with cirrhosis (Child-Pugh = 13)
- Stage I Lung Cancer 2012 – Stereotactic Body Radiation
- Hilar/Mediastinal Lymph Node Recurrence Jan 2014 – Treated with Lobectomy, post-op XRT (Pt unable to receive adjuvant chemo 2° to liver disease)
- Jan 2014 presents to ED with 1-2 days severe upper back/neck pain and confusion.
- Exam shows mild right leg weakness 4/5 strength, DTRs are hyper-reflexive in bilateral biceps, triceps and knee jerk
In a patient with newly diagnosed epidural spinal cord compression the optimal dexamethasone dose is:

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D. When it comes to steroids more is better.
Spinal Cord Compression

- Admitted to Hospitalist Service.

- MRI Spine showed 2.1cm intradural mass in posterior right spinal canal at C6. Marked mass effect on cervical cord.

- MRI Brain showed 2.5cm mass left parietal lobe with medial extension to lateral ventricle.

- Pt Started dexamethasone 10mg IV x1, then 4mg qid.
Spinal Cord Compression

- Any indentation/pressure on the thecal sac = SCC

- Cauda Equina Syndrome = lower level SCC (below the end of the cord ~ L1/2) – saddle numbness, urinary/stool incontinence/retention, lower extremity weakness/numbness/parasthesias

- Single most important prognostic factor in regaining function is pretreatment neurologic status.

- Cancer type also predicts response
  - Lymphoma, seminoma, small cell, breast, prostate do better (radiosensitive)
  - Sarcoma, renal cell, melanoma do very poorly (radioresistant)

- Early treatment is essential! (Start as soon as diagnosis is made with steroids and get radiation oncology/neurosurgery consult.)

- Median Survival is ~ 6 months
Management

• Steroids – typically dexamethasone
  o I like to start 10mg IV or orally, then 4mg QID and taper once radiation has started.
  o No data show improved outcomes for daily dexamethasone doses >16mg, higher doses associated with increased complications.
  o GI prophylaxis is important for patients on high dose steroids (Proton Pump Inhibitor or Ranitidine 150mg BID)

• Pain Management – in addition to steroids, opioid analgesics, Neurontin

• Surgery
  o Randomized data show posterior decompression with laminectomy no better than RT alone.
  o More aggressive resection (anterior and lateral approaches, that address the bulk of tumor in the vertebral body) with spine stabilization followed by XRT has been shown to improve ambulatory rate over XRT alone (84% vs 57%)

• Radiation
  o Primary XRT
    • ~1/3 of patients who are non-ambulatory at presentation will regain the ability to walk
    • Starting treatment (at least steroids) within 24 hours of loss of function is also important
    • 70-80% improvement in pain
    • Local control rate ~75%
  o Post-op XRT
  o Stereotactic Radiation Therapy
Spinal Cord Compression

- Pt initiated palliative radiation – 30Gy x factions after 18 hours IV steroids.

- Pain improved dramatically following day with reduced hyper-reflexia and improved Rt. LE strength

- Pt walking without difficulty or additional neurologic symptoms at completion of radiotherapy.

- Pt readmitted to hospital 2 weeks after treatment and ultimately expired
Whole Brain Radiation

- Most patients with brain metastases will receive whole brain radiotherapy

- Standard dose 30Gy in 10 daily fractions or 37.5Gy in 15 fractions

- Faster treatment for patients with poor performance status - 20Gy in 5 Fractions

- Generally speaking faster treatment results in more long term toxicity

- Long term toxicity – 8-12 months after treatment include neurocognitive and behavioral changes:
  - Short term memory loss
  - Flatter affect
  - Trouble with math skills

- Can be used after any form of partial brain treatment, such as gamma knife, SRS, surgery or post-op partial brain
What About Gamma Knife?

• GK is a form of radiosurgery (single, precise, high dose radiation treatment)

• GK is a brand (there is no knife. We now do similar treatment with True-beam (another brand) linear accelerator

• Appropriate Patients
  o 1-3 brain metastases (UW will often treat up to 10 for unknown reasons)
  o Performance Status ≥ 70
  o Systemic Control or new diagnosis 1-3 mets with plans for systemic treatment

• Advantages
  o Fast – single treatment (~1hr)
  o Minimizes delay to systemic treatment start
  o Minimal toxicity – essentially no neurocognitive

• Disadvantages
  o Inappropriate for many patients
  o 5% risk radio-necrosis at 1 year, 10% at 2 years
  o Ignores other brain which may have disease – risk of additional metastasis requiring treatment ~50%
  o Labor intensive for rad onc., requires neurosurgical collaboration