

HEMATOLOGY & ONCOLOGY CASES FOR THE HOSPITALIST NP PA

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MAYO CLINIC IN ARIZONA
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ADULT HOSPITAL MEDICINE
BOOT CAMP

SEPT. 18 - 22, 2024 | PHOENIX, AZ //

AAPA
American Academy of
Physician Associates

shm.
Society of Hospital Medicine

DISCLOSURE

- Non-Declaration Statement

I have no relevant relationships with ineligible companies to disclose within the past 24 months

EDUCATIONAL OBJECTIVES

At the conclusion of this session, participants should be able to:

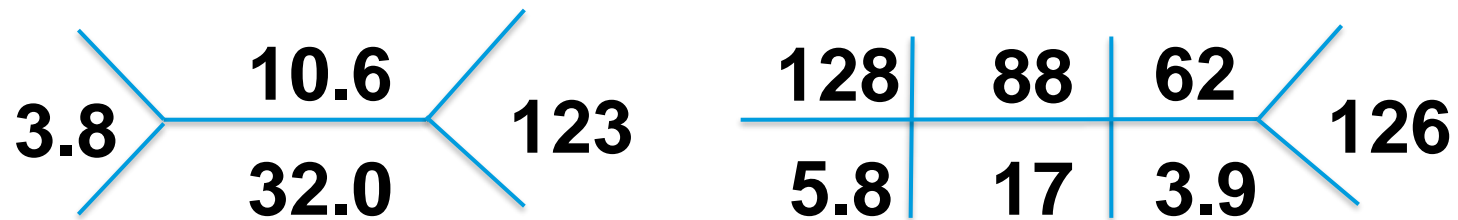
- Identify and develop treatment plans for hematologic and oncologic emergencies, such as tumor lysis syndrome and neutropenic fever.
- Outline the management of mucositis/esophagitis.
- Discuss the principles of management of malignant pain.
- List pharmacologic options for opioid-induced constipation.

MR. COOPER

- 30-year-old male with newly diagnosed Burkitt lymphoma presents to the ER with lethargy, nausea, vomiting, and decreased urination over the last 36 hours.
- He received chemotherapy 2 days prior.
- On exam:
 - Lethargic but responds to verbal stimuli, oriented
 - Palpable abdominal mass

T 37.8 - BP 104/57 – HR 115 – RR 17 – O2 98%

MR. COOPER'S LABS



Lab	Value	Reference Range
Calcium	6.9	8.5 – 10.2 mg/dL
Phosphate	8.9	2.4 – 4.1 mg/dL
Uric acid	19	3.5 – 7.2 mg/dL

TUMOR LYSIS SYNDROME

- Acute tumor cell lysis due to chemotherapy
 - ≥ 2 metabolic findings ($\uparrow K$, $\uparrow P$, \uparrow uric acid, $\downarrow Ca$)
 - Occurs within 3 days before or 7 days after chemo
- Can also be associated with seizures and cardiac arrhythmias/sudden death
- The Cairo-Bishop defines and grades TLS

RISK FACTORS



Hematologic malignancies (especially acute leukemia and high-grade lymphoma)



Rapidly growing tumors



Bulky disease



Chemosensitivity of the cancer



Pre-existing renal impairment, ↑lactate dehydrogenase, ↑uric acid, ↑phosphorous



Dehydration

PATHOPHYSIOLOGY

- Release of intracellular products
 - Uric acid → Hyperuricemia → AKI → Acidosis
 - Potassium → Hyperkalemia
 - Phosphates → Hyperphosphatemia
 - Calcium → Binds w/phosphate → Hypocalcemia

TREATMENT

- Prevention
- Aggressive IVF
- Treatment of electrolyte abnormalities
- Hemodialysis (if indicated)



TREATMENT

- [Allopurinol](#)

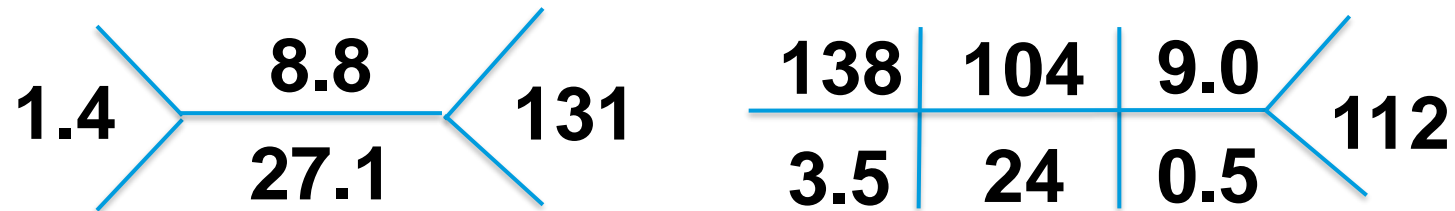
- Intermediate-risk patients
- Inhibits uric acid production
- Takes several days

- [Rasburicase](#)

- High-risk patients (+/- Intermediate-risk patients)
- Catalyses conversion of uric acid to allantoin
- Rapidly breaks down uric acid - works within 4 hours
- Contraindicated in G6PD deficiency 2/2 severe hemolysis

MRS. FIORITO

- 49-year-old female with breast cancer presents to the ER with a fever of 39.0. Her only other symptoms are an episode of chills and a vague HA.
- She received carboplatin and docetaxel 11 days prior.



ANC = 0.05

FEBRILE NEUTROPENIA

- Fever

- IDSA defines fever in a neutropenic patient as a single oral T $>38.3^{\circ}\text{C}$ OR
- T $>38.0^{\circ}\text{C}$ sustained for >1 hour

- Neutropenia

- Absolute neutrophil count (ANC) <500 cells/mm³
 - Profound neutropenia = ANC <100 cells/mm³

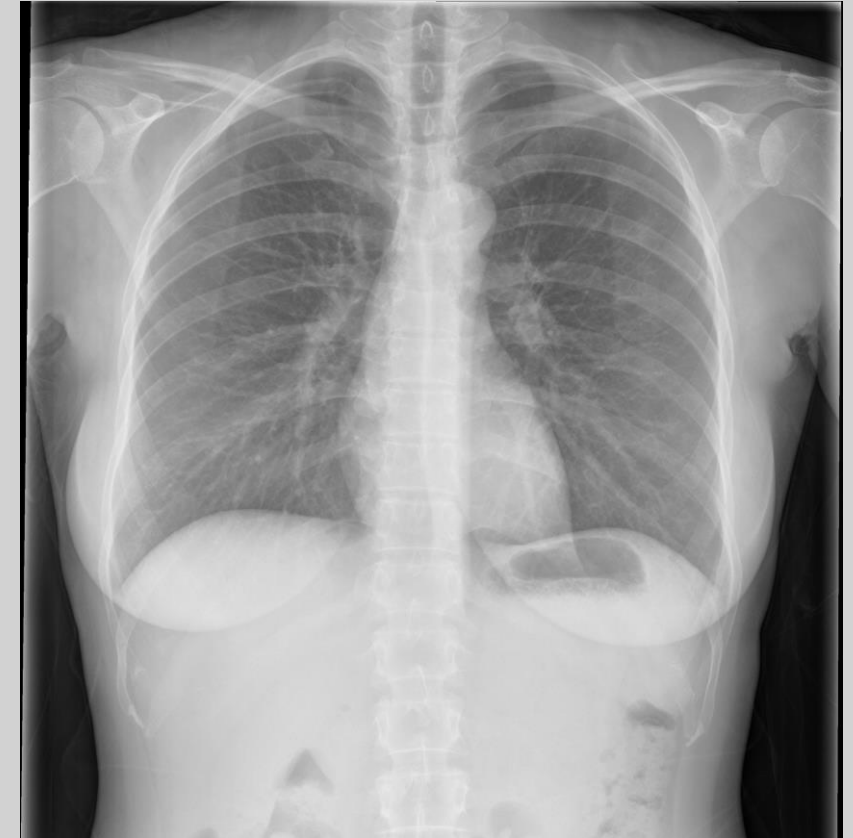
ANC = WBC X % of polymorphonuclear cells (PMNs) and bands

FEBRILE NEUTROPENIA

- Incidence
 - 10-50% patients with solid tumors
 - >80% patients with hematologic malignancies
- Guidelines
 - 2010 Infectious Diseases Society of America (IDSA)
 - 2018 American Society of Clinical Oncology (ASCO) and IDSA

DIAGNOSTICS

- H&P
- Labs
 - CBC with differential, CMP
 - Blood cultures X2
 - UA
 - Additional applicable cultures
- Radiographic studies



ETIOLOGY

- Bacterial > fungal source
 - HEENT, pulmonary, GI, GU, neuro, skin
 - Lines
- Acute neutropenia (<7 days) → bacterial
- Prolonged neutropenia (>7 days) → fungal
- Infection identified in 20-30% of cases
- Bacteremia identified in 10-25% of cases
 - Gram (+) most common

Commonly Identified Organisms

Escherichia coli
Klebsiella spp
Enterobacter spp
Pseudomonas aeruginosa
Acinetobacter spp
Staphylococcus aureus
Enterococcus spp
Viridans group
streptococci
Streptococcus

MASCC RISK INDEX

- Multinational Association of Supportive Care in Cancer

Characteristic	Weight
Burden of FN with no or mild symptoms	5
No hypotension (SBP>90 mmHg)	5
No COPD	4
Solid tumor or hematologic malignancy w/no previous fungal infection	4
No dehydration requiring IVF	3
Burden of FN with moderate symptoms	3
Outpatient status	3
Age <60 years	2

RISK ASSESSMENT

- High-risk patient

- Prolonged or expected neutropenia (>7 days) and
- Significant medical comorbidities
 - Hepatic and/or renal insufficiency
- MASCC score <21
- CAR-T w/in 2 months

- Low-risk patient

- Expected neutropenia ≤ 7 days
- No or few comorbidities , stable
- MASCC score ≥ 21

TREATMENT

- Goal directed therapy for SIRS/sepsis
- Empiric IV antibiotics
 - Cefepime, piperacillin-tazobactam, meropenem, imipenem, or ceftazidime
 - +/- Vancomycin
 - When to modify antibiotics?
- Start antibiotics after BCs have been obtained.
- Do not delay treatment and give antibiotics within 1 hour.

TREATMENT

- Empiric antifungals

- If no improvement/persistent fever after 4-7 days of broad-spectrum abx and no identified fever source
- Prolonged neutropenia (>7 days)
- *Candida* and *Aspergillus* are most common
 - Oral ulcers concerning for *Candida*
- ? Fluconazole
- Amphotericin B, voriconazole, caspofungin, itraconazole

- Empiric antivirals

- Oral ulcers concerning for HSV

GRANULOCYTE-COLONY STIMULATING FACTORS

- 2014 meta-analysis
 - Compared to abx alone, G-CSF did not significantly improve overall mortality or infection-related mortality.
 - ↑ incidence of bone or joint pain or flu-like sx
- IDSA does not recommend
- ASCO does not recommend
 - Consider for patients at high risk for infection-related complications or factors predictive of poor clinical outcome

DISCHARGE

- DC Criteria
 - Continue broad spectrum abx until afebrile for \approx 48 hours
 - ANC > 500 cells/mm³ and \uparrow
 - Resolution/improvement of source of infection (if identified)
- Median time frame for defervescence: 2 days for low-risk patients and 5 days for high-risk patients
- Consider ability to be evaluated post DC

DISCHARGE

- PO antibiotics

- Ciprofloxacin or levofloxacin + amoxicillin-clavulanate
 - Alternative: clindamycin or cefixime

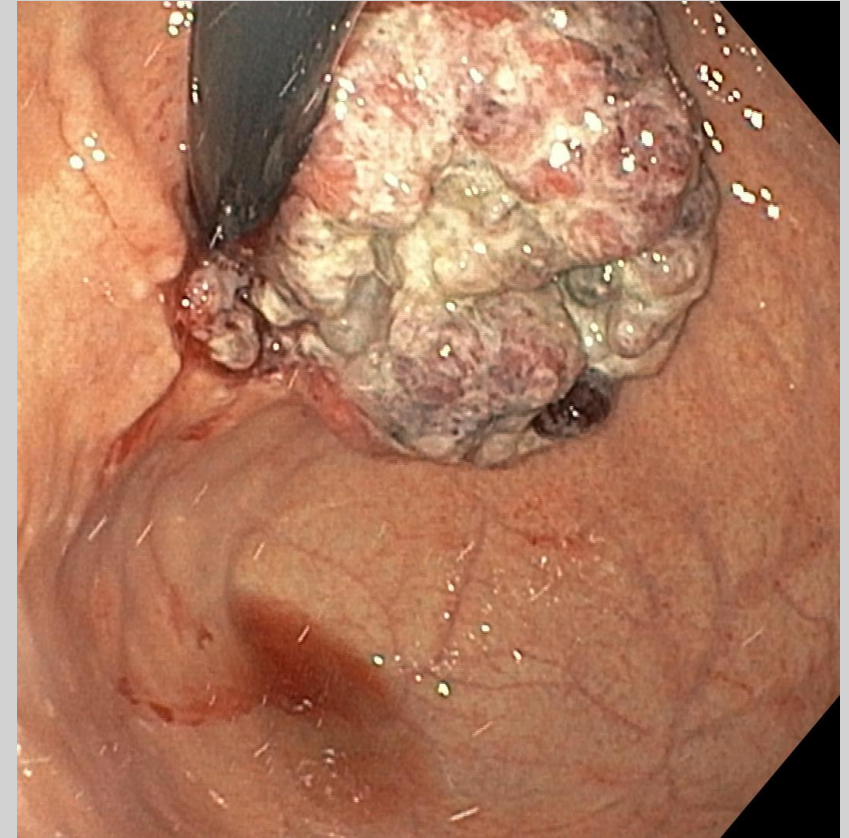
- Duration

- Identified organism/source: typical course for infection
- Unidentified source: dependent on treatment response
 - Treat until sustained defervescence (4-5 days for high-risk and 1-3 days for low-risk) and ANC recovery



MRS. POST

- 70-year-old female with esophageal cancer presents to the ER with odynophagia, nausea, and poor PO intake. She is also significantly weak.
- She received her 3rd cycle of chemotherapy 8 days prior and is currently undergoing radiation



MUCOSITIS

- Mucosal damage 2/2 chemo and/or radiation
 - Oral cavity, pharynx, larynx, esophagus
- Occurs in \approx 20-40% of patients receiving chemo and nearly all patients receiving radiation to the head and neck
- Erythema and ulcerations of mucosa, pain, N/V/D, \downarrow PO intake

COMMONLY ASSOCIATED AGENTS

- Doxorubicin
- Etoposide
- Methotrexate
- 5-fluorouracil (5-FU)
- Bleomycin
- Melphalan
- Cytarabine
- Sunitinib
- Sorafenib
- Erlotinib
- Temsirolimus
- Everolimus

*Can result in dose reduction of chemo or break in radiation

TREATMENT

- Symptomatic treatment
- Oral hygiene
- Salt and baking soda rinses
- Viscous lidocaine
- The benefit of “miracle mouthwash” is unclear.
 - Viscous lidocaine, diphenhydramine elixir, Mag AL Plus, sodium bicarbonate
- Pain medications
 - Acetaminophen, NSAIDs, opioids, gabapentin

TREATMENT

- Superinfections
 - **Candida albicans**
 - Clotrimazole troches, nystatin suspension
 - Systemic fluconazole if needed
 - **HSV**
 - Acyclovir
- Liquid or soft diet
 - Feeding tube in severe, prolonged cases

MRS. DENISON

- 51-year-old female with newly diagnosed pancreatic cancer with metastases to the liver, stomach, duodenum, and periportal lymph nodes.
- She presents to the ED with uncontrolled abdominal pain. She is taking prn Norco with minimal relief.
- A CT A/P showed a large pancreatic mass with hepatic metastases with complete occlusion of the SMV, portal vein and splenic vein and a new middle hepatic vein thrombosis.

MALIGNANT PAIN MANAGEMENT

- Comprehensive pain assessment
- Manage pain, minimize adverse effects
- Morphine equivalent daily dose
MEDD/OME/OMED



<https://www.capc.org/documents/download/20/>

Equianalgesic Conversion Table			
Drug Name	Equianalgesic Dose		Oral to Parenteral Ratio
	Oral (mg)	Parenteral (mg)	
Morphine	25	10	5:2
Hydromorphone	5	2	5:2
Oxycodone	20	n/a	n/a
Hydrocodone	25	n/a	n/a
Oxymorphone	10	1	10:1

Potency ratios:

- oral morphine: oral hydromorphone is 5:1
- oral morphine: oral oxycodone is 1.25:1
- oral morphine: IV hydromorphone is 12.5:1
- transdermal fentanyl 25mcg/hr: oral morphine 50mg/24hr

Oral hydromorphone is 5 times as potent (mg per mg) as oral morphine

This conversion table is adapted from: McPherson ML. *Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing*, 2nd ed. American Society of Health-System Pharmacists, Bethesda, Maryland, 2018.

INTRACTABLE MALIGNANT PAIN

- Mild

- Scheduled long-acting opioid plus short-acting opioid PRN

- Moderate-Severe

- PO/IV – Equivalent of 10-20% MEDD in last 24H
 - Pain unchanged/↑ → ↑ dose by 50-100%
 - Pain ↓ but not controlled → Repeat dose
 - Pain ↓/controlled → Continue effective dose prn 24H

- PCA

- Continuous and/or bolus

- Narcan

MRS. DENISON

- She was started on morphine but developed a morbilliform rash on her face, trunk, arms, and proximal thighs.
- She was transitioned to OxyContin 40 mg p.o. b.i.d. and oxycodone 10-20 mg p.o. q.4 hours p.r.n..



MALIGNANT PAIN MANAGEMENT

- Opioid tolerance

- Chronic use
- High MEDD

- Opioid rotation

- Renal function, delivery mechanism, efficacy
- ↓ MEDD by 30-50%

- Opioid reduction

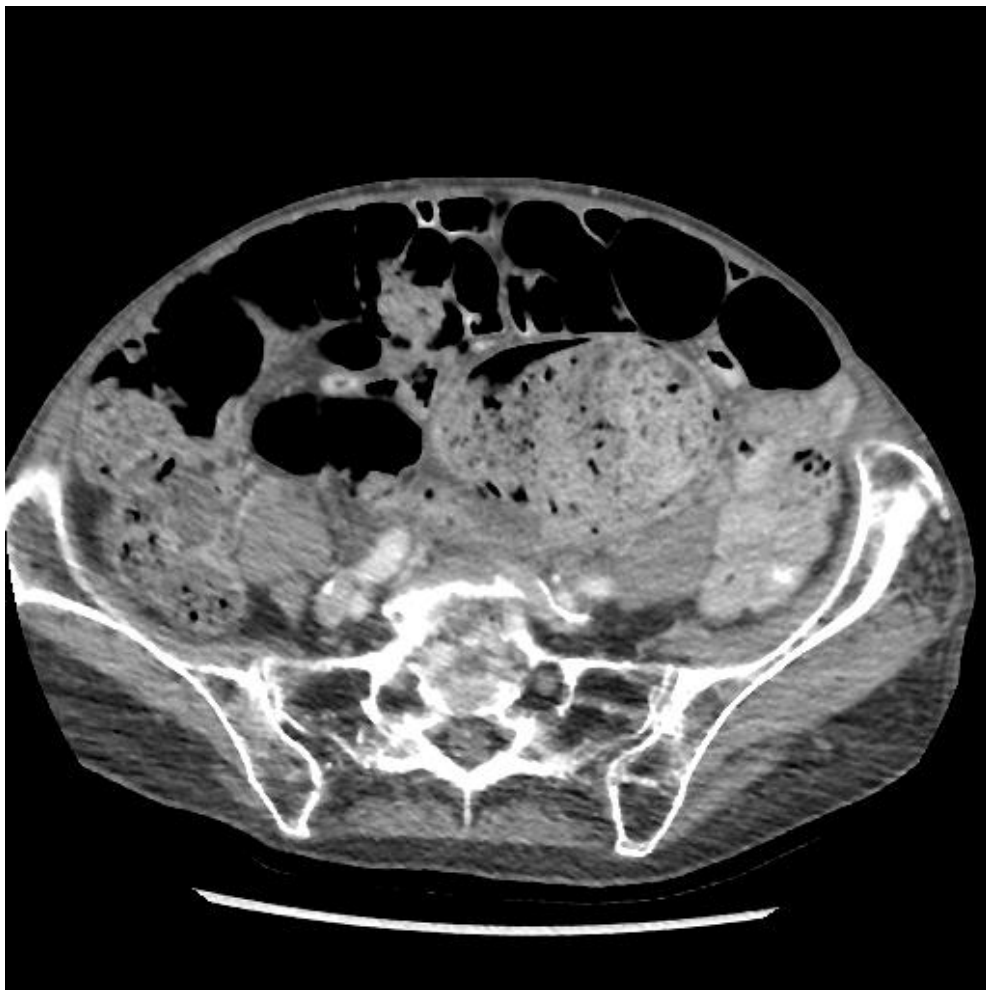
- May need to ↓ due to adverse effects
- ↓ 10-25% and reevaluate

MRS. CAMEL

- 65-year-old female with metastatic lung cancer to the bone (chest wall) and liver
- She was hospitalized two weeks ago with intractable cancer-associated chest pain. During that hospitalization, her OxyContin was increased to 80 mg BID and oxycodone to 15 mg Q 3hour prn pain.
- She returns to the ER with severe diffuse abdominal pain. She denies N/V/D. Her last BM was about 7 days ago.



MRS. CAMEL



OPIOID-INDUCED CONSTIPATION

- Most common side effect from opioids
 - Occurs in 60-90% of patients
- Opioids bind to receptors in GI tract and CNS system → ↓ bowel motility → excessive water and electrolyte reabsorption from feces → constipation
- R/O other causes

PREVENTION!

- Non-pharmacologic

- ↑ fluids
- ↑ dietary fiber
- ↑ mobility

- Pharmacologic

- Cathartic
- Osmotic laxative
- Both



TREATMENT

- Start treatment if not already on it
- Adjust dose and/or frequency of medications
- Add (or switch) additional medications
- Include non-pharmacologic methods
- If refractory, consider peripheral opioid antagonist

Senna
Polyethylene glycol
Lactulose
Bisacodyl
Suppository
Enema

TREATMENT FOR REFRACTORY CASES

- **Methylnaltrexone**

- SQ (and PO) opioid antagonist that crosses BBB but doesn't cause W/D sxs
- 12 mg SQ daily
- Use cautiously in for patients w/intestinal wall lesions

- **Naloxegol (Movantik)**

- PO opioid antagonist for treatment of opioid-induced constipation in cancer-related pain

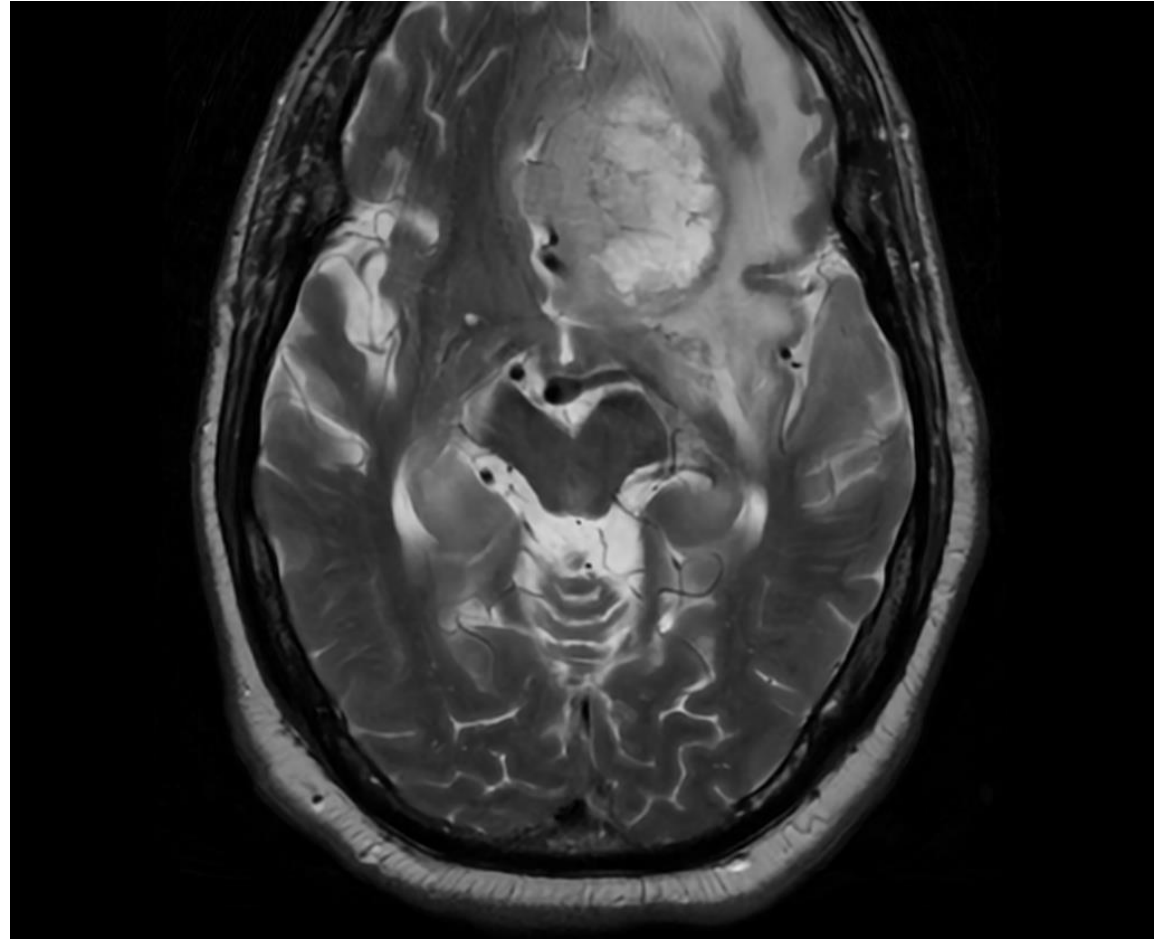
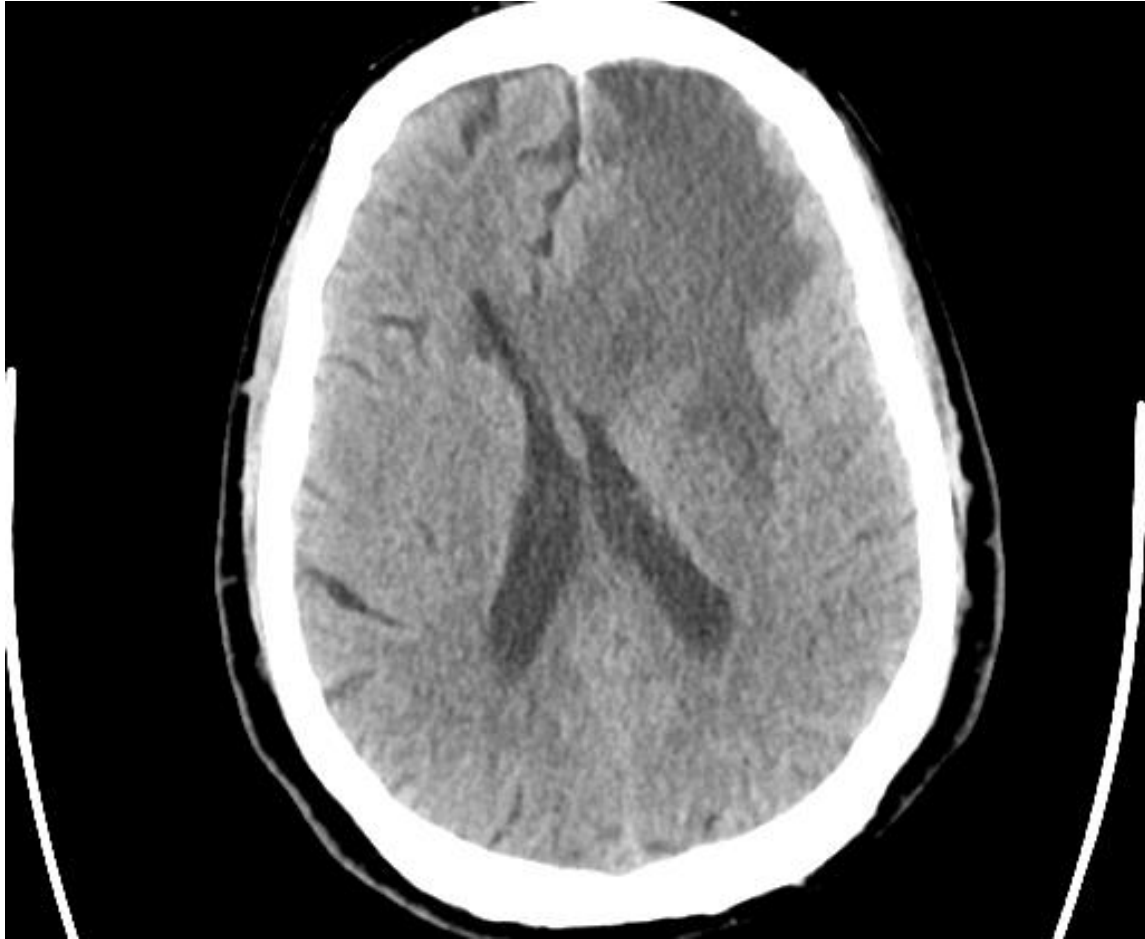
- **Naldemedine (Symproic)**

- PO opioid antagonist for treatment of opioid-induced constipation

MR. ROMO

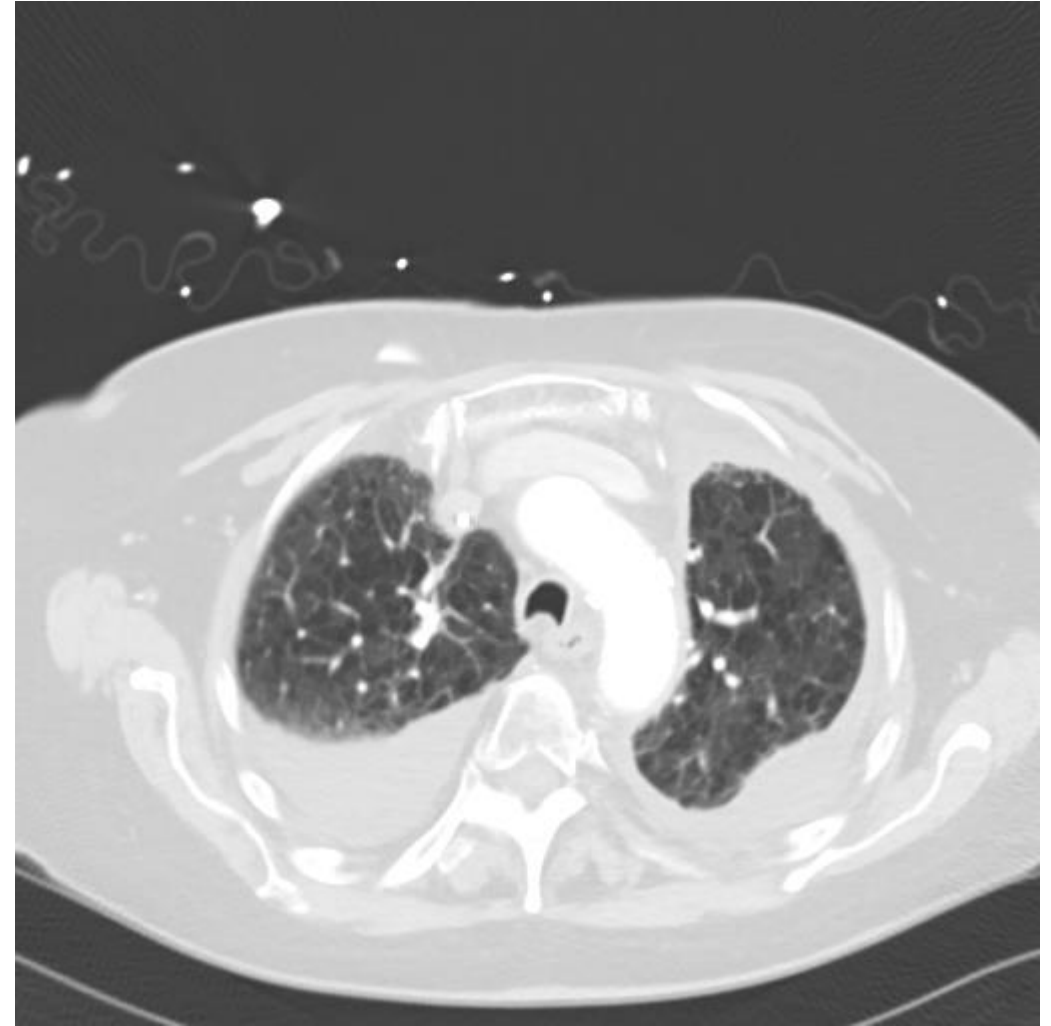
- 79-year-old male with CAD s/p, DES February 2023, chronic SHF s/p AICD/PPM, s/p bioprosthetic AVR, HTN, HLD, and hypothyroidism.
- He has CKD 5 and had a RUE AVF placed (about 8 years ago) in preparation for possible HD.
- He presented to the ED with confusion, and you were asked to admit him for uremia. The ED called Nephrology, and they will dialyze him tomorrow.

	2024 2/5/24 17:16	1/18/24 12:02	2023 12/18/23 12:53	11/13/23 11:27	11/13/23 11:26	9/18/23 12:37	6/13/23 09:32	6/6/23 10:06
GEN CHEMISTRY								
Sodium, S	143	143	145	144		143	138	142
EXT Sodium								
Sodium - Arterial								
Potassium, S	4.2	4.3	4.8	4.8		4.8	4.6	4.5
EXT Potassium								
Potassium - Arterial								
Chloride, S	100	105	101	104		105	100	102
EXT Chloride								
Bicarbonate, S	23	22	26	24		21 ▼	24	25
Anion Gap	20 ▲	16 ▲	18 ▲	16 ▲		17 ▲	14	15
EXT Anion Gap								
BUN (Blood Urea Nitrogen), S	79.0 ▲	67.9 ▲	64.5 ▲	54.1 ▲		60.2 ▲	75.7 ▲	66.4 ▲
EXT BUN								
Creatinine	8.81 ▲	8.30 ▲	7.45 ▲	7.09 ▲		6.60 ▲	6.92 ▲	6.79 ▲
EXT Creatinine								
Estimated GFR (eGFR)	<15 ▼	<15 ▼	<15 ▼	<15 ▼		<15 ▼	<15 ▼	<15 ▼



MS. GUNNELL

- 71-year-old female with metastatic mesothelioma, who is has had disease progression on multiple lines of treatment
- She was admitted with SOB and found to have.....



TAKE HOME POINTS

- The first key to managing TLS is considering it in your differential!
- Watch for candida superinfections in patients with mucositis.
- Consider coverage with vancomycin in patients with neutropenic fever and central lines.
- Manage cancer-associated pain with minimal adverse effects from opioids.
- Prevention is the key to opioid-induced constipation.

QUESTIONS & DISCUSSION



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