PHARMACY TO DOSE
THE CRITICAL CARE PODCAST

# Oncologic Emergencies

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I. Oncologic emergencies are life-threatening conditions that are directly or indirectly related to cancer or its treatment and can occur at any time in the disease process.
   a. Risk factors are specific to the different types of oncologic emergencies
      i. More severe symptoms can occur in those with a high cancer/tumor burden
   b. Can generally be broadly broken down into 4 categories
      i. Metabolic: tumor lysis syndrome (TLS), SIADH, hypercalcemia
      ii. Structural: superior vena cava syndrome, spinal cord compression, pericardial effusion
      iii. Hematologic: hyperviscosity syndrome, febrile neutropenia
      iv. Treatment-related: CAR-T cytokine release syndrome and immune-mediated toxicities

## Tumor Lysis Syndrome

MK is a 33 y/o M who presents with a 3-week history of malaise and weight loss. He has also had progressive shortness of breath and hypoxia requiring high-flow oxygen therapy since presentation. He was admitted to the ICU for close monitoring and his subsequent laboratory work-up revealed the following:

| | | |
|---|---|---|
| WBC: 110k | SCr: 0.7 mg/dL | K: 4.2 mmol/L |
| Uric acid: 7.5 mg/dL | LDH: 1750 U/L | |

MK was started on hydroxyurea for cytoreduction while awaiting a diagnosis from his bone marrow biopsy.

II. TLS occurs when cancer cells are destroyed, and the cells lyse releasing their contents (including K, P, and nucleic acid metabolized eventually into uric acid)
   a. Hyperuricemia: contributes to AKI d/t renal tubule crystallization
   b. Hyperphosphatemia: can cause soft tissue precipitation d/t Ca-P precipitation
   c. Hyperkalemia: can cause life-threatening arrhythmias
   d. Hypocalcemia (d/t hyperphosphatemia): can cause arrhythmias and precipitation
      i. These effects can compound upon themselves and further accumulate

III. Risk factors: higher tumor burden, cell lysis potential, chemotherapy intensity, impaired renal function, concomitant nephrotoxic agents/hyperuricemic agents

IV. TLS Diagnosis: Cairo-Bishop Classification

| **Lab Values** | | **Clinical Criteria** |
|---|---|---|
| Potassium | K > 6 mmol/L | Cardiac dysrhythmia or sudden death |
| Calcium | Corr. Ca < 7 mg/dL OR iCa < 1.12 mmol/L | Cardiac dysrhythmias, seizures, hypotension, neuromuscular irritability, or heart failure |
| Uric acid | UA > 8 mg/dL | Acute kidney injury (SCr increase >/= 0.3 mg/dL or oliguria) |
| Phosphorous | P > 4.5 mg/dL | |

   a. Occurs within first 7 days of therapy and more often occurring earlier (first 24-48 hrs)

V. TLS Prevention
   a. Prevention is key because once TLS occurs it's hard to reverse
   b. Strategy for prevention depends on TLS risk (low/intermediate/high)
      i. If you have 2+ risk factors: High risk for TLS
   c. Every patient should receive regular laboratory monitoring
      i. Moderate/high risk: q4h-q6h lab draw frequency
   d. Ensure adequate hydration with IV crystalloids to clear metabolites/electrolytes
      i. ~2x maintenance fluid rate (150-200 mL/hr)
   e. Consider IV diuresis in patients fluid overloaded or at risk of this
   f. No longer recommended to use acetazolamide or sodium bicarbonate for urine alkalinization due to risk of nephropathy
   g. Allopurinol is a xanthine oxidase inhibitor decreasing uric acid formation
      i. Start 2-3 days prior to chemotherapy initiation, esp. in high-risk pts
      ii. Continue for entire duration patient has risk of TLS (at least 10-14 days)
      iii. Dose: 300mg PO qDay to BID (BID early when highest TLS risk)
   h. Febuxostat is alternative treatment in case patients can't tolerate allopurinol (hypersensitivity or severe renal impairment) but use is limited d/t cost
   i. Treatment with rasburicase should be considered in high-risk patients
      i. Lowers uric acid by catabolizing uric acid into excretable metabolite
      ii. Typically give one dose to decrease uric acid and prevent TLS progression
         1. Recheck labs 6-12 hrs after and depending on results may repeat dose
      iii. Ensure to screen for G6PD deficiency, but might closely monitor for ADE if unable to wait for result prior to treatment

MK's bone marrow biopsy resulted and is suggestive for acute lymphoblastic leukemia (ALL). Hyper-CVAD was initiated, which consists of cyclophosphamide, vincristine, doxorubicin, and dexamethasone, with continued close monitoring of his labs in the ICU. On day 2 of chemotherapy, his labs reveal the following:

| | | | |
|---|---|---|---|
| SCr: 1.5 mg/dL | K: 5.8 mmol/L | Phos: 7 mg/L | Calcium: 6.8 mg/dL |
| | iCa: 0.8 mg/dL | Uric acid: 12 mg/dL | LDH 1800 U/L |

VI. TLS Treatment
   a. Ensure close clinical and laboratory monitoring
      i. Post-rasburicase treatment ensure uric acid lab is sent on ice/chilled
   b. Rasburicase is a recombinant urate-oxidase enzyme which converts uric acid to allantoin (inactive/soluble uric acid metabolite) and is the first-line TLS treatment
      i. Expensive treatment option led to use of fixed-dose single dose
         1. Found to be as effective as FDA dosing (0.2 mg/kg x5 days)
         2. Studied doses range from 1.5mg to 6mg (depending on lab values)
      ii. Consider repeat rasburicase dose at 6-12 hours if uric acid still elevated
      iii. Continue allopurinol prophylaxis even if treated with rasburicase

c. Allopurinol is a second-line treatment option if rasburicase is unavailable
    i. Less preferred since it only prevents formation of uric acid
d. May ultimately need hemodialysis to remove and lower uric acid levels

MK develops atrial fibrillation with his HR going up to the 150s and his SCr continues to increase up to 2.3 mg/dL. Stat labs are drawn revealing significant electrolyte disturbances:

| | | |
|---|---|---|
| K: 6.5 mmol/L | Ca: 6.5 mg/dL | Uric acid: 4 mg/dL |

VII. Electrolyte Management
a. Initiate hyperkalemia protocol when appropriate
b. Don't necessarily administer calcium as the arrhythmias may not be simply due to hypocalcemia (also carries risk of calcium-phosphate precipitation)
    i. But if symptomatic from hypocalcemia, should administer calcium
c. Consider phosphate binders but may not be the most effective

**Hypercalcemia of Malignancy**

A 46 y/o F, SP with a PMH significant for breast cancer presents to her outpatient heme/onc appointment complaining of increasing confusion and somnolence over the past week. Her CMP was notable for a serum calcium of 15 mg/dL and she was sent to the ED for re-draw of her labs for confirmation and further evaluation.

VIII. Common causes of hypercalcemia of malignancy
a. Bone metastases or osteolysis (common diagnosis: breast/prostate cancer and MM)
b. Humoral hypercalcemia of malignancy which increases parathyroid hormone-related protein (common diagnosis: squamous cell/renal/bladder/ovarian cancer)
c. 1,25-Dihhydroxyvitamin D secreting lymphomas (common diagnosis: Hodgkin's and Non-Hodgkin's Lymphoma)
d. Ectopic hyperparathyroidism (common diagnosis: parathyroid/ovarian/lung cancer)

IX. Diagnosis
a. Can diagnose based on clinical signs/symptoms:
    i. "Bones, stones, moans, and groans"
        1. Bones – bone pain
        2. Stones – flank pain d/t kidney stones
        3. Moans – GI symptoms including constipation, nausea, and vomiting
        4. Groans – AMS including coma/delirium/hallucinations
    ii. Other severe symptoms include:
        1. Arrhythmias (increased PR, widened QRS, shortened QT), muscle weakness, and dehydration (d/t urine sodium losses)

b. Laboratory diagnosis based on serum calcium:

| | |
|---|---|
| Mild | >10.5 – 11.9 mg/dL |
| Moderate | 12 – 13.9 mg/dL |
| Severe | >/= 14 mg/dL |

c. Ionized calcium is preferred, can use corrected calcium equation (see below) to diagnose based on serum levels (Measured $Ca^{2+}$ + 0.8*[4 – Albumin])
d. Hypercalcemia based on ionized calcium: >/= 1.3 mmol/L

X. Medication-induced Hypercalcemia
a. Highlights include: calcium-containing products, thiazide diuretics, vitamin D, and lithium

SP's labs in the ED are notable for the following:

| | | |
|---|---|---|
| Serum $Ca^{2+}$ 15.3 mg/dL | Alb: 3.1 g/dL | SCr: 1.9 mg/dL (0.6 mg/dL) |

She is still confused, but her vital signs are stable. SP will be admitted to the hospital for further treatment.

XI. Hypercalcemia treatment
a. Treatment is reserved for symptomatic or severe hypercalcemia (>/= 14 mg/dL)
b. Supportive care treatment:
i. IV crystalloid (balanced fluids or normal saline) for dehydration d/t urine sodium loss
1. Avoid LR as it's a calcium-containing product
2. Initial IV crystalloid rate: 200-500 mL/hr depending on volume status of patient
a. Can decrease rate or stop fluids if volume overload occurs
3. Goal is to maintain good urine output and volume repletion
ii. Loop diuretics
1. Avoid use up front d/t initial dehydration
2. Can use if patients are becoming volume overloaded
a. May cause calciuresis
c. Calcitonin antagonizes the effects of the parathyroid hormone decreasing calcium levels
i. SubQ route preferred in hypercalcemia
1. 4-8 IU/kg SubQ q12h
a. Typically start with 4 IU/kg and increase to 8 IU/kg if ineffective
2. Decreases calcium initially before bisphosphonate treatment starts to work
3. Tachyphylaxis is common after a few doses, typically use for first 24-48 hrs

SP's SCr continues to increase up to 2.8 mg/dL (estimated CrCl 25 mL/min), her ionized calcium is 3.3 mmol/L with a corrected serum calcium of 16 mg/dL. In addition to the aforementioned interventions, the team comes to you to discuss which IV bisphosphonate we should use for hypercalcemia treatment.

d. Bisphosphates
i. US treatment options: pamidronate and zoledronic acid
1. Most institutions preferentially use zoledronic acid for treatment
a. Generally speaking, both treatments have similar efficacy

b. Doesn't work immediately, consider up-front prescribing in severe cases

2. Zoledronic acid previously had a higher risk/concern of renal impairment, but some studies signal higher treatment efficacy
    a. Recent studies show similar safety in patients with renal impairment
3. IV administration times:

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|---|
| Zoledronic acid – 15 minutes |
| Pamidronate – 120 minutes |

    a. Consider prolonging infusion rate in renal impairment
4. If unresponsive to treatment, can repeat dose in 7 days with same agent

e. Salvage therapy
    i. Denosumab is a monoclonal antibody with affinity for RANKL, decreasing $Ca^{2+}$
        1. May be better tolerated in patients with renal impairment
    ii. Consider corticosteroids in patients with hypercalcemia d/t elevated calcitriol

## Superior Vena Cava Syndrome (SVCS)

DR is a 56 y/o M with a recent diagnosis of non-small-cell lung cancer (NSCLC) planned to initiate chemotherapy in the coming weeks, complaining of upper extremity edema, dyspnea, and cough. On physician exam he is hemodynamically stable with distended jugular veins and is hemodynamically stable with an $SpO_2$ of 98% on 2 L $O_2$ via NC.

XII. SVCS grading scale

| Grade | Severity | Definition |
|---|---|---|
| 0 | Aysmptomatic | Asymptomatic presentation |
| 1 | Mild | Head/neck edema, cyanosis |
| 2 | Moderate | Head/neck edema with functional impairment |
| 3 | Severe | Mild/moderate cerebal edema, laryngeal edema, impaired cardiac reserve |
| 4 | Life-threatening | Substantial cerebral edema, laryngeal edema, or hemodynamic compromise |
| 5 | Fatal | Death |

a. Urgent intervention needed in patients who present with severe or life-threatening symptoms such as airway obstruction or cerebral edema
b. Treatment is based on the underlying cause (found via diagnostic testing)

DR is admitted to the hospital for further work-up and imaging. A CT w/ IV contrast showed a mediastinal mass compressing and occluding his SVC. The ICU team is urgently called to his bedside for oxygen desaturation and is emergently intubated.

XIII. SVCS treatment
- a. Ensure airway is okay and not compromised
- b. Mild to moderate cases may just need supportive care
    - i. Elevation of the head, oxygen supplementation
- c. Make the diagnosis of what is causing the superior vena cava syndrome
    - i. If you know it is a mass/obstruction, obtain tissue diagnosis
- d. When patients have a known malignancy: treatment involves radiation
    - i. Depends on type of malignancy (preferred in less chemo-sensitive cancer)
- e. Chemotherapy is another treatment option for cancers that respond to chemotherapy (small cell lung cancer and lymphomas)
- f. Corticosteroids can be used in patients with lymphomas
- g. Consider intravascular stenting in severe cases to alleviate the life-threatening symptoms
- h. Thrombolytic administration could be used
    - i. Some patients may be at high risk for bleeding, so may be a risk:benefit scenario
        1. Risk of bleeding is already high in cancer patients
    - ii. Catheter-directed thrombolysis would be preferred to reduce the thrombolytic exposure

XIV. Oncologic emergencies take-home points
- a. Don't just treat the number, despite how out of range it may be, treat the symptoms
- b. Assist physician colleagues in choosing the right treatment agents and appropriate supportive care