Oncological Emergencies in the ICU

Daniel L Arellano, PhD(c), RN, ACNP-BC, CCRN, CEN, CFRN, EMT-P
University of Texas MD Anderson Cancer Center
Department of Critical Care
Houston, Texas
Disclosures

• Conflict of Interest: None
Objectives

• Demonstrate complex understanding of the etiologies of metabolic and structural oncological medical conditions.

• Identify treatment modalities for metabolic and structural oncological medical conditions in critical care.

• Apply evidence based practice to the treatment of oncologic emergencies to maximize the quality of care.
What is an Oncological Emergency?

• Clinical condition resulting from a metabolic, neurologic, cardiovascular, hematologic, and/or infectious change caused by cancer or its treatment that requires immediate intervention to prevent loss of life or quality of life.
Oncological Emergencies

• Neurological Emergencies
  • spinal cord compression
  • brain Metastasis and increased ICP
  • seizures

• Metabolic Emergencies
  • SIADH
  • hypercalcemia

• Hematologic Emergencies
  • hemorrhage
  • hyperviscosity
  • hyperleukocytosis and leukostasis
  • disseminated intravascular coagulation (DIC)
  • tumor lysis syndrome (TLS)
  • thrombosis

• Cardiovascular
  • cardiac tamponade
  • superior vena cava syndrome

• Pulmonary
  • malignant Airway Obstruction
  • pleural effusions

• GI
  • acute gastrointestinal bleed
  • typhlitis

• GU
  • hemorrhagic cystitis
  • urinary tract obstruction

• ID
  • neutropenic Sepsis
Oncological Emergencies Categories

• Metabolic
  • SIADH, hypercalcemia

• Structural
  • Spinal cord Compression, increased ICP, cardiac tamponade, SVC syndrome, malignant airway obstruction

• Treatment Related
  • TLS, neutropenic sepsis

• Hematological
  • hemorrhage, hyperleukocytosis/leukostasis
Metabolic: SIADH

• 1-2% of patients patient cancer
• Small-cell lung cancer is responsible for 60% cases
• Chemotherapy triggers
  • Cyclophosphamide
  • Vincristine
• ADH=WATER

SIADH

• Clinical Manifestations:
  • Hyponatremia (<130mEq/L)
  • Low urine output
  • Altered mental status, fatigue, headache.

• Treatment:
  • Treat underlying pathology
  • Strict I/Os
  • Correct electrolyte imbalance
  • Fluid restriction (500-1000mL/day)
  • Demeclocycline 600-1200mg/day inhibits ADH
  • Hypertonic saline for severe cases

Metabolic: Hypercalcemia

• Most common oncological metabolic emergency
• 10-20% of patients with cancer experience this condition
• Associated with lung, breast, kidney, myeloma and head and neck cancer
• High association with bone metastasis
• Can be a poor prognostic indicator

Minisola, S; Pepe, J; Piemonte, S; Cipriani, C (2015). The diagnosis and management of hypercalcaemia. BMJ. 350: h2723.
Hypercalcemia

Malignancy-Associated Hypercalcemia

Humoral Hypercalcemia
  PTHrP-related
  Non-PTHrP-related (including due to 1,25-vitamin D3)

Bone Invasion

Rare causes:
- Drug-related (retinoids)
- Immobilization
- PTH (parathyroid carcinoma)
Hypercalcemia

• Clinical Manifestations:
  • Serum calcium levels >11mg/dL
  • Hypophosphatemia
  • Lethargy, confusion, nausea vomiting, polyuria, dysrhythmias,

• Treatment:
  • Hydration (5-8L saline)
  • Diuretics (excretes calcium)
  • Calcitonin
    • Drug of choice. Acts immediately to decrease renal tubular reabsorption of calcium
    • Steroids may prolong action of calcitonin and given concurrently
  • Biphosphonates
    • Etidronate or Pamidronate. Inhibit osteoclast activity

Minisola, S; Pepe, J; Piemonte, S; Cipriani, C (2015). The diagnosis and management of hypercalcaemia. BMJ. 350: h2723.
Structural: Spinal Cord Compression

- Spinal cord compression occurs in approximately 5% of those with cancer
- Most associated breast, lung, prostate malignancy
- Occurs at the thoracic level in 70% of cases due to kyphosis and narrowed lumen at this level

Spinal Cord Compression

• Clinical Manifestations:
  • Back pain
  • Loss of motor function
  • Decreased sensation, unsteady gait, foot drop, bowel/bladder dysfunction

• Treatment:
  • Radiation therapy
  • Steroids
  • Surgery
  • Chemotherapy

Cauda Equina Syndrome

**Etiology**
- Compression of cauda equina by:
  - Herniated disk
  - Tumor
  - Abscess

**Diagnosis**
- Clinical suspicion
- MRI or CT myelogram

**Clinical**
- Urinary retention (most sensitive) followed by incontinence
- Post-void residual urine vol > 100 mL
- Bowel retention
- Saddle anesthesia
- Flaccidity of lower extremities (lower motor neuron symptoms)
- Loss of deep tendon reflexes (DTRs)
- Loss of rectal tone
Structural: Increased ICP

- Occurrence of primary brain tumors is 1% of all cancers
  - Metastatic brain lesions occur in 45% of patients with cancer
- Cancers with high rate of brain metastasis: lung, breast renal, thyroid, and melanoma
- Increased ICP can be caused by tumor expansion, brain edema, increased CSF, or intracranial hemorrhage

Increased ICP

• Clinical Manifestations:
  • Headache
  • Seizures
  • Nausea vomiting, altered mental status, cranial nerve abnormalities
  • ICP>10mmHg

• Treatment:
  • Corticosteroids
  • Anticonvulsants
  • Radiation therapy
  • Surgery
  • External Ventricular Drain

Increased ICP: Severe Cases

- Promote venous outflow
  - Positioning of head
  - Decrease abdominal pressure using muscle relaxants, laxatives, or decompression
  - Decrease intrathoracic pressure, especially in patients requiring high PEEP.
- Decrease metabolic rate demands
  - Treat pain and sedate
  - Treat fever
- Increase cerebral oxygenation/perfusion
  - Goal O2 sat > 90%
  - Goal PaO2 > 80
  - Goal Hgb > 8
  - Goal MAP > 90
- ABC’s
  - Control ICP/CPP (MAP-ICP=CPP)

Structural: Cardiac Tamponade

• Malignant pericardial effusions are the most common cause of tamponade
• Rarely caused by primary tumors and fibrosis of the heart
• Effusions are common in leukemia, lymphoma, breast, lung and melanoma malignancies
Cardiac Tamponade

• Clinical Manifestations:
  • Chest pain, SOB
  • Pulsus Paradoxicus
  • Tachycardia, Beck’s triad, electrical alternans

• Treatment:
  • Pericardiocentesis
  • Radiation
  • Pericardial window
  • Volume replacement
Structural: SVC Syndrome

• Associated with lung cancer, mediastinal tumors, lymphoma, breast cancer, and even a large thrombus
• SVC obstruction resulting in decreased superior venous return
SVC Syndrome

Figure 3. Symptoms of Superior Vena Cava Syndrome and Their Progression

SVC Syndrome

• Treatment:
  • Radiation
  • Chemotherapy
  • Stent Placement
  • Diuretics
  • Corticosteroids
  • Thrombolytic agents

• Nursing:
  • Increase HOB 45 degrees
  • Avoid brachial BPs
  • Minimize energy expenditure

Structural: Malignant Airway Obstruction

- Airway obstruction resulting from endobronchial lesions or extrinsic compression from adjacent structures
- Presentation can be acute or “subacute”
- Most common in patients with bronchogenic, head and neck, lymphoma, thymoma, and thyroid malignancies
Malignant Airway Obstruction

• Clinical Manifestations:
  • Neck fullness
  • Cough
  • SOB, dysphagia, stridor

• Treatment:
  • Corticosteroids
  • Intubation or tracheostomy
  • Radiation
  • Chemotherapy
  • Stent Placement
1. Assess the likelihood and clinical impact of basic management problems:
   - Difficulty with patient cooperation or consent
   - Difficult mask ventilation
   - Difficult supraglottic airway placement
   - Difficult laryngoscopy
   - Difficult intubation
   - Difficult surgical airway access

2. Actively pursue opportunities to deliver supplemental oxygen throughout the process of difficult airway management.

3. Consider the relative merits and feasibility of basic management choices:
   - Awake intubation vs. intubation after induction of general anesthesia
   - Non-invasive technique vs. invasive techniques for the initial approach to intubation
   - Video-assisted laryngoscopy as an initial approach to intubation
   - Preservation vs. ablation of spontaneous ventilation

4. Develop primary and alternative strategies:

   **AWAKE INTUBATION**
   - Airway approached by Noninvasive intubation
     - Invasive Airway Access
       - Succeed
       - FAIL
     - Cancel Case
     - Consider feasibility of other options
       - Invasive airway access

   **INTUBATION AFTER INDUCTION OF GENERAL ANESTHESIA**
   - Initial intubation attempts successful
   - Initial intubation attempts UNSUCCESSFUL
     - FROM THIS POINT ONWARDS
     - 1. Calling for help
     - 2. Returning to spontaneous ventilation
     - 3. Awakening the patient

   **FACE MASK VENTILATION ADEQUATE**
   - Ventilation adequate, intubation unsuccessful
     - Alternative approaches to intubation
       - Successful intubation
       - FAIL after multiple attempts
         - Invasive airway access
         - Consider feasibility of other options
   - SGA ADEQUATE
   - SGA NOT ADEQUATE
   - EMERGENCY PATHWAY
     - Ventilation not adequate, intubation unsuccessful
     - Emergency noninvasive airway ventilation
     - Successful ventilation
     - Emergency invasive airway access

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*a, Other options include (but are not limited to): surgery utilizing face mask or supraglottic airway (SGA) anesthesia (e.g., LMA, ILMA, laryngeal tube), local anesthesia infiltration or regional nerve blockade. Pursuit of these options usually implies that mask ventilation will not be problematic. Therefore, these options may be of limited value if this step in the algorithm has been reached via the Emergency Pathway.
b. Invasive airway access includes surgical or percutaneous airway, jet ventilation, and retrograde intubation.
c. Alternative difficult intubation approaches include (but are not limited to): video-assisted laryngoscopy, alternative laryngoscope blades, SGA (e.g., LMA or ILMA) as an intubation conduit (with or without fiberoptic guidance), fiberoptic intubation, intubating stylet or tube changer, light wand, and blind oral or nasal intubation.
d. Consider re-preparation of the patient for awake intubation or canceling surgery.
e. Emergency non-invasive airway ventilation consists of a SGA.
Treatment Related: Tumor Lysis Syndrome
Tumor Lysis Syndrome

### Table 1: Cairo-Bishop Definition of Laboratory Tumor Lysis Syndrome

<table>
<thead>
<tr>
<th>Element</th>
<th>Value</th>
<th>Change from Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uric acid</td>
<td>≥476 micromol/L (8 mg/dL)</td>
<td>25% increase</td>
</tr>
<tr>
<td>Potassium</td>
<td>≥6.0 mmol/L (or 6 mEq/L)</td>
<td>25% increase</td>
</tr>
<tr>
<td>Phosphorous</td>
<td>≥2.1 mmol/L (6.5 mg/dL) for children or 1.45 mmol/L (4.5 mg/dL) for adults</td>
<td>25% increase</td>
</tr>
<tr>
<td>Calcium</td>
<td>≤1.75 mmol/L (7 mg/dL)</td>
<td>25% decrease</td>
</tr>
</tbody>
</table>

Note: Two or more laboratory changes within the period from 3 days before to 7 days after cytotoxic therapy are required to establish the diagnosis of tumor lysis syndrome.

From Coiffier et al. [43] Reproduced with permission.

### Table 2: Risk of TLS According to Tumor Type

<table>
<thead>
<tr>
<th>Degree of Risk</th>
<th>Tumor Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Burkitt’s lymphoma</td>
</tr>
<tr>
<td></td>
<td>High-grade non-Hodgkin’s lymphoma</td>
</tr>
<tr>
<td></td>
<td>Lymphoblastic lymphoma</td>
</tr>
<tr>
<td></td>
<td>T-cell acute leukemia</td>
</tr>
<tr>
<td></td>
<td>Other acute leukemias</td>
</tr>
<tr>
<td>Moderate</td>
<td>Low-grade lymphoma treated with chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Radiation/corticosteroids</td>
</tr>
<tr>
<td></td>
<td>Multiple myeloma</td>
</tr>
<tr>
<td></td>
<td>Breast carcinoma treated with chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Hormonal therapy</td>
</tr>
<tr>
<td></td>
<td>Small-cell lung carcinoma</td>
</tr>
<tr>
<td></td>
<td>Germ-cell tumors (seminoma, ovarian)</td>
</tr>
<tr>
<td>Low</td>
<td>Low-grade lymphoma treated with interferon</td>
</tr>
<tr>
<td></td>
<td>Merkel’s cell carcinoma</td>
</tr>
<tr>
<td></td>
<td>Medulloblastoma</td>
</tr>
<tr>
<td></td>
<td>Adenocarcinoma of the gastrointestinal tract</td>
</tr>
</tbody>
</table>

TLS: tumor lysis syndrome
Source: Reference 3.

Tumor Lysis Syndrome

• Treatment:
  • IV fluids (>100mL/hr)
  • Allopurinol
  • Rasburicase
    • Check uric acid level and hospital protocol
  • Treat electrolyte abnormalities
  • Treat only symptomatic hypocalcemia
  • Monitor labs frequently
    • Minimum every 8 hours
  • Cardiac monitoring
  • Early hemodialysis

Hematological: Hyperleukocytosis and Leukostasis

- Damage related to leukemic infiltration and to the effects of leukemic cells on the vasculature.
- Intravascular sludging and leukostasis can develop along with white thrombus formation.
- Tissue damage occurs as a result of local hypoxia
- Occurs in patients with AML, CML in blast crisis with WBC count >100,000/mL
Hyperleukocytosis and Leukostasis

• Clinical Manifestations:
  • WBC count >100,000/mL
  • Neuro: AMS, dizziness, retinal hemorrhage
  • Pulmonary: Fever, hypoxia, respiratory failure
  • Other: renal failure, priapism, peripheral vascular occlusion

• Treatment:
  • Chemotherapy
  • Corticosteroids (high dose)
  • Leukopheresis
  • Oxygen
Treatment Related: Neutropenic Sepsis

Neutropenic Sepsis

• Factors that Predispose to Infection:
  • Immunosuppression
    • Chemotherapy, steroids
  • Indwelling devices
    • Implanted port, peripherally inserted central catheter, tunneled central venous catheters, urinary catheters, chemotherapy delivery devices
  • Epidemiology
    • Hospitals, clinics, long-term care centers
  • Age
  • Comorbid conditions
  • Invasive procedures

Neutropenic Sepsis

• Antibiotic Principles:
  • “Hit hard and Hit Fast” ANTIBIOTICS ASAP
  • CULTURES BEFORE ANTIBIOTICS
  • Empiric therapy is acceptable in this population
  • Initial therapy should be broad spectrum
  • Broad spectrum antibiotics markedly alter the normal host flora in 3 days AND cultures should be back in 3 days reassess antibiotic choices and narrow it when possible
  • Consider antifungals if high risk and persistent fevers
  • Viral treatment should be considered for respiratory illness and herpes simplex.
Common Antibiotic Regimens in Cancer Patients

Option 1

1) Vancomycin
   • Gram positive
2) Piperacillin-tazobactam
   • **Gram negative**
   • Pseudomonas Coverage
   • Anaerobes
3) Levofloxacin
   • **Gram negative**/Atypical coverage
   • Optional:
4) Fluconazole
   • Antifungal
5) Acyclovir
   • Antiviral

Option 2

1) Linezolid
   • Gram positive
2) Meropenem
   • **Gram negative**
   • Pseudomonas Coverage
   • Anaerobes
3) Amikacin
   • **Gram negative**
   • Optional:
4) Caspofungin
   • Antifungal
5) Valacyclovir
   • Antiviral
Hematological: Hemorrhage

• Common hemorrhage in cancer patients:
  • Massive hemoptysis
  • Diffuse Alveolar Hemorrhage (DAH)
  • GI Bleed
  • Hemorrhagic cystitis

• Common causes of hemorrhage in cancer patients:
  • Thrombocytopenia
  • Erosion into vasculature
  • DIC
  • Use of anticoagulants
Massive hemoptysis

• MD Anderson Algorithm:
  • 50cc at once or 200 over 24 hours
  • Thoracic Surgery Fellow on-call - First Response/Consult
    • Alert the ICU team of need for an ICU bed and possible need for medical assistance/resuscitation
    • Alert the Anesthesiologist on-call in-house for airway management and possibly need for emergent surgery
    • Alert Interventional Radiology through the radiology resident in-house for possible emergent IR procedures
    • The Pulmonary medicine will be notified as needed by the Thoracic Team Fellow, in cases where their input and care is more appropriate
Massive hemoptysis

- Nursing Interventions:
  - Know the site of bleeding
    - Left lung? Right mainstem intubation
  - ETT Epinephrine
  - Patient positioning. Lateral decubitus
  - Presumed bleeding lung in the dependent position.
Diffuse Alveolar Hemorrhage

• Bleeding into the alveolar spaces of the lungs
• Often due to disruption of the alveolar-capillary basement membrane.
• Hemoptysis is the usual presenting symptom; however it is not always present, even when hemorrhage is severe
Diffuse Alveolar Hemorrhage

• Clinical Manifestations:
  • Hemoptysis
  • Hypoxia
  • Cough
  • Fever
  • SOB
  • Radiographic findings

• Treatment:
  • Supportive Care
  • Corticosteroids
  • Treat thrombocytopenia
  • Treat coagulopathy
  • Aminocaproic acid
  • Tranexamic acid
GI Bleed

- Multifactorial Causes:
  - Thrombocytopenia
  - Erosion into vasculature

- Often unstable for diagnostic procedures or treatment

- Supportive Care
  - Reverse coagulopathy
  - Treat thrombocytopenia
  - Consider Aminocaproic acid or Tranexamic acid
  - Massive Transfusion protocol
Hemorrhagic Cystitis

• Causes:
  • Chemotherapeutic agents (busulfan [Myleran], cyclophosphamide, ifosfamide, thiotepa)
  • Pelvic irradiation
  • Viruses (BK Virus, CMV)
  • Invasive urothelial tumors

Hemorrhagic Cystitis

• Treat underlying cause
• Correct coagulopathy and thrombocytopenia
• Administration of the uroprotective agent mesna (Mesnex)
• Vigorous hydration to encourage frequent urination
• Continuous bladder irrigation (1:1 nursing care?)
Disseminated intravascular coagulation (DIC)

**Pathophysiology**
- Hyper-activated coagulation system.
- Hyper-activated fibrin-lytic system, or both simultaneously.
- Coagulation factors and platelets consumed as soon as they are made.
- Secondary to an underlying disease or condition. Example: sepsis, placenta abruption, snake bites, toxin, trauma, graft vs. host disease, and burns.

**Clinical Finding**
- Patients are at risk of bleeding and thrombosis.

**Laboratory Finding**
- Thrombocytopenia.
- Prolonged PT, APTT, thrombin time.
- Decreased fibrinogen.
- Elevated D-dimers.
- Schistocytes on the peripheral blood smear.

**Treatment of DIC**
- Treatment of the underlying disorder.
- Transfusion support of Red Blood Cells or Fresh Frozen Plasma (FFP) to replace coagulation factors.
General Strategies

• Stay prepared.
• Anticipate potential emergencies and recognize them early
  • High degree of suspicion
• Monitor lab values closely in unstable patients.
• Identify risk factors
• Ask for help/consultations
  • Difficult airway. Early anesthesia involvement
• Educate the patient and family
MD Anderson Treatment Algorithms

Questions?

Daniel L Arellano, PhD(c), RN, ACNP-BC, CCRN, CEN, CFRN, EMT-P
University of Texas MD Anderson Cancer Center
Department of Critical Care
Houston, Texas

• DLArellano@MDAnderson.org
References

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