Oncologic Emergencies in the ICU

Just the pearls and a tidbit of patho...

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Commonality of Oncologic ICU Emergencies

**Common**
- Neutropenic Septic Shock
- Cytokine Release Syndrome
- Pulmonary Embolism
- Bleeding (hemoptyisis, DIC, tumor invasion)

**Uncommon (predicted)**
- Pericardial Tamponade
- Acute Tumor Lysis
- SVC Syndrome
- Spinal Cord Compression

*from experience at MSKCC*
Disclosures

• None

(but I wouldn’t mind some)
Neutropenic Septic Shock
...it was the host, not the germ, that drove the pathogenesis of sepsis.

Angus DC., & van der Poll, T. Critical Care Medicine, August 29, 2013
Systemic Inflammatory Response Syndrome

• Criteria\(^1\)-must have 2 or more of the following:
  – Body temperature >38° C
  – Heart rate > 90 bpm
  – Respiratory rate >20 rpm or PACO\(_2\) <32 mm Hg
  – WBC >12,000/mm\(^3\) or <4000/mm\(^3\) or “bands” >10%

\(^1\) defined by the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference in Chicago. (Bone et al., 1992)
Host Response in Septic Shock

Tissue hypoperfusion

Increased coagulation

- Monocyte
- Tissue factor pathway inhibitor
- Antithrombin
- Protein C
- Activated protein C
- PAI-1
- Fibrinolysis
- NETs with trapped platelets
- Thrombus
- Thrombosis

Decreased anticoagulation

- TM
- Endothelial protein C receptor
- S1P3 and S1P1
- PAR1
- Angiopoietin 2
- VE cadherin and Tight junctions
- Capillary leak and interstitial edema
- Loss of barrier function

Loss of barrier function

- S1P3
- S1P1

Vasodilatation

- Red-cell deformability
- Blood pressure

Tissue hypoperfusion

- Release of mitochondrial contents
- Mitochondrial dysfunction
- Mitochondrial dysfunction
- Tissue oxygenation

Organ failure
Management

Recognize & Act Quickly!

• IV antimicrobials within the first hour of recognition
• Combination therapy with extended spectrum β-lactam and either an aminoglycoside, fluoroquinolone or Azithromycin for neutropenic pts plus Vancomycin 1 g q 12 hrs or Linezolid
• Liposomal amphotericin B, voriconazole or micafungin with hx of HSCT and/or not responding to therapy (fluconazole- abdominal surgery)
• Antivirals (CMV, RSV) and Anti-PCP (steroids)
• Crystalloids/Colloids
• Norepinephrine or Epinephrine +/- Vasopressin

Cytokine Release Syndrome
Inflammation cascade

- Magnitude differs w/ each pt
- ↑ cytokines (IL-6)
CRS Management

- Hypotension SBP < 90 refractory to IVF challenge or requiring vasopressors OR
- Respiratory distress/hypoxia requiring increasing supplemental oxygen or ventilatory support OR
- Acute coronary syndrome with positive troponin and/or ECG changes OR
- Seizure, clinically suspected and/or documented on EEG

Tocilizumab 8mg/kg IV once

Worsening CRS within 12 hours
- Increasing vasopressors dose OR
- Increasing ventilatory support OR
- Persistent seizure activity

Dexamethasone 10mg IV q6h

Taper as clinically indicated

No clinical improvement ≥ 24 hours

Clinical improvement < 24 hours
- Decreasing vasopressor dose OR
- Decreasing ventilatory support OR
- No further seizure activity

Observe

Worsening CRS
- Increasing vasopressors OR
- Increasing ventilatory support OR
- New seizure
Pulmonary Embolism
Pathophysiology of Major PE

BP = blood pressure; CO = cardiac output; LV = left ventricular; RV = right ventricular; TV = tricuspid valve.

Konstantinides et al. European Heart Journal, 2014
Presentation

Dyspnea (79%)

Tachypnea (57%)

Pleuritic pain (47%)

Leg edema, erythema, tenderness, palpable cord (47%)

Cough/ hemoptysis (43%)

Elevated Troponin?

In hemodynamically stable PE patients, elevated troponin levels increase mortality 6-fold.

Embolectomy

Surgical

• Operative mortality: 10-75%; 50-95% in pts who have had cardiopulmonary arrest
• Complications: ARDS, acute renal failure, mediastinitis, severe neurologic sequelae
• Critical to have an experienced and aggressive CT surgery team that can be rapidly mobilized

Catheter

• Transvenous insertion of embolectomy catheter $\rightarrow$ suction and pulverization by a high-speed rotor or fluid jet, and physical fragmentation with the catheter tip
• Limited studies, but survival rate ~70%-90%

Disseminated Intravascular Coagulation
DIC

• Persistent activation of the coagulation cascade
• Widespread (micro) vascular thrombosis
• Excess circulating thrombin assists in the conversion of plasminogen to plasmin, resulting in fibrinolysis
• Ongoing activation exhausts factors and platelets resulting in profuse bleeding

DX:
• Thrombocytopenia
• ↑ PT and APTT
• ↓ Fibrinogen
• ↑ Fibrin degradation products or (FDP) or fibrin split products
• 10-15% of patients with metastasized tumors have evidence of DIC
  – Mucin-secreting adenocarcinomas; prostate, lung, breast, pancreas, stomach, bladder
• 15% of patients with acute leukemia have evidence of DIC (promyelocytic leukemia)
DIC: Management

- Treat the cause
- PRBC (hgb >8d/dl), platelet transfusion (maintain platelet count > 20,000/ul (50,000 preferred)
- Fibrinogen > 100
- PT, APTT q 4-6 hrs

<table>
<thead>
<tr>
<th></th>
<th>FFP</th>
<th>Cryo</th>
</tr>
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<tbody>
<tr>
<td>Factors</td>
<td>II, V, X, XII, XIII</td>
<td>II, V, X, XII, XIII</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>vWB</td>
<td>No</td>
<td>Yes</td>
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</table>
Pericardial Tamponade
Pericardial Tamponade

- A **pericardial effusion** occurs when the production of fluid exceeds the rate of resorption

- **Tamponade**: rapid accumulation of fluid in the pericardial space causing compression of the heart faster than the pericardium can distend
  - Rapid increase of only a very small volume
  - Slow increase over weeks may never lead to tamponade

- Malignant - 13-23%
  - Lung cancer #1 cause of malignant effusions

- Physical Signs: Increased JVD, peripheral edema, pulses paradoxus (Drop of 10-12 mmHg in SBP on inspiration), tachycardia, hypotension, respiratory failure, hemodynamic collapse
Pericardial Tamponade

• **Echo Findings**
  
  – **Right atrial systolic collapse (RASC)**
    • Right atrial inversion
    • About 100% sensitive, but low specificity (33-94% in some series)
  
  – **Right ventricular diastolic collapse (RVDC)**
    • 75-93% sensitive and 85-100% specific

Singh S. et al. 1986
Gilliam LD et al. 1983
Pericardial Tamponade: Surgical Management

• Pericardiocentesis
  – Remove 10-50 cc of fluid to see improvement
  – Should be ultrasound guided unless in an emergency
  – Low risk
• Pericardial Window (subxiphoid, transthoracic)
  – Pericardial drain
Pericardial Tamponade: Post-op

- Rapid improvement in hemodynamics
- Decrease O2 requirements
- Lasix due to increase RA and RV filling pressures
- Mild symptoms of right heart failure initially after surgery
  - Improves with diureses
  - Lasix often given in the OR to reduce this risk

- But some get worse...
Pericardial Tamponade

- **Paradoxical hemodynamic Instability**
  - Instead of improving, patients worsen after tamponade is released
  - Unknown etiology
  - Poor prognosis

- Review of MSKCC data on pericardial effusions over 5 years
  - Evaluated survival, predictive factors and incidence of paradoxical hemodynamic instability (PHI)
Paradoxical Hemodynamic Instability

- Occurred in 11% of all patients
  - 84% of patients in tamponade
  - Only 4% of those not in tamponade
- Acute cardiogenic pulmonary edema
- Hemodynamic instability
- Often normal findings on echo
  - Biventricular function is usually preserved
- Respiratory failure
- Median survival is 35 days
  - Majority do not survive their hospital stay
Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>PHI (n = 19)</th>
<th>No PHI (n = 160)</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>54.0 ± 13.8</td>
<td>55.8 ± 15.3</td>
<td>.6</td>
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<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6 (31.6%)</td>
<td>59 (36.9%)</td>
<td>.8</td>
</tr>
<tr>
<td>Female</td>
<td>13 (68.4%)</td>
<td>101 (63.1%)</td>
<td></td>
</tr>
<tr>
<td>Primary malignant disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>8 (42.1%)</td>
<td>70 (43.8%)</td>
<td>.9</td>
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<tr>
<td>Breast</td>
<td>5 (26.3%)</td>
<td>30 (18.8%)</td>
<td></td>
</tr>
<tr>
<td>Hematologic</td>
<td>2 (10.5%)</td>
<td>15 (9.4%)</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>2 (10.5%)</td>
<td>11 (6.9%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (10.5%)</td>
<td>34 (21.2%)</td>
<td></td>
</tr>
<tr>
<td>Malignant cells identified, cytology or pathology</td>
<td>13 (68.4%)</td>
<td>65 (40.6%)</td>
<td>.03</td>
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<tr>
<td>Volume of pericardial fluid drained, mean ± SD, mL</td>
<td>674 ± 217</td>
<td>495 ± 231</td>
<td>.003</td>
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<tr>
<td>Preoperative atrial fibrillation</td>
<td>2 (10.5%)</td>
<td>9 (5.6%)</td>
<td>.3</td>
</tr>
<tr>
<td>Concurrent pulmonary embolism</td>
<td>2 (10.5%)</td>
<td>8 (5.0%)</td>
<td>.3</td>
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<tr>
<td>Prior anthracycline exposure</td>
<td>5 (26.3%)</td>
<td>39 (24.4%)</td>
<td>.8</td>
</tr>
<tr>
<td>Prior thoracic radiation</td>
<td>5 (26.3%)</td>
<td>65 (40.6%)</td>
<td>.3</td>
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</table>

Table 2. Echocardiographic findings

<table>
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<th>PHI (n = 19)</th>
<th>No PHI (n = 160)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Preoperative echocardiogram</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Tamponade present</td>
<td>16/19 (84%)</td>
<td>87/155 (56%)</td>
<td>.01</td>
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<tr>
<td>LV dysfunction, moderate-to-severe (EF &lt; 40%)</td>
<td>0/19 (0%)</td>
<td>2/115 (2%)</td>
<td>.7</td>
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<tr>
<td>Postoperative echocardiogram</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV dysfunction, moderate-to-severe (EF &lt; 40%)</td>
<td>2/18 (11%)</td>
<td>3/90 (3%)</td>
<td>.16</td>
</tr>
<tr>
<td>RV dysfunction, moderate-to-severe</td>
<td>4/17 (24%)</td>
<td>9/75 (12%)</td>
<td>.25</td>
</tr>
<tr>
<td>RV dilatation, moderate-to-severe</td>
<td>2/18 (11%)</td>
<td>3/83 (4%)</td>
<td>.22</td>
</tr>
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</table>

Table 3. Multivariate analysis of factors associated with PHI

<table>
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<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
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</thead>
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<tr>
<td>Malignant cells identified, cytology or pathology</td>
<td>5.8</td>
<td>1.2–28.3</td>
<td>.029</td>
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<tr>
<td>Volume of pericardial fluid drained, per mL</td>
<td>1.003</td>
<td>1.0001–1.005</td>
<td>.043</td>
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<tr>
<td>Presence of tamponade</td>
<td>4.1</td>
<td>0.8–20.3</td>
<td>.082</td>
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</table>

PHI, Paradoxical hemodynamic instability; SD, standard deviation.
Paradoxical Hemodynamic Instability

• Prevention of PHI
  – Slow drainage of fluid
    • Similar to re-expansion pulmonary edema phenomenon
  – Early prophylactic drainage of effusions
    • Only 4% of non-tamponade patients developed PHI
  – Massive hemodynamic support in the first 24-48 hours
    • If no early improvement, unlikely to every recover
    • Must explain this all to the family

Wagner et al. JTCVS 2011
Acute Tumor Lysis
Acute Tumor Lysis

- Destruction of tumor cells with treatment → Metabolic derangements (Hyperkalemic, Hyperphosphatemic, Hyperuricemia and Hypocalcemic) and release of intracellular debris or spontaneous d/t rapid growth
- High Risk: Tumors with high growth fraction, bulky disease (leukemias, lymphomas, solid tumors (small cell lung, breast)
- Can occur 24-72 hrs after initiation of therapy
- Treatment (prevent AKI)
  - HYDRATION, HYDRATION, HYDRATION (200 ml/hr)
  - DIURESIS (urine output 150-200ml/hr)
  - Allopurinol (prophylaxis only) (inhibits production)
  - Rasburicase – catabolizes uric acid
    - Cannot use if pt has glucose-6-phosphate dehydrogenase (G6PD) deficiency (hemolytic anemia or methemoglobinemia)
  - Sodium bicarb- Urine alkalization- less favorable d/t nephropathy
  - Phosphate binding aluminum antacids- Sevelamer
SVC Syndrome
Pathophysiology

- Occlusion of the SVC resulting in an increase in venous pressure which leads to venous stasis and engorgement
- Causes - Lung Cancer (Small Cell - 65-80%)
  - Catheters, thrombosis, aneurysm, vasculitis, sarcoidosis
- Symptoms: periorbital edema, facial fullness, dyspnea, cough, arm swelling, chest pain, dysphagia
- Late signs: Dysphagia and hoarseness due to the entrapment of the laryngeal nerve and laryngeal edema, Increasing intercranial pressure, cerebral edema, heart failure
- Treatment: chemotherapy, radiation, stenting, thrombosis
- Adjunct management: diuretics, steroids, avoid CVC insertion
Kumaer & Hosn, 2014, NEJM
Spinal Cord Compression
High Risk for SCC

- High Risk: Primary Intramedullary Tumors (Ependymoma, Astrocytoma, Glioma, Hemangioblastoma), Metastatic Intramedullary Tumors (Lymphoma, Neuroblastoma) Metastatic Bone/Epidural Tumors (Breast, Lung, Prostate, Renal, Myeloma, Thyroid, Sarcoma), vertebral fractures or intraspinal abscesses
- Symptoms: Pain ➔ parethesias ➔ motor loss ➔ loss of proprioception
- Treatment: High dose corticosteroids, laminectomy, radiation, chemo