emDocs

The EM Educator Series

The EM Educator Series: The Sick Oncology Patient

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Case 1:
A 55-year-old female with a history of breast cancer presents with progressively worsening shortness of breath.

Case 2:
A 60-year-old male with a history of metastatic renal cell cancer presents with nausea, vomiting, acute on chronic abdominal pain, and poor pain control.

Case 3:
A 30-year-old male with no past medical history presents with stroke-like symptoms and chest pain.

Questions for Learners:

1. What is the ED approach and management for SVC syndrome?
2. What is the ED approach and management for pericardial effusion? Cardiac tamponade?
3. What is the ED approach and management for spinal cord compression?
4. What is the ED approach and management for hypercalcemia?
5. What is the ED approach and management for tumor lysis syndrome?
6. What is the ED approach and management for hyperviscosity syndrome?
7. What is the ED approach and management for neutropenic fever?

Suggested Resources:

- FOAMed
  - emDocs – Oncology emergencies Part I
  - emDocs – Oncology emergencies Part II
  - EM Cases – Oncology emergencies
  - REBEL EM - Oncology emergencies
- Journal Articles
  - Western Journal of Emergency Medicine
  - Emergency Medicine Clinics of North America

Answers for Learners:

1. What is the ED approach and management for SVC syndrome?

SVC syndrome is due to **obstruction of blood through the SVC, caused by internal vascular invasion or external compression. Malignancy** such as lung cancer is most common (60%), whereas **intravascular catheters** account for 40% of presentations. External compression can be due to the right lung/mass, lymph nodes, or other mediastinal structures**. Malignancy is the predominant cause**, commonly non-small cell and small cell **lung cancer**, followed by lymphoma. **Thrombosis** of the SVC accounts for the majority of nonmalignant causes of SVC syndrome, usually a result of an indwelling intravascular device. Post-radiation fibrosis and fibrosing mediastinitis are other causes. The time of symptom onset depends on the **rate of obstruction and venous collateral formation. Dyspnea** is the most common symptom, with patients also complaining of face fullness/swelling. Cough, chest pain, and dysphagia are other symptoms. Unfortunately if rapid onset of symptoms occurs and no collateral flow is present, **rapid onset of airway edema may present necessitating intubation**. Facial edema and distension of neck and chest wall veins are commonly seen, though facial plethora and arm edema are rare. Usually symptoms are gradual over weeks with increase in venous pressure, and then improve with collateral vessel formation. **Chest xray is abnormal in 84% of patients**, often demonstrating widening of the mediastinum and pleural effusion. **The optimal imaging is CT of the chest with contrast**, which shows venous drainage, point of blockage, and identifies the cause of obstruction. Collateral vessel presence on CT has a specificity of 96% and sensitivity of 92%. MRV, US, and cavogram are other imaging options. Biopsies are often taken of the mass if cancer is found. Treatment involves symptom relief and disease management. If a malignancy is chemotherapy sensitive, systemic chemotherapy is warranted**. A stent can be placed by interventional radiology for severe symptoms**. **Radiotherapy** is done for non-small cell lung cancer following stent placement. If thrombus is present, **systemic anticoagulation with heparin** is needed. If airway edema is present, emergent stenting with radiation is necessary, **with high-dose steroids**. Though classically included in the treatment in boards review, **diuretics are not supported in the literature**. Unfortunately survival is around six months on average once the diagnosis is made.

2. What is the ED approach and management for pericardial effusion? Cardiac tamponade?

Malignant pericardial disease is present in up to **one third** of cancer patients and is most commonly due to **metastases from lung or breast cancer**. The majority of pericardial effusions (90%) are not malignancy-related. Most patients will present with **exertional dyspnea (80%)**. A slow accumulation of fluid can allow up to 2L in the pericardial sac to collect with no change in hemodynamics. **The acute accumulation of fluid causes decompensation. Ultrasound** is the key to diagnosis and allows evaluation for tamponade (right atrial collapse in late diastole and right ventricular collapse in early diastole). **Pericardiocentesis** is often the necessary treatment, with ultrasound guidance preferred. **Unfortunately up to 60% of patients will have recurrent pericardial effusions after drainage**. Most patients have a poor prognosis following diagnosis, with median survival two to four months.

3. What is the ED approach and management for spinal cord compression?

Malignant spinal cord compression is a common cancer complication resulting from thecal sac compression, usually from local disease progression from vertebral body metastases from lung, kidney, or breast cancer, as well as multiple myeloma. There are **three types of**

compression: **intramedullary** (metastasis in the dura mater), **leptomeningeal** (metastasis on top of the dura mater), and **external compression** (90% of cases). The **thoracic spine has the most blood supply and greatest number of vertebrae**, so it is most susceptible (60-70% of cases). Unfortunately it also possesses the least amount of space in the spinal canal. Prostate cancer will often metastasize to the lumbar region, breast to the thoracic, lung to the thoracic, and kidney to thoracic or lumbar. Median survival is six months**. Back pain** is the most common complaint found in 80-95% of patients, which often precedes other symptoms by two months. **Half of patients will have bowel/bladder dysfunction at presentation**, so obtaining a post-void residual or ultrasound can be helpful in the evaluation. The most important aspect is diagnosis, and the best prognostic factor, is pretreatment ambulation and neurologic status. **MRI of the whole spine is needed for adequate visualization**, as one third of patients will have multiple sites of metastasis and/or compression. Pain management is the first item of treatment, with **opiate analgesics and glucocorticoids** both supported by literature. If severe neurologic deficits such as paraparesis or paraplegia is present, then some recommend using high-dose steroids (dexamethasone 96mg IV), though risk of side effects is increased with greater steroid doses. With minimal symptoms, dexamethasone 10mg IV can be given. If no neurologic symptoms are present, no steroids are needed. As in common back pain, bedrest is not recommended. Definitive treatment involves **surgery, external beam radiotherapy, or stereotactic body radiotherapy**. If the spine is unstable, surgery is usually needed. Ultimately the course of treatment will be up to your spine surgeon and oncologic specialist

4. What is the ED approach and management for hypercalcemia?

Hypercalcemia of malignancy occurs in 20 to 30% of cancers and is due to three different mechanisms: **parathyroid-related protein (PTHrP) production** seen in squamous cell carcinoma and lymphoma (80%), **osteoclast activating factor** seen in multiple myeloma or metastases causing osteolysis (20%), and **endogenous calcitriol** (1,25-dihydroxyvitamin D) production seen in lymphomas (<1%). Unfortunately hypercalcemia of malignancy is associated with poor prognosis. The most common cancers with bone involvement are **breast and lung cancer and multiple myeloma.** Patients will present with **dehydration, polydipsia, fatigue, confusion, nausea/vomiting, constipation, decreased urine output, and ECG changes** (bradycardia, prolonged PR, widened QRS, short QT). Management includes obtaining an ionized calcium and electrolyte panel with ECG. Patients with mild hypercalcemia (<12mg/dL) with no symptoms do not need immediate treatment, but need **adequate fluid intake**. Mild symptoms with levels of 12-14mg/dL is often chronic, and treatment should be aimed at rehydration and finding the cause.

This post will focus on severe hypercalcemia, defined by levels **> 14mg/dL with severe** symptoms. **Initial treatment is with crystalloids, crystalloids, and more crystalloids at 200-300ml/hr. Loop diuretics are not recommended in the absence of renal or heart failure because of potential complications**. **Calcitonin** is the fastest acting medication, given at 4 international units/kg IM or subcutaneously, but unfortunately tachyphylaxis is common after the first dose. **Bisphosphonates** such as pamidronic acid (60-90mg IV over 2 hours) and zoledronic acid (4mg IV over 15 minutes) are the mainstays of therapy after adequate rehydration. **Hydration and calcitonin will lower levels by 12 hours, with bisphosphonates working within 24 to 72 hours**. These patients should be admitted. If neurologic deficits are found with a level of 18mg/dL or greater, then **dialysis** is warranted. Glucocorticoids are also commonly quoted as treatment, but this is only warranted if mechanism of hypercalcemia is due to calcitriol overproduction (lymphoma, sarcoidosis).

5. What is the ED approach and management for tumor lysis syndrome?

TLS is due to **massive tumor cell lysis with release of potassium, phosphorus, and uric acid into the body.** TLS occurs **after treatment initiation for high grade lymphomas and ALL, but any malignancy with aggressive therapy or high tumor burden can result in TLS**. Treatment with radiation, chemotherapy, and/or steroids is the instigating factor. Patients often present with **nausea/vomiting, diarrhea, anorexia, lethargy, low urine output, cramps, and dysrrhythmias. Low calcium** is the most common electrolyte abnormality, usually due to release of phosphorus from dying cells binding free calcium. **Hyperkalemia** can result in arrhythmias, phosphorus elevation can cause calcium phosphate deposits in the kidneys, and high uric acid can lead to uric acid precipitation in the renal tubules, renal vasoconstriction, and acute kidney injury**.** Hyperuricemia is due to the breakdown of purine nucleic acids via xanthine oxidase. Uric acid is not very soluble in water, resulting in crystal formation. Phosphorus is produced in tumor cells at four times the amount of normal tissue cells. Secondary hypocalcemia results, and calcium phosphate deposits will develop when calcium times phosphate is greater than $60mg^2/dL^2$.

Two classifications exist via the **Cairo-Bishop definition**. The first is **laboratory TLS** (two or more laboratory abnormalities) and the second is **clinical TLS** (one laboratory abnormality plus increased creatinine, cardiac arrhythmia, or seizure). Patients at risk for TLS are followed closely by oncologists, who usually place them on allopurinol for prophylaxis. The most important aspect of this disease is avoiding it! **Adequate hydration and allopurinol** are essential in prevention. Allopurinol only prevents the formation of uric acid, but does not improve metabolism of the already present uric acid. For treatment of established TLS, there are several avenues to address. **First is hydration.** IV hydration is vital to maintain the glomerular filtration rate of the kidneys. These patients are often dehydrated, so several boluses of IV fluids (normal saline works well) are usually necessary to correct the dehydration**. Next is electrolyte management**, especially **hyperkalemia** (calcium for cardiac membrane stabilization, beta agonists and insulin/glucose for shift) and **hyperphosphatemia** (restrict intake and use phosphate binders such as calcium carbonate or sevelamer). **Renal protection is the next step**, which is assisted with your fluid boluses and electrolyte monitoring/management. **Rasburicase is vital in this step**, which oxidizes uric acid to allantoin. This metabolite is ten times more soluble than uric acid. Unfortunately this **does not prevent renal failure or lower mortality**! Rasburicase is dosed at 0.2mg/kg one time per day. Urinary alkalinization using sodium bicarbonate is **controversial**, with no data to support this, and this has been shown to increase formation of calcium phosphate crystals in the kidneys! These patients require admission, often to the **ICU** for monitoring.

6. What is the ED approach and management for hyperviscosity syndrome?

Hyperleukocytosis occurs with **WBC greater than 50,000** (classically greater than 100,000). **Leukostasis occurs in the setting of hyperleukocytosis with symptoms and is an emergency**. It is seen with **acute myeloid leukemia (20% of patients) or chronic myeloid leukemia with blast crisis** most commonly, but it can occur with other malignances. Symptoms are due to white cells plugging microvasculature and/or tissue hypoxemia with cytokine damage, often resulting in **respiratory (30% of patients) and neurologic (40%) symptoms.** If untreated, mortality at one week reaches 40%. Pulmonary symptoms include **dyspnea and hypoxia**. Of note, arterial pO_2 levels may be falsely decreased due to the elevated WBCs utilizing O_2! Neurologic signs/symptoms include **vision changes, headache, dizziness, tinnitus, ataxia, confusion, and coma**. Patients with hyperleukocytosis have increased risk of intracranial hemorrhage for at least one week after treatment! **Close to 80% of patients will display fever**, so most specialists and studies recommend **antibiotic treatment concurrently**. Myocardial ischemia, limb

ischemia, and renal disease may also be present. Labs will show high WBC (often above 100,000), falsely elevated platelets, and hyperkalemia; however, **DIC** is present in 40% of patients!
Management involves **lowering the WBC count by cytoreduction (induction chemotherapy or leukopheresis), so hematology/oncology must be emergently consulted. Adequate fluid resuscitation** is vital to maintain perfusion to end organs. **Only chemotherapy has been shown to reduce mortality**, as opposed to leukopheresis. However, if chemotherapy is unobtainable emergently, then speak with your blood bank and oncologist about leukopheresis! Hydroxyurea (50-100 mg/kg/day) is also an option for asymptomatic hyperleukocytosis patients. **DIC and tumor lysis syndrome are major risks** during the treatment of leukostasis, and coagulation panel, CBC, and renal function panel with urinalysis are vital in monitoring. Prophylaxis with allopurinol with hydration is usually started with cytoreduction treatment to decrease the risk of tumor lysis syndrome. Disposition is simple: these patients must be **admitted, preferentially to the ICU**.

7. What is the ED approach and management for neutropenic fever?

Neutropenic fever is a commonly treated condition in the ED. The cytotoxic medications used to treat malignancy have several effects on the body besides killing the cancer**: the medications affect myelopoiesis** (or production of blood/immune cells) and **destroy the integrity of the gastrointestinal mucosa**, allowing microbe translocation. **Fever is often the earliest, and sometimes only**, manifestation of an infection in these patients due to the muted inflammatory response. Many patients with cough and pneumonia will not show an infiltrate on chest Xray, which depends on the body's neutrophil response to infection. The Infectious Diseases Society of America defines a neutropenic fever as a **single oral temperature greater than 38.3°C or temperature >38.0°C for one hour. Notice this is an oral temperature**, but if the patient has mucositis, then use tympanic membrane or axillary thermometry. Classically, rectal temperatures are avoided due to risk of local mucosal trauma and bleeding. **Neutropenia requires an absolute neutrophil count (ANC) of < 1500 cells/microL, with severe defined as an ANC less than 500 cells/microL or an expected drop to < 500 over 48 hours**. How is this calculated?

ANC = WBC count X ((PMN/100) + (Bands/100))

High-risk patients are those presenting with shock, ANC levels < 500, ANC levels that are low for > 7 days, or other organ dysfunction (liver/kidney). The **Multinational Association for Supportive Care in Cancer (MASCC) risk index** is a validated tool often used to calculate the risk of medical complications in neutropenic patients, with those **above 21 points at low risk (often quoted as patients worthy of discharge and home treatment) and those below 20 points at high risk**. To be considered low risk, the patient must have no hypotension, no COPD, age less than 60 years, no dehydration, have a solid tumor or hematologic malignancy, and minimal symptoms. Most importantly, talk to your oncologist about disposition and treatment of these patients early!

Surprisingly only 20 to 30% of fevers in neutropenic patients are due to infection. Bacteria are the most common infectious cause, and the species is usually part of the endogenous flora (up to 80%)! For bacterial pathogens, up to the mid-1980s the most common bacilli were gram-negative, but after that period, **gram-positive** bacteria became most common (60% of cases). Why is this? Increasing use of long-term central venous catheters, prophylactic and empiric antibiotics targeting *Pseudomonas*, and newer chemotherapeutic regimens are all causes of this transition. However, **gram-negative infections are more serious**, and with more resistant strains, there has been a slight shift back towards gram-negative infections. ***S. epidermidis*** is the most common gram-positive cause. Fungal pathogens are

more common in high-risk patients with prolonged antibiotic use and increasing number of treatment cycles. Most viral pathogens affect those high-risk patients and are due to reactivation (70%), rather than primary infection.

Management of these patients revolves around **early recognition of neutropenic fever**. First, obtain a quick set of vital signs with an accurate temperature, IV access, and labs including CBC and blood cultures with lactate. Chest Xray, urinalysis, renal function panel, liver function panel, and ECG are also recommended. Then complete a thorough exam including mucous membranes/HEENT, skin, lungs, heart, and perianal region (though no digital rectal exam)! Make sure to ask when their last dose of treatment was, as the ANC reaches its nadir of <500 at 12-14 days after day one of chemotherapy. If criteria for sepsis are met, then the clock starts! **Start your resuscitation with fluids, with IV antibiotics right after blood cultures are obtained.** Guidelines quote **60 minutes** as the timeframe within which patients should be given bug juice after recognition. If antibiotics are delayed, mortality rates can reach **70%**! **Each hour delay of antibiotics in those with septic shock increases mortality by 8%**![14] One United Kingdom audit demonstrated that only 18-26% of patients receive antibiotics within one hour. **Remember, these patients are tricky in that often no clinical signs will be apparent due to the muted immune response**, so once you have the ANC count with fever, start your treatment and talk with oncology! If suspicious before the ANC comes back, then start resuscitation and antibiotics as soon as you can. Infections in these patients can progress rapidly, leading to hypotension, shock, and death.

High risk patients (MASCC less than 20):
Empiric treatment within sixty minutes is aimed at treating the most likely and virulent pathogens. Broad-spectrum coverage includes gram-positive and negative bacteria. IDSA guidelines state those high-risk patients should start with **cefepime 2g, meropenem 1g, or zosyn 4.5g**. Ceftazidime 2g monotherapy has increasing resistance among gram-negative bacteria and does not adequately cover gram-positive bacteria. **Vancomycin** should only be added in the setting of the following: skin/soft tissue/central line infections, pneumonia, mucositis, or hemodynamic shock. If necrotizing mucositis, intraabdominal/pelvic infection, sinusitis, or perirectal cellulitis is present, then add anaerobic coverage. **Monotherapy against *Pseudomonas,* as opposed to dual coverage, has equivalent outcomes with less adverse events**! If penicillin allergic, use ciprofloxacin plus clindamycin or aztreonam plus vancomycin. An empiric antifungal agent should be added if fungal infection is suspected, after 4-7 days in high-risk patients with no change in temperature, and if reassessment/clinical studies have not demonstrated a cause of infection.

For central lines, there is a great deal of controversy surrounding the removal of these lines if they are suspected as the source. There is a grade 1B recommendation for removal of the central line for *S. aureus, P. aeruginosa,* or *Candida*. A pocket infection or deep infection along the central line track or port is also cause for removal. First, talk with your oncologist. They may want to keep the line and use it for antibiotics!

Low risk patients (MASCC greater than 20):
Success rates in outpatient treatment are actually around 80% in these patients, with 20% needing readmission. Those at risk for failing outpatient treatment includes age > 70 years, poor performance status at home, severe mucositis, and neutropenia less than 100. If you are sending home one of these patients, please s**peak with their oncologist and obtain follow up** (next day would be nice). Teuffel found that **inpatient versus outpatient treatment had no difference in efficacy**. What regimen is used for outpatient treatment? **Ciprofloxacin plus augmentin** is classic, with ciprofloxacin and clindamycin another option for penicillin-allergic patients.