CLINICAL COMMENTARY

Oncologic Emergency Essentials for Non-Oncology Physicians

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Busy primary care physicians are bound to see oncologic emergencies. Non-oncologists must promptly recognize these emergencies and start the proper basic interventions as they seek consultation. This clinical commentary will review the crucial aspects of common oncologic emergencies and provide essential management suggestions. The oncologic emergencies are categorized as metabolic, structural, or hematologic.

Metabolic Oncologic Emergencies

1. **Hypercalcemia of malignancy** is a common (10-30%) complication and may be a diagnostic dilemma due to non-specific presenting symptoms. Nausea, constipation, weakness, vomiting, and declining performance status are common clinical manifestations. Clinicians may attribute these symptoms to the malignancy and/or the ongoing treatments.

    a. *Diagnosis:* Obtain serum calcium level with albumin or preferably ionized calcium levels. Additional tests such as parathyroid hormone-related peptide, PTH, or serum Vitamin D levels may be academically useful but are not immediately applicable in emergencies. Serum phosphorous is important because concurrent hypophosphatemia may be clinically detrimental.

    b. *Treatment:* Treatment is generally aggressive hydration with saline followed by forced diuresis. Careful repletion of the phosphorous is important and intravenous bisphosphonates are often used immediately upon diagnosis. While these agents are excellent in the long-term management of the hypercalcemia as they reduce skeletal events, their role in the acute setting is limited. Additionally, patients presenting with renal failure have increased risk for added renal toxicities. Steroids, calcitonin, or gallium nitrate are marginally useful in selected cases. Intravenous bisphosphonates are best given once the acute complications of the hypercalcemia have resolved.

2. **Tumor lysis syndrome** is usually associated with acute cancer therapy, so the oncologist is generally actively involved. However in rapidly progressive cancers such as high-grade lymphomas, non-oncologists may need to initially manage this complication. Unfortunately, the diagnosis may be delayed in newly diagnosed patients as the clinical clues are vague and nonspecific.

    a. *Diagnosis:* Obtain a comprehensive metabolic panel, phosphate, and uric acid levels at diagnosis. Severe cases may have DIC, which may be missed as DIC panels are rarely ordered.

    b. *Treatment:* IV hydration is the mainstay of therapy. Involvement of primary care physicians may help avoid common iatrogenic complications such as fluid overload. This is especially important if renal injury is present at diagnosis. Routine alkalization of the urine should be discouraged due to risk of calcium phosphate deposition. Alkalization may be helpful with metabolic acidosis. Hyperuricemia is often controlled with allopurinol and urate-oxidase (rasburicase) infusions. The urate-oxidase therapy is particularly useful in the setting of renal failure with extremely high uric acid levels. Rasburicase is especially useful when very rapid control is desired as it lowers the uric acid levels within 4 hours of administration. Consider nephrology consultation as management of the electrolytes could be challenging, and there may be need for temporary hemodialysis.

Structural Oncologic Emergencies

1. **Epidural spinal cord compression** is common and often present at cancer diagnosis. However, the diagnosis is often delayed by weeks or months as the initial symptoms may be minimal with occult neurologic manifestations. Primary care physicians may address back pain symptomatically especially if malignancy is not in their initial differential. The diagnosis may also be delayed as patients may not seek timely medical care. Eventually, most patients develop motor or sensory findings, ataxia, or possibly bowel or bladder incontinence. A thorough history and physical examination may reveal clues, including pain worse with lying down and/or vertebral body tenderness with percussion. This is especially important in the high-risk population, including smokers, the elderly, or those with history of cancer. An early and accurate diagnosis of cord compression may prevent irreversible neurologic complications.

MRI of the spinal column is the most sensitive diagnostic test. Prompt treatment should be initiated with dexamethasone followed by definitive therapy with radiation and/or surgical decompression.

2. **Superior vena cava (SVC) syndrome** is a subacute or acute impediment of the normal blood flow to the right atrium. This results in retrograde flow to the head and neck regions. The retrograde flow may clinically translate into discoloration (cyanosis) and swelling of the neck, upper extremities, and face (plethora). Patients commonly describe a sensation of fullness, headaches, and dyspnea. Cancer patients presenting with SVC syndrome have poor prognosis. The SVC diagnosis is often delayed as the clinical progression may be gradual and both the symptoms and the chest radiographic findings may be nonspecific.

   Chest CT is usually diagnostic. Recommended treatment is high-dose steroids (to allow for collateral venous flow) and diuretics. These interventions are excellent temporizing methods allowing for a prompt histologic diagnosis. Thereafter, treatment specific to the biopsy are initiated. The treatments may include chemotherapy, radiation, or a combination.

3. **Malignancy associated pericardial effusion** may be present in about 10% of newly diagnosed malignancies. The main neoplasm responsible for this complication is lung cancer. The diagnosis is difficult and may be missed in patients with an established malignancy. The common symptoms are non-specific palpitations, dyspnea, fatigue, orthopnea, and dizziness and may be attributed to the underlying malignancy. Prompt diagnosis of a pericardial effusion is frequently made when cancer is not in the differential. This paradox may result from referral bias: symptomatic patients without known malignancy are referred to the cardiologist for evaluation. True oncologic emergency occurs only with acute or possibly a subacute cardiac tamponade. Clinical clues include hypotension, increased heart rate, elevated jugular venous pressures, muffled heart sounds, and pulsus paradoxus greater than 10 mmHg change in systolic blood pressure on inspiration. Unfortunately, clinicians may not have familiarity with this physical examination test. Therefore, the diagnosis is frequently determined by echocardiography.

   Treatment involves removal of the pericardial effusion via subxiphoid pericardiocentesis. This immediately restores the hemodynamic parameters. Patients are usually offered a pericardial window and are initiated on individualized oncologic care.

Hematologic Complications of Malignancy

1. **Hyperviscosity syndrome** is the most elusive of all oncologic emergencies. It is most commonly associated with hematologic malignancies such as Waldenstrom's macroglobulinemia. The diagnosis is almost invariably delayed until the patient is seen by the oncologist. Patients have nonspecific symptoms such as epistaxis, headaches, blurred vision, and confusion. They may be anemic and receive blood transfusions with disastrous consequences.

   a. *Diagnosis* is generally established serum viscosity levels. The literature promotes the merits of retinal exams to identify "sausage-like" hemorrhagic changes; however, only the most astute physicians are able to diagnose hyperviscosity by this rare physical finding. As the serum viscosity levels are often not readily available, the diagnosis is rather challenging.

   b. *Treatment* involves immediate plasmapheresis. This is usually followed by disease directed interventions. However, the therapeutic interventions are invariably delayed pending oncology evaluation. Most importantly, blood transfusions may be ordered as patients are often anemic. Blood transfusions should initially be avoided since they may results in further elevation of the serum viscosity. Indiscriminate blood transfusions may be associated with adverse cardiovascular complications.

2. **Febrile neutropenia** is often easily diagnosed but can be very challenging to manage. Non-oncologists should be familiar with the treatment of the neutropenic fevers as this common condition is associated with high mortality rates. The prompt recognition of neutropenic fevers and initiation of antibiotic therapy are crucial. Clinicians should be comfortable with the definition of this entity, the timing of growth factors, and the proper antibiotic management. Delays (each hour delay increases the mortality by 8%) in antibiotic delivery to the patient are common and mostly relate to logistical issues (patients waiting to be admitted or pharmacy preparing the antibiotics, etc.). It is important to note that temperature measurements might be unreliable and that rectal thermometry should be avoided.

   a. *Diagnosis:* The diagnosis requires neutropenia (ANC < 500 micg/L) and fevers (temp > 101^{o}F/38.3^{o}C or more). Physicians should be aware that persistent temperatures of > 100.4^{o}F/38.0^{o}C for more than one hour also qualify for the diagnosis. The blood cultures commonly show either gram positive or gram negative organisms. Interestingly, the blood cultures are noncontributory in a sizable portion of the cases.

   b. *Treatment:* It is recommended that the first dose of the empiric antibiotic be given within the first hour of the diagnosis, a goal

rarely achieved in the hospitals. The treating physician must take personal charge to ensure that the first dose of the antibiotic is given within one hour of patients' diagnosis. In general, the patients are classified as either high or low risk, (< 7 day of projected neutropenia and no medical comorbidities or end organ dysfunction). The low-risk patients do not necessarily require hospitalization, but each case must be individualized. These patients are usually treated with a combination of a fluoroquinolone and amoxicillin/clavulanate. Penicillin allergic patients should receive clindamycin. The treatment of high-risk patients requires hospitalization for parenteral antibiotics. The mainstay of therapy includes antipseudomonal beta-lactam agents such as ceftazidime, cefepime, or meropenem. The immediate use of concurrent vancomycin is discouraged and should be reserved for suspected skin infections, catheter-related infections, or when their hemodynamic compromise. If no improvement is noted within 3 days of empiric antibiotics, then antifungals are added.

- Duration of therapy: The antibiotics are continued until the neutropenia has resolved or the proper length of therapy for a specific organism is completed (despite resolution of the neutropenia).

This summarizes an approach to oncologic emergencies for non-oncology physicians. Prompt treatment can be initiated without waiting for oncology consultation in many instances.

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