

Treatment of Oncologic Emergencies

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Most oncologic emergencies can be classified as metabolic, hematologic, structural, or side effects from chemotherapy agents. Tumor lysis syndrome is a metabolic emergency that presents as severe electrolyte abnormalities. The condition is treated with allopurinol or urate oxidase to lower uric acid levels. Hypercalcemia of malignancy is treated with aggressive rehydration, furosemide, and intravenous bisphosphonates. Syndrome of inappropriate antidiuretic hormone should be suspected if a patient with cancer presents with normovolemic hyponatremia. This metabolic condition usually is treated with fluid restriction and furosemide. Febrile neutropenia is a hematologic emergency that usually requires inpatient therapy with broad-spectrum antibiotics, although outpatient therapy may be appropriate for low-risk patients. Hyperviscosity syndrome usually is associated with Waldenström's macroglobulinemia, which is treated with plasmapheresis and chemotherapy. Structural oncologic emergencies are caused by direct compression of nontumor structures or by metastatic disease. Superior vena cava syndrome presents as neck or facial swelling and development of collateral venous circulation. Treatment options include chemotherapy, radiation, and intravenous stenting. Epidural spinal cord compression can be treated with dexamethasone, radiation, or surgery. Malignant pericardial effusion, which often is undiagnosed in cancer patients, can be treated with pericardiocentesis or a pericardial window procedure. (*Am Fam Physician* 2006;74:1873-80. Copyright © 2006 American Academy of Family Physicians.)

Family physicians are more likely to encounter emergencies related to the treatment or presence of cancer because of increases in outpatient cancer treatments and improved survival rates. Physicians should be familiar with these oncologic emergencies because treatment often is necessary before consultation with a subspecialist.¹ Some oncologic emergencies are insidious and take months to develop, whereas others manifest over hours, causing devastating outcomes such as paralysis and death.² In many patients, cancer is not diagnosed until a related condition emerges. Various clinical syndromes often are evident before an emergency occurs; therefore, a patient-focused approach that includes education and cancer-specific monitoring is needed.³ Most oncologic emergencies (*Table 1*^{1,2,4-12}) can be categorized as metabolic, hematologic, structural, or side effects from chemotherapy agents.⁴

Metabolic

Metabolic emergencies include tumor lysis syndrome, hypercalcemia of malignancy, and

syndrome of inappropriate antidiuretic hormone (SIADH).

TUMOR LYSIS SYNDROME

Tumor lysis syndrome is acute cell lysis caused by chemotherapy and radiation therapy. The release of intracellular products (e.g., uric acid, phosphates, calcium, potassium) overwhelms the body's homeostasis mechanisms.⁵ Tumor lysis syndrome is more common with hematologic malignancies or cancers with rapidly growing tumors, particularly acute leukemias and high-grade lymphomas. Tumor lysis syndrome usually presents within one to five days of chemotherapy or radiation.⁶

Patients with tumor lysis syndrome commonly present with azotemia, acidosis, hyperphosphatemia, hyperkalemia, hypocalcemia, and acute renal failure.¹³ Treatment includes inpatient monitoring, vigorous fluid resuscitation, allopurinol (Zyloprim) or urate oxidase (uricase) therapy to lower uric acid levels, urinary alkalization, and hemodialysis.¹

SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
Intravenous bisphosphonates are recommended for treating hypercalcemia of malignancy to improve quality of life and to reduce skeletal complications, bone pain, and the need for analgesic medications.	B	14, 19, 20
Outpatient treatment should be considered for patients with febrile neutropenia who are older than 16 years and who have a low risk of infection.	B	27
Routine use of antivirals, granulocyte transfusions, and colony-stimulating factors is not recommended for patients with febrile neutropenia.	C	23
Patients with epidural spinal cord compression should receive prompt treatment to improve outcomes.	C	2, 31
Patients with cancer who have new-onset back pain should be evaluated for epidural spinal cord compression.	C	32

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1821 or <http://www.aafp.org/afpsort.xml>.

HYPERCALCEMIA OF MALIGNANCY

Hypercalcemia of malignancy occurs in 20 to 30 percent of patients with cancer.¹⁴ This condition most commonly is associated with multiple myeloma and cancers of the lung, breast, and kidney. Mechanisms that are thought to be important in the development of hypercalcemia of malignancy include bone-resorbing cytokines; parathyroid hormone-related peptide, secreted by the tumor, that binds to parathyroid hormone receptors; tumor-mediated calcitriol production; and, occasionally, ectopic parathyroid hormone secretion.^{7,14}

Symptoms of this condition include nausea, vomiting, constipation, progressive decline in mental function, renal failure, and coma.^{14,15} Occasionally, serum calcium levels are 14 mg per dL (3.50 mmol per L) or more.¹⁶ Hypercalcemia of malignancy is associated with a poor prognosis, with more than 50 percent of patients dying within 30 days of diagnosis.¹⁴ However, treating hypercalcemia of malignancy allows time for treatment of the underlying tumor.¹⁴

Treatment of hypercalcemia of malignancy (Table 2^{14,17}) includes aggressive rehydration followed by diuresis with furosemide (Lasix). Serum phosphorus should be monitored because hypophosphatemia is common and can worsen the condition.¹⁴

Phosphorus should be replaced orally or via a nasogastric tube.^{8,14} Intravenous bisphosphonate therapy can inhibit osteoclastic bone resorption. Although pamidronate (Aredia) and zoledronic acid (Zometa) can effectively manage hypercalcemia of malignancy, a pooled analysis of two clinical trials showed that the more potent zoledronic acid is superior.¹⁸ Zoledronic acid and pamidronate have been shown to improve quality of life in patients with metastatic bone disease by reducing skeletal complications, bone pain, and the need for analgesic medications.^{19,20} Adjunctive treatments include dialysis and glucocorticoid, calcitonin (Miacalcin), plicamycin (Mithracin), and gallium nitrate (Ganite) therapies.¹⁴

SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE

When a patient with cancer presents with normovolemic hyponatremia, SIADH should be suspected. A bronchogenic carcinoma often is the ectopic source of antidiuretic hormone production, although certain chemotherapy agents can cause SIADH.¹ Patients may present with anorexia nervosa, nausea, myalgia, headaches, and severe neurologic symptoms (e.g., seizures, coma). Laboratory testing may reveal hyponatremia (i.e., serum sodium level less than 135 mEq per L [135 mmol

TABLE 1
Summary of Oncologic Emergencies

<i>Emergency</i>	<i>Associated cancer or cause</i>	<i>Signs and symptoms</i>
Metabolic		
Hypercalcemia of malignancy	Lung, breast, and kidney cancers; multiple myeloma	Fatigue, anorexia, nausea, vomiting, constipation, mental decline, renal failure, coma, myalgia, headache, altered sensorium
Syndrome of inappropriate antidiuretic hormone	Bronchogenic carcinoma	Anorexia, nausea, vomiting, constipation, muscle weakness, myalgia, polyuria, polydipsia, severe neurologic symptoms (e.g., seizures, coma)
Tumor lysis syndrome	Hematologic malignancies; cancers with rapidly growing tumors, particularly acute leukemias and high-grade lymphoma	Azotemia, acidosis, hyperphosphatemia, hyperkalemia, acute renal failure, hypocalcemia
Hematologic		
Febrile neutropenia	Chemotherapy-associated bacterial or fungal infections	Temperature greater than 101°F (38.3°C), absolute neutrophil count less than 500 per mm ³ (0.5×10^9 per L)
Hyperviscosity syndrome	Waldenström's macroglobulinemia, multiple myeloma, leukemia	Spontaneous bleeding, "sausage-like" hemorrhagic retinal veins, neurologic defects, serum viscosity levels greater than 5 cP
Structural		
Epidural spinal cord compression	Breast, lung, renal, and prostate cancers and myeloma	New back pain that worsens when lying down, late paraplegia, late incontinence, and loss of sensory function
Malignant pericardial effusion	Metastatic lung and breast cancer, melanoma, leukemia, lymphoma, chemotherapy to the chest wall	Dyspnea, fatigue, distended neck veins, distant heart sounds, tachycardia, orthopnea, narrow pulse pressure, pulsus paradoxus, water-bottle heart
Superior vena cava syndrome	Lung cancer, metastatic mediastinal tumors, lymphoma, indwelling venous catheters	Cough; dyspnea; dysphagia; head, neck, or upper extremity swelling or discoloration; development of collateral venous circulation
Side effects from treatment agents		
Diarrhea	Chemotherapy	Dehydration, poor skin turgor, dry mucous membranes, weight loss
Extravasations	Current chemotherapy infusion	Pain and erythema at infusion site, swelling, necrosis, contractures
Obstipation	Narcotic medications, chemotherapy (specifically neurotoxic agents)	Abdominal pain, constipation, hard stools every three to five days

Information from references 1, 2, and 4 through 12.

per L]), decreased serum osmolarity (less than 280 mOsm per L [280 mmol per L]), and concentrated urine (100 mOsm per L or more). There are few physical examination findings associated with SIADH, although papilledema and pathologic reflexes occasionally are present.⁴

Treatment of the underlying tumor is the cornerstone of therapy. Acute care includes fluid restriction (limit of 500 to 1,000 mL per day) and furosemide therapy. Slow correction of serum sodium levels is necessary to avoid central pontine myelinolysis. Hypertonic saline should be considered for patients with severe neurologic symptoms.¹

Demeclocycline (Declomycin) is recommended for persistent hyponatremia or for outpatient treatment of minor symptoms.^{1,21}

Hematologic

Hematologic emergencies include febrile neutropenia and hyperviscosity syndrome.

FEBRILE NEUTROPENIA

Febrile neutropenia is one of the most common complications related to cancer treatment, particularly chemotherapy. The condition contributes to 50 percent of deaths associated with leukemia, lymphomas, and solid tumors.²² Bacterial infections are common in patients

TABLE 2
Treatment of Hypercalcemia of Malignancy

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TABLE 3
Clinical Decision Rule for Determining Infection Risk in Patients with Febrile Neutropenia

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with febrile neutropenia, but fungal sources are increasingly prevalent.²³ Symptoms include a temperature of 101°F (38.3°C) or more and an absolute neutrophil count (ANC) less than 500 per mm³ (0.5 x 10⁹ per L).²

A patient usually is considered to have low risk if he or she has a cancer that is under good control or is in remission and has no evidence of hepatic insufficiency, hypotension, or comorbid conditions.²⁴⁻²⁶ However, patients with cancer presenting with fever soon after chemotherapy should receive inpatient treatment with empiric antibiotics until the ANC is more than 500 per mm³ for 72 hours.²³ Initial laboratory evaluation includes targeted cultures; complete blood count; and serum creatinine, blood urea nitrogen, and transaminase measurements. If respiratory symptoms are present, chest radiography is recommended, although it may not detect an infiltrate until the patient's ANC has improved enough to enable an inflammatory response.²³ Outpatient treatment of low-risk patients who are older than 16 years has been validated in several clinical trials.²⁷

Antibiotic treatment for febrile neutropenia depends on the patient's risk of life-threatening infection. A prospective, multinational study of 1,139 patients with febrile neutropenia validated a scoring system (Table 3²³) to classify patients as high or low risk.²⁷ Generally, multi-drug regimens are used when gram-positive and gram-negative organisms are suspected.²³ Empiric vancomycin therapy is added in hospitals where methicillin-resistant, gram-positive organisms are common or if specific clinical findings are present.²³ Antifungals are recommended if there is no improvement within the first three days of treatment. Routine use of antivirals, granulocyte transfusions, and colony-stimulating factors is not recommended.²³ Figure 1 is an algorithm for the treatment of febrile neutropenia.^{22,23}

HYPERVISCOSITY SYNDROME

Hyperviscosity syndrome is most common in patients with Waldenström's macroglobulinemia (although most patients with Waldenström's macroglobulinemia do not experience hyperviscosity syndrome),

Treatment of Patients with Febrile Neutropenia

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Figure 1.

leukemia, or multiple myeloma.^{9,28} Elevated levels of circulating serum immunoglobulins coat the cells, causing increased blood viscosity, sludging of blood, and hypoperfusion.²⁸

Signs and symptoms of hyperviscosity syndrome include spontaneous bleeding, neurologic defects (e.g., peripheral neuropathies), and vision changes (“sausage-like” hemorrhagic retinal veins are pathognomic). A serum viscosity of more than 5 cP suggests hyperviscosity syndrome.²⁸ Treatment includes plasmapheresis followed by targeted chemotherapy. Occasionally, repeat plasmapheresis is needed to control refractory episodes.⁴

Structural

Structural emergencies include superior vena cava syndrome, epidural spinal cord compression, and malignant pericardial effusion.

SUPERIOR VENA CAVA SYNDROME

This syndrome is caused by the gradual compression of the superior vena cava, leading to edema and retrograde flow.¹⁰ Lung cancer is the most common malignant cause, although lymphoma, metastatic mediastinal tumors, and indwelling catheters also can cause superior vena cava syndrome. Symptoms may include cough; dyspnea; dysphagia; and swelling or discoloration of the neck, face, or upper extremities.²⁹ Often, collateral venous circulation causes distension of the superficial veins in the chest wall.^{5,11}

Although superior vena cava syndrome is a clinical diagnosis, plain radiography, computed tomography, and venography are used for confirmation. Recommended treatments include chemotherapy and radiation to reduce the tumor that is causing the obstruction. However, treatment with

intravenous stents is becoming increasingly common.³⁰ Tissue diagnosis (i.e., sputum cytology, thoracentesis, bronchoscopy, or needle aspiration) often is necessary to direct treatment decisions. Adjunctive therapies include diuretics, corticosteroids, thrombolytics, anticoagulation, and elevating the head of the patient's bed.⁵ Patients with superior vena cava syndrome usually have advanced disease, and less than 10 percent survive more than 30 months after treatment.¹⁰

EPIDURAL SPINAL CORD COMPRESSION

Epidural spinal cord compression is caused by a tumor compressing the dural sac. This can cause permanent neurologic impairment even if treatment is delayed for only a few hours. Epidural spinal cord compression is associated with renal, prostate, and, most commonly, breast and lung cancers. The thoracic spine is most often affected, accounting for 70 percent of patients with the condition.¹² Patients with epidural spinal cord compression should receive prompt treatment to improve outcomes.^{2,31} Approximately 90 percent of patients who are ambulatory at the time of diagnosis do not lose this ability posttreatment.^{2,32}

New back pain in patients with cancer suggests epidural spinal cord compression. Pain that worsens when the patient is lying down or with percussion of vertebral bodies is characteristic of this condition.³² Late neurologic signs such as incontinence and loss of sensory function are associated with permanent paraplegia.² Plain radiographs usually show lesions in patients with solid tumors.^{2,33} Magnetic resonance imaging (MRI) has surpassed myelography as the imaging study of choice.^{2,32} If possible, the spinal column should be imaged with non-contrast MRI.^{2,32} *Figure 2* is an MRI scan showing spinal cord compression.³² If neurologic symptoms are present, the patient should receive a dexamethasone (Cortastat) bolus (10 mg intravenously) followed by 4-mg doses every six hours. This treatment should not be delayed while awaiting diagnostic study results.³⁴ Use of high-dose dexamethasone (up to 100 mg) is controversial;



Figure 2. Epidural spinal cord compression on magnetic resonance imaging (MRI). Sagittal T1-weighted MRI through the thoracic spine demonstrates lymphoma (arrows) involving the T5 and T12 vertebral bodies extending posteriorly into the spinal canal and compressing the spinal cord (c) at both levels. T8 indicates the T8 vertebral body, and A indicates anterior.

Adapted with permission from Quint DJ. Indications for emergent MRI of the central nervous system. JAMA 2000;283:854.

clinical trials have shown that it has unclear benefits and significantly more serious side effects at higher doses.^{33,35,36} Most patients with epidural spinal cord compression need radiation treatment (up to 3,000 Gy) or surgery.^{1,2,4} Asymptomatic patients should be considered for immediate radiation therapy, and patients with progressive symptoms despite radiation therapy should be considered for surgical intervention.^{31,33}

MALIGNANT PERICARDIAL EFFUSIONS

Malignant pericardial effusions often are undiagnosed in patients with cancer, although as many as 10 to 15 percent of patients with cancer will have some degree

of pericardial effusion at autopsy,¹ and some patients with otherwise treatable cancer succumb to undiagnosed pericardial effusion.⁴ Most effusions develop from metastatic lung or breast cancer. Other causes include malignant melanoma, leukemia, lymphoma, radiation therapy to the chest wall, and chemotherapy agents.^{4,37}

Clinical symptoms include dyspnea, orthopnea, fatigue, heart palpitations, and dizziness. Pulsus paradoxus, tachycardia, distended neck veins, narrow pulse pressure, and distant heart sounds may be present.^{5,29} Echocardiography is the preferred diagnostic study. Acute symptoms are treated with pericardiocentesis or a pericardial window procedure.^{4,37} Fluid samples should be analyzed with cytology. Chemotherapy, radiation, or sclerosis therapy can prevent fluid reaccumulation.⁵

Side Effects of Chemotherapy Agents

There are a multitude of side effects and allergic reactions associated with the use of chemotherapy agents. Many of these adverse reactions initially are managed by family physicians.

EXTRAVASATION INJURIES

Many chemotherapy agents (e.g., anthracyclines, vinca alkaloids) are irritants or vesicants.⁵ Leakage of these agents onto the skin during infusion therapy can cause extravasation injuries such as severe scarring or contractures if the injury is near joints.³⁸ Clinical signs of extravasation injuries include erythema, swelling, and necrosis at the infusion site, usually occurring within hours of chemotherapy. Prompt diagnosis is crucial to avoid extensive skin damage.

Treatment includes cessation of infusion treatments, application of heat or ice, avoidance of site compression, and initiation of antidotes.^{4,5} Patients presenting with erythema should receive rapid referral to an oncologist or plastic surgeon, because extensive debridement occasionally is needed.⁴

GASTROINTESTINAL COMPLAINTS

Dehydration is a serious side effect of cancer treatment that often is missed. Up to 30 percent of patients with cancer who have

delirium are dehydrated, and as many as 50 percent of patients treated for colon cancer develop dehydration from vomiting, diarrhea, and mucositis.^{3,5} Treatment includes fluid resuscitation and initiation of antiemetics and antidiarrheals.

Obstipation, characterized by hard stools every three to five days and abdominal pain, also is commonly associated with narcotic medications and occasionally with neurotoxic chemotherapy agents. If severe, an oncologist should be consulted to consider a change of treatment.⁵

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the U.S. Army or the U.S. Army Service at large.

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