Emergencies in Hematology and Oncology

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CME Activity

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Statement of Need: General internists and primary care physicians must maintain an extensive knowledge base on a wide variety of topics covering all body systems as well as common and uncommon disorders. *Mayo Clinic Proceedings* aims to leverage the expertise of its authors to help physicians understand best practices in diagnosis and management of conditions encountered in the clinical setting.

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Learning Objectives: On completion of this article, you should be able to (1) recognize both common and uncommon hematologic and oncological emergencies in patients with cancer, (2) identify which patients need emergent or urgent initiation of therapy and admission to the hospital for an optimal outcome, and (3) promptly initiate the appropriate therapy for life-threatening complications of both the cancer itself and the therapy directed against the cancer.

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Abstract

The development of medical emergencies related to the underlying disease or as a result of complications of therapy are common in patients with hematologic or solid tumors. These oncological emergencies can occur as an initial presentation or in a patient with an established diagnosis and are encountered in all medical care settings, ranging from primary care to the emergency department and various subspecialty environments. Therefore, it is critically important that all physicians have a working knowledge of the potential oncological emergencies that may present in their practice and how to provide the most effective care without delay. This article reviews the most common oncological emergencies and provides practical guidance for initial management of these patients.

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Cancer is expected to be diagnosed in more than 1.6 million people in the United States in 2017. A small percentage of these patients will experience an emergent cancer-related complication at some point during the disease course. For some patients, an emergent complication is the first manifestation of the cancer.[1] Given the large number of patients with active cancer, many practicing physicians can expect to encounter patients with a cancer-related emergency. It is therefore imperative that practitioners, especially primary and emergency care physicians, are able to rapidly recognize and effectively manage patients with these complications. Emergencies in hematology

and oncology can be broadly classified as conditions resulting from the cancer itself and complications related to therapy directed against the malignant disease, although there can be some overlap between the 2 categories. The emergencies can also be classified according to organ systems, which is the approach taken in this review.

METABOLIC EMERGENCIES

Hypercalcemia of Malignancy

Hypercalcemia is common in patients with advanced cancer and has been reported in up to 30% of patients with cancer.[2] The incidence varies greatly among cancer types, and hypercalcemia is most commonly associated with multiple myeloma, non–small cell lung cancer (especially squamous cell cancer), renal cell carcinoma, breast cancer, non-Hodgkin lymphoma, and leukemia but can also be seen in multiple other malignant disorders.[3] The presence of hypercalcemia in a patient with cancer is an adverse prognostic factor predicting a shorter survival, but effective therapy, both for the hypercalcemia and the underlying cancer, may improve outcomes.[4-7]

Pathophysiology. The pathophysiology of hypercalcemia of malignancy can be divided into 3 major categories.[8] The first category, often called humoral hypercalcemia of malignancy, usually results from tumor production of parathyroid hormone–related peptide (PTHrP) and less commonly intact parathyroid hormone (PTH). It is the most common underlying cause of hypercalcemia of malignancy. The second category is hypercalcemia from bone destruction and dissolution (osteolysis) from extensive bone metastases. The third and least common category is excess production of vitamin D analogues by the malignant cells. Humoral hypercalcemia of malignancy accounts for up to 80% of hypercalcemia that occurs in patients with cancer and is the dominant cause in patients with solid tumors.[2,9] Structurally, PTHrP is closely related to PTH and exerts many of the functions of PTH itself. It binds to receptors on osteoblasts and stimulates their activity through receptor activator of nuclear factor κB ligand (RANKL) signaling. This process in turn stimulates the osteoclasts, increasing their activation and proliferation and subsequently releases calcium into the circulation.[8,10,11] The presence of elevated PTHrP in humoral hypercalcemia of malignancy portends poorer prognosis and decreased response to therapy with bisphosphonates.[12-14] Osteolysis as a cause of hypercalcemia is commonly seen in patients with breast cancer, lung cancer, and multiple myeloma. Several cytokines have been implicated in the pathogenesis of cancer-induced osteolysis, including tumor necrosis factor, macrophage inflammatory protein 1a, and lymphotoxin.[15,16] Local production of PTHrP may also result in osteolysis, which is in part mediated through the RANKL pathway.[17,18] Extrarenal production of 1,25-dihydroxyvitamin D (calcitriol) can occur in patients with both Hodgkin and non-Hodgkin lymphomas as well as nonmalignant granulomatous diseases such as sarcoidosis.[19,20] Very rarely, ectopic production of PTH by tumors causes hypercalcemia.[21] Hypercalcemia of malignancy can also be exacerbated by factors unrelated to the malignant disorder itself such as the intake of calcium, vitamin D, lithium, and thiazides. Thiazides are thought to reduce urinary calcium excretion as a result of increased passive calcium reabsorption at the proximal tubule and increased distal reabsorption at a thiazide sensitive site.

Clinical Presentation and Diagnosis. Hypercalcemia is caused by either primary hyperparathyroidism or malignant disease more than 90% of the time. Therefore, it is important to distinguish between these 2 entities early on. In hypercalcemia associated with cancer, there are frequently overt signs of malignant disease at presentation. Hypercalcemia can cause a multitude of nonspecific symptoms. Lethargy, confusion, anorexia, nausea, constipation, polyuria, and polydipsia are all common symptoms of hypercalcemia, and the severity may correlate with the degree of hypercalcemia and the rapidity of onset.[22,23] Severe hypercalcemia, especially of rapid onset, may cause cardiac dysrhythmias such as bradycardia, shortening of the QT interval, and even cardiac arrest.[24] The physical examination is generally not helpful in making the diagnosis but can reveal signs of volume depletion and impaired cognitive function as well as signs of the underlying cancer such as enlarged lymph nodes.

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