Cancer patients commonly present on an emergent basis, either due to sequelae of neoplasia itself or due to iatrogenic causes. Cancer can affect any organ system in the body, causing patients to present with a wide variety of emergencies: pathologic fracture from osteosarcoma, hemoabdomen from hemangiosarcoma, seizures from brain tumors, vomiting from tumors of the gastrointestinal tract, or respiratory distress from primary or metastatic pulmonary tumors, just to name a few examples. Often the primary care veterinarian or emergency veterinarian are the first to recognize symptoms that are suspicious for cancer, and are instrumental in recommending further diagnostics, treatments, or referral for their patients. Primary care and emergency veterinarians are also important partners in their patients’ cancer care team, especially in the management of treatment-related side effects. Many clients travel to an oncologist from a distance, and it may be more convenient or more beneficial to the patient to seek emergency care closer to home when necessary. While our goal is always to minimize treatment complications, knowledge of how to manage common side effects can help ensure the fastest recovery possible for our patients.

Cancer-Related Emergencies

Hypercalcemia of Malignancy:

Cancer is the most common cause of hypercalcemia in dogs, and hypercalcemia of malignancy is one of the most common paraneoplastic syndromes, particularly in dogs with lymphoma. Hypercalcemia of malignancy can also be seen in dogs with apocrine gland anal sac adenocarcinoma, thyroid carcinoma, and multiple myeloma, among other tumors. In cats, hypercalcemia of malignancy is most often associated with lymphoma, multiple myeloma, squamous cell carcinoma, and mammary adenocarcinoma. Primary hyperparathyroidism can also cause hypercalcemia in both species.

There are a variety of mechanisms of hypercalcemia of malignancy. A primary parathyroid tumor will release excess parathyroid hormone, and multiple lytic bone lesions can also cause an increase in calcium. In dogs, lymphoma and apocrine gland anal sac adenocarcinoma produce PTH-related peptide (PTH-rp), resulting in hypercalcemia.

Patients with hypercalcemia should be evaluated for any of the tumor types listed above, starting with physical exam (lymph node palpation, neck palpation, rectal exam, oral exam), and then complete minimum database (CBC, chemistry, urinalysis), thoracic radiographs, and abdominal ultrasound.
Hypercalcemia results in decreased sensitivity of the distal tubule to antidiuretic hormone (ADH), decreased renal blood flow, and decreased glomerular filtration rate (GFR). The renal epithelium then undergoes degeneration, necrosis, and calcification, leading to polyuria, polydipsia, and progressive dehydration. Excess calcium can also cause vomiting, anorexia, hypertension, bradycardia, weakness, depression, coma, or even death.

A serum calcium > 18 mg/dL is considered a medical emergency, and appropriate supportive care, including fluid diuresis, should be instituted as soon as possible. Treatment of the underlying neoplasia, such as initiation of chemotherapy for lymphoma or surgical removal of an anal sac tumor, can also result in resolution of hypercalcemia. While corticosteroids can decrease calcium levels, they should not be given until a definitive diagnosis is made, particularly in suspect cases of lymphoma. Steroids can preclude definitive diagnosis of lymphoma, and can also induce resistance to certain chemotherapy drugs. Severe cases of hypercalcemia that are refractory to other treatments may be treated with bisphosphonates, which inhibit bone resorption.

Hemoabdomen:

Hemoabdomen most commonly results from bleeding tumors of the spleen or liver, both highly vascular organs. Hemoretroperitoneum may result from bleeding tumors of the kidneys or other retroperitoneal structures. While reported percentages vary, approximately 70% of canine non-traumatic hemoabdomens are caused by neoplasia, primarily hemangiosarcoma, with other differentials including splenic hematoma, splenic torsion, hepatocellular carcinoma, and splenic lymphoma. Patients with visceral hemangiosarcoma often present with a history of acute weakness and collapse, although owners may also report episodes of transient weakness in the preceding days to weeks prior to presentation. These transient episodes are thought to represent microhemorrhages that were subsequently reabsorbed, allowing the patient to recover. Dogs often have pale mucous membranes, delayed capillary refill time, tachycardia, poor pulse quality, and a palpable fluid wave in the abdomen.

The diagnosis of hemoabdomen is typically made by diagnostic abdominocentesis, which yields serosanguineous effusion or frank blood. Usually this effusion does not clot. Frank blood will have the same PCV as the patient’s peripheral blood. Further work-up for dogs with hemoabdomen includes complete minimum database (CBC, chemistry, urinalysis), staging with thoracic radiographs and abdominal ultrasound, and coagulation profile, +/- echocardiogram to check for a right atrial mass. As most patients are also anemic, blood typing +/- cross-matching should be considered, especially prior to surgery. Electrocardiogram and blood pressure should also be monitored closely.

Following appropriate treatment for hypovolemic shock, along with correction of any coagulation abnormalities, surgery is the treatment of choice for dogs with hemoabdomen without obvious evidence of metastatic disease. A careful abdominal exploratory exam should be conducted at the time of surgery, in order to identify any
gross liver or omental lesions that were not visible on pre-operative imaging. Any suspicious lesions should be removed and submitted for biopsy. Post-operatively, patients should be placed on continuous ECG monitoring to watch for ventricular arrhythmias.

Due to the high risk of metastasis associated with hemangiosarcoma, post-operative chemotherapy is recommended, with the best outcomes associated with doxorubicin-based protocols. Continued treatment with oral metronomic-based protocols following completion of doxorubicin is being evaluated, as well as combination or single-agent treatment with I’m Yunity(R), a commercially-available Coriolus versicolor mushroom extract. The Chinese herbal supplement Yunnan Bai Yao is helpful to treat episodes of recurrent bleeding, and has also been shown to have activity against hemangiosarcoma cells in vitro. A new clinical trial is also available at Penn Vet evaluating an antibody therapy that is designed to inhibit vascular endothelial growth factor (VEGF), a growth factor that may contribute to growth and spread of hemangiosarcoma.

**Treatment-Related Emergencies**

**General Chemotherapy Side Effects:**

Chemotherapy drugs target rapidly-dividing cells, such as cancer cells, but in the process of this may also damage normal, rapidly-dividing cells in the body. These include the gastrointestinal mucosal cells and the bone marrow stem cells.

**Gastrointestinal**

Chemotherapy drugs can cause gastrointestinal side effects either by direct damage of the gastrointestinal mucosal cells, or indirectly through stimulation of the chemoreceptor trigger zone. Nausea and vomiting as a result of direct damage to the mucosal cells is more common, and usually occurs 2-5 days following a chemotherapy treatment. The timing of development of clinical signs reflects the turnover time of the rapidly-dividing mucosal cells. Chemotherapy drugs that commonly cause nausea via this mechanism include doxorubicin and vincristine. Vincristine also has a unique mechanism of causing nausea by induction of gastrointestinal ileus. While the exact mechanism of vincristine-related ileus is unknown, it is thought to be related to vincristine’s effects on the nervous system.

Chemotherapy drugs such as dacarbazine (DTIC), Cisplatin, and Streptozotocin, while used less commonly in practice, are all associated with development of acute nausea via stimulation of the chemoreceptor trigger zone in the vomiting center. These drugs are all given as infusions over several hours, and patients should be prophylactically treated with antiemetics throughout the infusion.

Our chemotherapy patients are typically prescribed prophylactic maropitant or ondansetron to help treat or prevent nausea, along with metronidazole to have on hand in case diarrhea develops. Patients with severe nausea or loss of appetite may need to
be hospitalized for intravenous fluids and injectable antiemetics. Metoclopramide can be particularly useful in treating patients with vincristine-related ileus.

**Bone Marrow Suppression**

Chemotherapy drugs may cause damage to bone marrow stem cells, leading to bone marrow suppression. Neutrophils are most susceptible because they are the cells with the shortest circulating lifespan, about 10 hours. The body has about a 5-day reserve of neutrophils, so chemotherapy nadirs typically occur around 7 days after treatment. Platelets circulate for about 5-9 days, so chemotherapy-related thrombocytopenia typically occurs later after treatment. For example, we often see thrombocytopenia two to three weeks following treatment with Carboplatin or Mitoxantrone. Red blood cells circulate the longest, for about 4 months, and therefore anemia is rarely seen as a complication of chemotherapy.

Thankfully, despite the frequency of neutropenia, sepsis occurs in less than 5% of patients. This is partly due to our careful monitoring with regular CBCs at defined intervals following treatment with a particular chemotherapy drug. Penn has also started to routinely prescribe prophylactic antibiotics to patients following administration of chemotherapy drugs which are most likely to result in neutropenia; this has been shown in two studies to reduce the risk of sepsis.

In cases where prophylactic antibiotics are not prescribed, antibiotic therapy should be initiated if a routine post-treatment CBC shows a neutrophil count less than 1000, or if patients are febrile or clinically ill. Since there is an increased risk of exposure to pathogens in the hospital, we typically only recommend hospitalization for patients who are febrile or clinically ill, particularly if they are showing signs of sepsis. These patients should have an IV catheter placed using sterile technique, and should be handled with reverse isolation practices. In addition to fluids, they may need intravenous antibiotics and other supportive care. Vomiting patients are at increased risk for aspiration pneumonia, and patients with severe gastroenteritis are at risk for bacterial translocation across the gut; both conditions can potentially lead to sepsis.

Neutrophils usually recover on their own within 5-7 days of the nadir. For patients who are severely ill or septic, and whose neutrophils are not adequately rebounding on their own, treatment with Neupogen (granulocyte colony stimulating factor) can be considered.

**Acute Tumor Lysis Syndrome:**

Acute tumor lysis syndrome (ATLS) most commonly occurs in patients with high grade, lymphoblastic lymphoma or leukemia. It is caused by rapid lysis of tumor cells following initiation of treatment, either with chemotherapy or radiation therapy. Lymphoblasts contain increased concentrations of phosphorus, potassium, and uric acid. As a result, rapid death of lymphoblasts will lead to characteristic biochemical changes: hyperphosphatemia, hyperkalemia, hypocalcemia, and metabolic acidosis, with or
without azotemia. ATLS is overall rare in veterinary patients, reported in a handful of case reports in dogs and in one case report in a cat. Patients who are volume-depleted, have underlying renal disease, or who have a high tumor burden (Stage IV or Stage V lymphoma) with a rapid response to treatment are at greatest risk for ATLS. Clinical signs usually manifest within 24-48 hours of treatment and include depression, severe lethargy, vomiting, diarrhea, and in severe cases cardiovascular collapse and shock. Early recognition of clinical signs is essential for successful treatment, and it is important that owners recognize the difference in the acute timing of these signs, versus the more delayed timeframe in which we expect to see chemotherapy-related gastrointestinal upset. Treatment for ATLS involves aggressive fluid diuresis and correction of electrolyte and acid-base imbalances.

Selected References


