Antimicrobial Use in the Veterinary Cancer Patient

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KEYWORDS

• Chemotherapy • Antimicrobial • Neutropenia • Radiation • Sepsis

KEY POINTS

- Veterinarians are constantly challenged regarding prudent use of antimicrobials.
- Any patient that is displaying clinical signs around the time of the neutrophil nadir, regardless of the absolute neutrophil count, should be aggressively treated.
- Critically ill or septic patients often have special considerations that should be recognized so as to institute appropriate dosing and therapies.
- Prophylactic prescription of antimicrobials is limited to those patients considered at high risk of developing a febrile neutropenic episode after chemotherapy.
- Appropriate dosages and dosing schemes still need further work to determine the ideal treatment plan if doxycycline is to be incorporated into standard low-dose chemotherapy protocols.

ANTIMICROBIAL USE IN THE CANCER PATIENT

With the increased emergence of antimicrobial resistance in human medicine, veterinarians are constantly challenged regarding prudent use of antimicrobials. The goal of this article is to discuss the clinical indications for antimicrobial use in veterinary oncology. Areas discussed include general considerations of antimicrobial use, antimicrobials in the neutropenic patient, prophylactic antimicrobial usage, antimicrobials in radiation therapy, and antimicrobials in metronomic chemotherapy protocols.

ANTIMICROBIAL USE IN THE NEUTROPENIC PATIENT

Bone marrow suppression is the most common consequence of chemotherapeutic administration and is the dose-limiting toxicity of many chemotherapy agents.[1] Neutrophils are the cell line affected most often by chemotherapy, as they have a short life span in circulation and these cells are replenished frequently by the bone

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marrow.[2,3] Neutropenia frequently becomes clinically relevant approximately 7 days after administration of chemotherapeutics.[4] However, the nadir can be prolonged with the administration of certain chemotherapy drugs, including carboplatin and lomustine, which can have nadirs as late as 3 weeks after administration.[1,3,5–8]

The Veterinary Cooperative Oncology Group has established a grading scheme for neutropenia in our veterinary patients.[9] In general, most oncologists believe that if the neutrophil count is approximately 1000/μL that the body's immune system is adequate to fight an infection and the risk of infection is low.[10] However, it is critical when evaluating a patient's blood work after chemotherapy to remember that a complete blood count is simply a "snapshot in time" and there is no way to predict if the absolute neutrophil count is increasing or decreasing. Nonetheless, this number is regularly used as a set point to guide antimicrobial therapy in neutropenic chemotherapy patients as well as dose adjustments for future chemotherapy agent administrations (Table 1).

The greatest concern for patients that are neutropenic is for the risk of infection and subsequent sepsis. As the neutrophil count decreases, the risk of infection and septicemia increases, particularly when patients have fewer than 500 neutrophils/μL. The risk for significant side effects requiring hospitalization is less than 5%, with treatment-associated fatalities being less than 1%.[1,11]

RISK FACTORS

Two recent studies have evaluated risk factors associated with chemotherapy-induced sepsis and outcomes in veterinary patients.[12,13] Risk factors that have been identified potentially associated with chemotherapy-induced neutropenia include lower body weight, hematological tumors, chemotherapy drug used (doxorubicin/vincristine), and induction phase of chemotherapy. Additionally, factors that have been associated with a negative prognosis in dogs presenting for neutropenia episodes include hypotension, granulocyte colony-stimulating factor use, and lower rectal temperature on presentation. If any of these risk factors are identified, it may be necessary to be more aggressive with appropriate antimicrobial therapy.

FEBRILE NEUTROPENIA MANAGEMENT

Most patients with septicemia are brought to the veterinary hospital with nonspecific clinical signs and a concurrent fever. However, neutropenia by itself does not typically cause clinical signs. Therefore, any patient that is displaying clinical signs around the time of the neutrophil nadir, regardless of the absolute neutrophil count, should be aggressively treated (Table 2). Additionally, in some cases of severe neutropenia, the patient may have such immune dysfunction that they are unable to adequately release the necessary cytokines to produce a fever.[13] In the author's experience

Table 1
Veterinary Cooperative Oncology Group: common terminology criteria for adverse events v1.1

Hematologic Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutropenia	1500/μL – lower limit of normal	1000–1499/μL	500–999/μL	<500/μL	Death

From VCOG. Veterinary Co-operative Oncology Group – common terminology criteria for adverse events (VCOG-CTCAE) following chemotherapy or biological antineoplastic therapy in dogs and cats v1.1. Vet Comp Oncol 2011. http://dx.doi.org/10.1111/j.1476-5829.2011.00283.x; with permission.