Main Points:

1. Haematologic complications include myelosuppression should be transient, so if they do not resolve, keep looking for cause
2. Certain chemo drugs have specific +/- dose dependant reactions such as Doxo with DCM, and cyclophosphamide with hemorrhagic cystitis
3. Many of the drug reactions produce consequences that should be treated no differently than these signs caused by other diseases

Most Common complications of chemo

- Anorexia
- Fever
  Vomiting
- Neutropenia
- Resp Distress
- Diarrhea

Questions to ask during history

- Previous reactions to the drugs?
- Previous antibiotic therapy

Haematologic complications

- Myelosuppression
    - Neut <3k
        - Severe risk of sepsis at <1k
        - Risk of infection rises exponentially under 500
    - Typically transient
        - If unresolved, requires additional bone marrow diagnostics
    - Most nadirs 5-7 days post therapy
        - Doxorubicin is day 10
        - Cisplatin has double nadir at day 6 and 15
    - Most common sites of infection are GI, urogenital, resp tracts
        - Signs of inflammation are absent due to lack of WBCs
- Recombinant granulocyte colony stimulating factor (rh-G-CSF) can promote neutrophil and (to a less extent) monocyte production and prime neutrophils for cell killing
    - Some evidence for prophylactic use, evidence for either febrile or afebrile neutropenia is contradictory and use is not widely recommended
    - Despite being human, no evidence yet for development of antibodies

Gastrointestinal complications

- Anorexia, pancreatitis, enterocolitis are most common
- Pancreatitis more often associated with
    - L-asparaginase, cisplatin, doxorubicin, methotrexate, azathioprine, steroids

Cardiotoxicity

- Doxorubicin, epirubicin, and daunorubicin
    - Cats rarely experience cardiotoxicity from doxo
    - Acute cardiotox
        - Mild, uncommon, transient
        - Acute dysrhythmias, hypotension during doxo administration
        - Acute pericarditis is reported as an idiosyncratic reaction
    - Doxorubicin-induced cardiomyopathy in dogs that got more than 150-240 mg/m2
        - DCM
        - Possibly due to oxidant injury of myocytes

Neurotoxicity

- Rare
- 5-Fluorouracil has been reported to cause refractory seizures, tremors, hyperexcitability, ataxia, mucositis, diarrhea
- Vincristine has caused direct axonal injury to spinal cord, peripheral nerves and CNS

Nephrotoxicity

- AKI has been reported with cisplatin
    - Due to decreased renal blood flow, acute tubular necrosis, reduced GFR
    - Saline diuresis greatly reduces nephrotoxicity due to high chloride content

Hemorrhagic cystitis

- Cyclophosphamide
    - More common with long term use
    - In one study, 14 of 203 dogs (7%) and 1 of 32 cats (3%) treated with oral cyclophosphamide had hemorrhagic cystitis
    - UA will reveal many RBCs but few WBCs
        - Diagnosis made with UA and negative culture

Dermatologic toxicity

- Extravasation of chemo
    - Vesicants
        - Induce blister with or without necrosis
    - Irritants
        - Pain and inflammation
    - non vesicants
        - Rarely cause problem
    - Worst offenders
        - *Doxorubicin*
        - Vincristine, vinblastine, actinomycin D, DTIC, and streptozocin

        - Signs are usually evident within 1 to 10 days after the incident at the site of injection
- Treatment
    - Dilution with saline, bicarb, or dexamethasone SP
    - Hyaluronidase
    - These are all controversial, as may expose larger tissue area to effects
    - Treat with bandage changes, surgical debridement, etc…

Acute Tumor Lysis Syndrome

- Death of massive amounts of primary malignant cells
- Lymphoma, leukemia most common
    - Dehydrated patients with stage IV or V lymphoma is highest risk
- Can cause shock - treat as such
- Causes hyperkalemia, hyperphosphatemia, hypocalcemia,

Allergic or hypersensitivity reactions

- L-asparaginase, doxorubicin, are more common
- L-asp associated with type I IgE mediated reactions
- Doxo can cause acute mast cell degranulation without IgE

Questions

1. You are presented with a patient that is undergoing treatment for lymphoma. The chief complaint is bloody urine. The owner reports that the dog is not having any increased urgency or discomfort. Its last treatment was 6 days ago but the owners are unsure of which chemo drug was used. The patient has been undergonig therapy for 4 months. A CBC reveals a neutrophil count of 2.8k, with no other abnormalities. A UA reveals moderate red blood cells and a large amount of white blood cells. A culture is pending. Which of the following is the most appropriate treatment protocol?
    a. oral enrofloxacin until results of UCS
    b. parenteral amikacin until results of UCS
    c. IV ampicillin/sulbactam until results of UCS
    d. IV fluid therapy alone until results of UCS

2. Which of the following drugs is the most potent dermatologic irritant?
    a. Cisplatin
    b. Vincristine
    c. Doxorubicin
    d. Hyaluronidase

3. True/False: human recombinant granulocyte colony stimulating factor greatly increases production of neutrophils, monocytes, and eosinophils

4. Which of the following electrolyte abnormalities would be expected with acute tumor lysis syndrome?
    a. Hypophosphatemia
    b. Hypomagnesemia
    c. Hyperkalemia
    d. Hypercalcemia

Answers:

1. You are presented with a patient that is undergoing treatment for lymphoma. The chief complaint is bloody urine. The owner reports that the dog is not having any increased urgency or discomfort. Its last treatment was 6 days ago but the owners are unsure of which chemo drug was used. The patient has been undergonig therapy for 4 months. A CBC reveals a neutrophil count of 2.8k, with no other abnormalities. A UA reveals moderate red blood cells and a large amount of white blood cells. A culture is pending. Which of the following is the most appropriate treatment protocol?
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    This is likely NOT sterile cystitis since there is a large amount of WBC. Also, patient is neutropenic which may explain lack of inflammatory signs

2. Which of the following drugs is the most potent dermatologic irritant?
    a. Cisplatin
    b. Vincristine
    c. Doxorubicin
    d. Hyaluronidase

3. True/**False**: human recombinant granulocyte colony stimulating factor greatly increases production of neutrophils, monocytes, and eosinophils

    It only greatly increases neuts

4. Which of the following electrolyte abnormalities would be expected with acute tumor lysis syndrome?
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