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UPDATE ON FERRET LYMPHOMA

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Lymphoma is one of the most commonly diagnosed conditions in ferrets in the USA.[1] A viral etiology of the disease, like the viral leukemia in cats, has recently been proposed[2] but no scientific evidence of this proposed etiology exists to date.

Unfortunately, in spite of the frequency of occurrence, lymphoma is one of the more difficult diseases to accurately diagnose. Two distinct forms of this disease are commonly discussed in the literature. The first is the 'juvenile' form, which usually affects ferrets younger than 2-3 years. It is also known as the 'lymphoblastic' form. In this case, many visceral organs are infiltrated by lymphocytes with resulting enlargement of these organs. The most common presentation is a young ferret with respiratory distress. This is due to significant enlargement of the thymus, and can be clearly seen on chest radiographs.

The second form of lymphoma is often described in the literature as the 'lymphocytic' form, or the adult/chronic presentation. It is usually seen in ferrets older than 3 years. In this form of the disease the most common presentation is a 'healthy' animal with significantly enlarged peripheral lymph nodes. Over time, lymphocytes will eventually infiltrate every organ and the cause of death in the advanced state is usually organ failure. While the distinction between the two forms of the disease can be very useful, it is possible for this disease to present in many different ways. It is therefore important to include lymphoma in the differential list for most sick ferret patients until proven otherwise.

In order to appropriately **diagnose** lymphoma in a ferret, a biopsy is needed. In only in a few cases can the diagnosis be made with a fine needle aspirate, and almost never based on the complete blood count alone. The popliteal lymph node is easily removed and biopsy of this tissue is often the best diagnostic choice. Fine needle aspirates obtained via the ultrasound exam can be suggestive of lymphoma but often don't provide a definitive diagnosis.

TREATMENT

Several different treatment options are available and before starting any particular treatment the owner should be informed about the character of this disease and warned that a complete cure is rarely achieved.

Chemotherapy is one option and the simplest form is the use of prednisolone alone. This is an extremely effective treatment resulting in rapid remission even within a few days. Therefore it should never be started before a biopsy is taken. However, in most cases, if not all, the lymphoma will recur within a few months after initiation of this treatment and then can be considered as a multi-drug resistant (MDR) lymphoma. These animals will usually lose ground rapidly and euthanasia is often indicated due to quality of life issues.

Other chemotherapeutic protocols have been published for ferrets and are usually modified from canine or feline protocols.[3,4] All of these published protocols include chemotherapeutic agents, which are extremely caustic to tissue and must be given intravenously with strict care. For example one of the most popular protocols consists of vincristine, asparaginase, cyclophosphamide and doxorubicin. Any extravasation of these drugs has the potential to cause tissue necrosis leading to sloughing or self-mutilation resulting in severe damage. Repeated careful venous access can sometimes be a challenge in the small ferret patient. The use of subcutaneous venous access-ports can be helpful in this regard and techniques for their use have been published previously.[5]

Often however, owners may shy away from treatment choices involving either invasive surgeries or these aggressive chemotherapeutic agents. A novel lymphoma protocol has been developed at the Tufts Cummings School of Veterinary Medicine and includes drugs that are given only by oral or subcutaneous routes, completely avoiding the need for weekly venipuncture or surgical procedures. The following drugs are used:

1. prednisolone
2. L-asparaginase
3. cyclophosphamide
4. cytarabine
5. methotrexate
6. chlorambucil
7. procarbazine

The preliminary results over the last 3 years of trials are promising and owners have been very pleased with the efficacy of the drugs. The only drawback of this protocol is that it extends over a 26 week period and 19 visits are required during this time, making it relatively involved for the owner.

For this protocol we stage the disease prior to treatment. The staging process should include a complete blood count with a platelet count, a chemistry profile, whole body radiographs (2 views), abdominal ultrasonography, a biopsy of affected tissue and a bone marrow aspirate. Currently, we distinguish four stages in the manifestation of lymphoma:

- Stage 1: the tumor involves only a single site
- Stage 2: multiple sites are involved, on the same side of the diaphragm
- Stage 3: spleen, and lymph nodes on both sides of the diaphragm are involved.
- Stage 4: multiple sites on both sides of the diaphragm are affected

Blood work (CBC only in most cases) is repeated 7 times during the protocol to monitor the affect of the myelosuppressive drugs (cyclophosphamide, chlorambucil, procarbazine and cytarabine). Also, depending on the location of the disease, imaging of the abdomen or chest may need to be repeated to assess response to therapy.

This protocol appears promising. However, due to the low number of animals that have been treated with it thus far, conclusions are only preliminary. It does appear that in animals that have been treated previously with prednisone for an extended period of time, the protocol appears not to be as effective. For exact details and instructions on this protocol, please contact the author (joerg.mayer@tufts.edu).

In cases where the lymphoma is resistant to drugs and or the owners do not feel comfortable with chemotherapy, the option of **radiation treatment** is also available. The use of radiation treatment in ferrets has been reported in the literature.[6] The author has managed different neoplastic conditions in ferrets with the help of radiation therapy including an animal with MDR lymphoma. While the treatment is not curative, it is simple to use if a radiation therapy facility is available and side effects are negligible.

CONCLUSION

While lymphoma remains a very common diagnosis in the ferret patient, it is important not to overdiagnose the disease by CBC results. For a definitive diagnosis of lymphoma, a tissue biopsy or sometimes a fine needles aspirate is needed as a minimum diagnostic workup. Different chemotherapy options are available to the client including radiation therapy.

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