

RADIOTHERAPY WITH AND WITHOUT CHEMOTHERAPY FOR LOCALIZED LYMPHOMA IN 10 CATS

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A retrospective study was undertaken to determine the efficacy of radiotherapy with and without chemotherapy for treatment of localized lymphoma in 10 cats. Tumor location included nasal cavity (3 cats), retrobulbar area (3 cats), mediastinum (1 cat), subcutaneous tissue (1 cat), maxilla (1 cat) and mandible (1 cat). Six cats were treated with radiation alone and 4 cats also received chemotherapy during and/or after radiotherapy. Complete remission was achieved locally in 8 of 10 cats, whereas 2 cats had partial remission. Five of the 6 cats treated with radiotherapy alone achieved complete remission. Overall mean and median remission times for the 8 cats with complete remission were 123 weeks and 114 weeks, respectively (range 4 to 277 weeks). Three of the 8 cats have been in complete remission for more than 131 weeks and are still alive. Three cats achieving complete local remission developed lymphoma outside the radiation field. One cat had recurrence at the site of irradiation. Results of the retrospective study suggest that radiotherapy with and without chemotherapy may be effective for the treatment of localized lymphoma in the cat. *Veterinary Radiology, Vol. 32, No. 6, 1991, pp 277-280.*

Key words: feline, lymphoma, radiotherapy

Introduction

ALTHOUGH LYMPHOMA is the most frequent hematopoietic neoplasm of the cat,¹⁻⁴ extranodal, localized forms of feline lymphoma are rare.⁵⁻⁸ Traditionally, feline lymphoma has been treated with chemotherapy. The extreme radiosensitivity of lymphoid tumors⁹ suggests that radiotherapy may be a logical treatment option for localized forms of lymphoma. The purpose of this study was to retrospectively evaluate the response of localized malignant lymphoma in cats to radiotherapy with and without chemotherapy. Due to the scarcity of information available in the literature concerning the biologic behavior and treatment of localized lymphoma in the cat, the information in this study may be useful in the design of more effective therapeutic protocols in the future.

Methods

Criteria for patient selection—Ten cats with localized lymphoma were evaluated at the Colorado State University

Comparative Oncology Unit between 1983 and 1989. Cats were included for study when clinical staging procedures confirmed stage I lymphoma according to the World Health Organization clinical staging system¹⁰ and cats were treated with radiotherapy, either alone or in combination with chemotherapy. All cats were clinically staged using the following criteria: complete blood count, serum biochemical profile, urinalysis, thoracic radiographs, lymph node aspirates and FeLV ELISA test.* Additional evaluation included skull radiographs (9 cats) and bone marrow aspirates (3 cats). Lymphoma was diagnosed by histologic examination of a biopsy specimen in 9 cats and by cytologic examination of lesion aspirates in 1 cat (cat 7, Table 1).

Patient characteristics—The median age of cats in this study was 13 years (range 1.5 to 16 years). Seven of the 10 cats were castrated males. There was 1 intact male, 1 neutered female and 1 intact female. There were 3 domestic shorthair cats, 3 domestic longhair cats, 3 Siamese cats, and 1 Rex cat. Two of the 10 cats (cats 1 and 10) were FeLV-positive. Of the 9 cats that had radiographs of the skull, 5 cats (cats 1, 2, 5, 6 and 9) had evidence of bony involvement. Five cats (cats 1, 2, 3, 5, and 7) were symptomatic (stage Ib¹⁰) at the time of diagnosis. The time from diagnosis to initiation of radiotherapy ranged from 5 to 10 days.

Tumor sites included nasal cavity (3 cats), retrobulbar area (3 cats), mediastinum (1 cat), subcutaneous tissue in

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*FeLV CITES, Norden Company, Lincoln, Nebraska.

the temporal region (1 cat), maxilla (1 cat) and mandible (1 cat) (Table 1). Three cats received chemotherapy prior to radiotherapy. Two cats received 5 to 10 mg of prednisone daily for 3 days (cat 4) to 1 month (cat 2) prior to irradiation. One cat was treated with a combination of cyclophosphamide, vincristine and prednisone⁷ for 1.5 weeks (cat 7) prior to irradiation. Clinical improvement did not occur in all cats (cats 2, 4 and 7) treated with these chemotherapeutic agents prior to radiotherapy. Six of 10 cats received radiation as the sole treatment. Total minimum tumor dose varied from 6 Gy to 40 Gy, delivered by a 6 MV linear accelerator. Bolus (tissue equivalent material) was used in all cats to achieve an appropriate surface dose. The nasal, retrobulbar area, mediastinal and maxillary tumors were treated with photon radiotherapy given in 2.5 to 4 Gy fractions. The subcutaneous and mandibular tumors were treated with 6 MeV electron radiation given in 3.6 Gy and 5 Gy fractions, respectively.

Four cats received chemotherapy during and/or after radiotherapy. Cats 2 and 10 received 5 mg of prednisone daily for 2 to 3 months after radiotherapy. Cats 1 and 7 each received one treatment of vincristine (0.75 mg/m² IV) 1

week after radiotherapy, as well as oral prednisone for 4 to 5 months after the end of radiation treatment.

Response criteria—All cats responded to treatment with either complete remission or partial remission (Table 1). Complete remission was defined as absence of clinical disease. Partial remission was defined as a 50% or greater decrease in tumor volume. Stable disease was defined as <50% increase or decrease in tumor volume, and progressive disease was defined as a 50% or greater increase in tumor volume. After treatment, cats were evaluated at 1- to 3-month intervals for 1 year. After 1 year, follow-up was done by the Comparative Oncology Unit staff via questionnaire or telephone.

Results

Eight of the 10 cats (80%) attained complete remission. The overall mean and median remission times for those 8 cats were 123 and 114 weeks, respectively, with a range of 4 to 277 weeks (Table 1). Complete remission occurred in the 3 cats with nasal lymphoma (cats 1, 2 and 3). Cat 1 has been in complete remission for 277 weeks and is still alive.

TABLE 1. Results of Radiotherapy of Cats with Solitary Lymphoma

Cat	Site	Radiation			Response	Duration ⁺⁺ of CR (weeks)	Survival ⁺⁺⁺ (weeks)	Necropsy	Comments
		Total Dose (Gy)	No. of Fractions	Days for Completion of Treatment					
++++	1 Nasal	8	2	3	CR*	277	277	—	Alive
	2 Nasal	40	10	20	CR	97	97	Not done	Chronic renal failure; CR at death
++++	3 Nasal	40	10	22	CR	180	180	—	Lost to follow-up
	4 Retrobulbar	37.5	15	25	CR	26	26	CR primary site; lymphoma in lymph nodes	Lymphoma in lymph nodes 20 wk post-XRT* ⁺
	5 Retrobulbar	40	10	22	PR#	—	6	Not done	Euthanatized
	6 Retrobulbar	35	10	22	CR	220	220	—	Alive
	7 Mediastinal	8	2	2	CR	131	131	—	Alive
	8 Subcutaneous	36	10	22	CR	4	21	Not done	Lymphoma at treatment site and outside XRT field
	9 Maxilla	6	2	2	CR	47	47	Not done	Lymphoma in lymph nodes at 21 wk post-XRT; CR at primary site
10 Mandible	25	5	10	PR#	—	9	Lymphoma at primary site and outside XRT field	Euthanatized	

⁺⁺ Duration of CR: duration of complete remission at primary site of irradiation

⁺⁺⁺ Survival time: time from diagnosis to death or lost to follow-up

*CR: complete remission, absence of any clinical evidence of tumor

#PR: partial remission, 50% or greater decrease in tumor volume

*XRT: radiation treatment

⁺⁺⁺⁺ Previously reported by Straw et al⁸

Cat 2 was euthanatized at 96 weeks post-irradiation due to progressive chronic renal failure that was initially identified at the time the lymphoma was diagnosed. At the time of death, lymphoma clinically appeared to be in complete remission. Cat 3 received radiotherapy as the sole form of treatment for nasal lymphoma. This cat was lost to follow-up after complete remission was documented at 178 weeks.

Two of the 3 cats with retrobulbar lymphoma (cats 4 and 6) attained complete remission with only radiotherapy. Cat 4 was euthanatized 24 weeks after irradiation due to extension of lymphoma to cervical lymph nodes. Necropsy confirmed complete remission at the site of radiotherapy. Cat 6 has been in complete remission for 220 weeks and is still alive. The third cat with retrobulbar lymphoma (cat 5) was euthanatized 2 weeks after radiotherapy. Clinically, tumor tissue was still present, but necropsy was not done.

Complete remission occurred in 1 cat (cat 7) with mediastinal lymphoma. Cat 7 has been in complete remission for 131 weeks and is still alive (Table 1).

Six weeks following electron radiotherapy, cat 8 (subcutaneous lymphoma) had evidence of lymphoma at the treatment site, as well as adjacent to the radiation field. For palliative purposes, the site was re-irradiated with photon radiotherapy at a total dose of 7.2 Gy given in 2 fractions. Chemotherapy (cyclophosphamide, vincristine and prednisone⁷) was administered concurrently. Partial remission was attained 2 weeks after reinstatement of therapy. This cat was euthanatized upon owner request 5 weeks after the second course of radiotherapy due to lack of complete response and clinical evidence of progressive chronic renal failure.

Cat 9 (maxillary lymphoma) achieved complete remission following radiation treatment without adjuvant chemotherapy. Twenty-one weeks after radiotherapy, lymphoma was present in cervical lymph nodes. Adjuvant chemotherapy (cyclophosphamide, vincristine and prednisone⁷) was given. The tumor size remained unchanged for 13 weeks, at which time chemotherapy was discontinued due to clinical evidence of progression of lymphoma. The cat was euthanatized 46 weeks after radiotherapy. Necropsy was denied, though clinically tumor recurrence at the site of radiotherapy was not observed.

Cat 10 (mandibular lymphoma) was treated with electron radiotherapy and adjuvant prednisone. At the time of diagnosis, bone involvement was not evident radiographically. Complete remission was not attained. The cat was euthanatized upon owner request 5 weeks after radiation treatment. Necropsy revealed lymphoma at the site of radiation treatment, with extension to the mandible.

Discussion

Chemotherapy has been recognized as the treatment of choice for systemic lymphoproliferative neoplasms in hu-

mans and animals.^{1,7,11-13} Localized lymphoma has been managed with surgery, hyperthermia and radiotherapy, with or without adjuvant chemotherapy, in humans and dogs.^{1,5,6,9,12-17} Radiotherapy is effective for treatment of localized forms of Hodgkin's and non-Hodgkin's lymphoma in humans.^{12,13,16,17,18,19} Similarly, solitary forms of lymphoma in dogs have been reported to respond favorably to irradiation.⁹ The study reported here reviews the benefits of radiotherapy with and without concurrent chemotherapy for the treatment of localized lymphoma in the cat.

There are few reports of the efficacy of radiotherapy with and without chemotherapy for control of localized feline lymphoma.^{3,8,20} An interpretation of this study must be done with knowledge of the confounding variables that are inherent in many retrospective studies. The use of chemotherapy in 4 of 10 cats during or after radiotherapy may have enhanced the control of tumor. Two of the cats were given prednisone, which has been shown to be relatively ineffective as a single agent for complete control of lymphoma in the cat, and cats that do respond to glucocorticoids generally do so for a relatively short time.²¹ The other 2 cats in this study were given one dose of vincristine and subsequently 4 to 5 months of prednisone therapy. Cotter reported that only 27% of cats with lymphoma treated more aggressively with these two drugs achieved a complete remission.⁷

The median age of cats reported in this study, 13 years, is older than that reported for cats with all forms of lymphoma,^{2,4,7,22} suggesting that localized or extranodal lymphoma may be a more indolent form of the disease. Eight of the 10 cats reported here were males. One study reports an incidence ratio of 2:1 for lymphoma in male cats.⁴

Eight of the 10 cats (80%) in this study achieved complete remission. This is similar to percent remission achieved with chemotherapy reported by other authors for multicentric lymphoma.^{3,7} Five of the 8 cats attaining complete remission were treated with radiotherapy alone. There were insufficient numbers of cats and too many confounding variables in this study to allow accurate comparison of response to treatment in the cats receiving radiotherapy alone versus those treated with radiotherapy and adjuvant chemotherapy but, in our opinion, local control was most likely due to irradiation.

Turrel²⁰ reports complete and partial responses in some cats with intranasal lymphoma using a moderate dose of radiation. One of the 3 cats with intranasal lymphoma in our study received a low dose of radiation (8 Gy), whereas the other 2 received 40 Gy. All 3 cats remained in complete remission for greater than 97 weeks, which suggests that a dose of radiation lower than 40 Gy may be adequate, in some cats, to achieve complete remission at this site. This

conclusion must be tempered with the knowledge that lymphoma typically responds in a heterogeneous manner to radiation treatment²⁰ and would, therefore, respond most consistently to the highest dose of radiation tolerated by normal tissue.

Two of the 8 cats attaining complete local remission (cats 4 and 9) had evidence of lymphoma in cervical lymph nodes 20 weeks after radiation treatment of the primary site. Although complete remission was attained at the primary tumor site after radiotherapy, adjuvant chemotherapy or prophylactic irradiation of cervical lymph nodes may have been useful to delay or prevent progression of lymphoma in these cats.

Cats 8 and 10 received electron radiotherapy, as radiographs of the skull did not reveal bony involvement. Four to 6 weeks after radiotherapy, both cats had lymphoma at the treatment site, as well as outside the radiation field. Results in these 2 cats suggest that the extent of tumor and radiation field were underestimated.

At the initial presentation for lymphoma, cats 2 and 8 were diagnosed as having chronic renal failure as deter-

mined by blood tests, urinalysis and abdominal radiographs. Renal lymphoma was considered to be unlikely due to small kidney size, as determined by radiographs; however, a biopsy would have been necessary to ascertain the cause of renal failure in these two cats.

Results of this study suggest that radiotherapy is effective in attaining complete remission with and without chemotherapy in localized forms of feline lymphoma. Since lymphoma responds to radiotherapy in a heterogeneous manner, the maximum dose of radiation tolerated by normal tissue should be employed. The radiation field must be sufficiently wide to avoid underestimation of tumor volume and progression of lymphoma outside the field of radiation. It is difficult to predict which cases of localized lymphoma will extend to regional lymph nodes; therefore, chemotherapy combined with radiotherapy may be more effective than radiation alone. The information obtained from this report may be of value to design prospective studies to determine the benefit of combined chemotherapy and radiotherapy, and to design optimum treatment protocols for localized lymphoma in cats.

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