Radiographic Differentiation of Cranial Mediastinal Lymphomas from Thymic Epithelial Tumors in Dogs and Cats

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ABSTRACT

In both dogs and cats, the most common cranial mediastinal masses (CMMs) are lymphoma and thymic epithelial tumors (TETs). Pretreatment differentiation of these tumors using fine needle aspiration or biopsy is essential because lymphomas are treated medically, whereas TETs are treated surgically. The purpose of this retrospective study was to determine whether thoracic radiographic findings can be used to aid clinicians in preliminarily differentiating the two tumor types before cytology or histopathology results become available. Medical records, available cytologic or histologic samples, and thoracic radiographs were evaluated for 62 dogs and 28 cats. Seventeen radiographic criteria were assessed by two examiners, and regression modeling was performed to test for significant predictors of tumor type. In dogs, CMMs with at least two well-defined radiographic margins on a lateral view and CMMs causing a rightward shift of the cardiac silhouette on a ventrodorsal or dorsoventral view were significantly more likely to be TETs than lymphomas ($P < .001$ and $P < .01$, respectively). No significant predictive variables were identified in cats. Radiographic findings do not eliminate the need for invasive sampling, but in dogs, they may guide the clinician in providing preliminary information to owners regarding the staging and therapeutic measures that may eventually be recommended. (*J Am Anim Hosp Assoc* 2019; 55:187–193. DOI 10.5326/JAAHA-MS-6907)

Introduction

In both dogs and cats, the most common cranial mediastinal mass (CMM) is lymphoma, followed by thymic epithelial tumors (TETs).[1,2] Other types of CMM may occur in both species but are relatively rare. In both humans and dogs, TETs are known to include thymomas, which are most common, as well as atypical thymomas and thymic carcinomas.[3–5] The umbrella term TETs better captures the concept that the tumors may have variable histologic appearances and prognoses than does the term thymoma. Pretreatment differentiation of lymphomas from TETs in dogs and cats is essential because lymphomas are often treated medically, whereas TETs may be treated with a combination of surgery and/or radiotherapy. A definitive diagnosis is generally established through fine needle aspiration or biopsy of the CMM or, in the case of lymphomas, of

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CMM (cranial mediastinal mass); CT (computed tomography); DV (dorsoventral); TETs (thymic epithelial tumors); VD (ventrodorsal)

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other tissues that are affected. However, because CMMs are often associated with respiratory signs, thoracic radiographs are commonly obtained as part of the minimum database and could potentially help to differentiate the two tumor types.[6,7] Identification of radiographic criteria suggestive of either lymphoma or TET could aid clinicians in providing owners with preliminary guidance regarding the staging and therapeutic measures that might eventually be recommended.

To date, little information has been published regarding the utility of any imaging modality for differentiating the two tumor types. A study evaluating radiographic predictors of diagnosis in dogs with CMMs reported no correlation between histologic diagnosis and either the size of the mass or the presence of pleural effusion; however, megaesophagus was more commonly identified in dogs with thymoma than in dogs with other CMMs.[8] Compared with thoracic radiographs, computed tomography (CT) has the benefits of increased contrast resolution and lack of anatomic superimposition. As a result, CT has been demonstrated to provide valuable additional information about the anatomic extent and distribution of diseases involving the mediastinum and other thoracic structures.[9] However, in a study that included nine dogs and five cats with thymoma or lymphoma, CT findings that were predictive of tumor type could not be identified.[10] The ultrasonographic appearance of CMMs in dogs and cats has been described, but the use of ultrasound in differentiating tumor types has not been investigated.[11]

The purpose of this study was to determine whether radiographic criteria can aid in the differentiation of lymphomas from TETs in dogs in cats. Our null hypothesis was that, in both dogs and cats, there would be no significant differences in radiographic criteria between patients with lymphoma and patients with thymoma.

Materials and Methods

Canine and feline electronic medical records at Cummings School of Veterinary Medicine at Tufts University were queried for patient visits between the years of 2001 and 2015. Criteria for inclusion in the study were the presence of a CMM on available two- or three-view thoracic radiographs obtained prior to surgical or chemotherapeutic intervention; a diagnosis of lymphoma based on cytology, histology, or polymerase chain reaction for antigen receptor rearrangements; or a diagnosis of TET based on cytology or histology. For each animal meeting the inclusion criteria, all available cytologic or histologic preparations were re-evaluated, and a final diagnosis was made by a single board-certified clinical (PJB) or anatomic (SHJ) pathologist. When cytologic or histologic slides were unavailable for review, diagnoses were based on the original clinical reports provided by board-certified pathologists.

If three-view thoracic radiographs were available, the lateral view with the best subjective combination of mass visibility and radiographic technique was used for data collection. The same criteria were used to select a view when both ventrodorsal (VD) and dorsoventral (DV) views were available. All radiographs were digital[a] and were reviewed by a board-certified radiologist (TJO) and a small animal rotating intern (PEH) at a dedicated picture archiving and communication system workstation[b]. Evaluations were performed without knowledge of the cytologic or histologic diagnoses. When there was disagreement, the assessment of the board-certified radiologist was used. Fifteen categorical and two continuous radiographic variables were evaluated for each animal (**Tables 1, 2**). To evaluate CMM margination, the cranial, caudal, dorsal, and ventral margins were individually evaluated on the lateral view, and CMMs with two or more individual discretely defined margins were recorded as well defined. Displacement of the cardiac silhouette in the VD or DV view was subjectively determined based on deviation from the typical appearance in which most of the cardiac silhouette is on midline (VD or DV view) and the cardiac apex is to the left of midline (VD view). Similarly, tracheal deviation on the VD or DV view was subjectively determined based on deviation from the typical appearance in which the trachea is on midline or slightly to the right of midline. CMM location in the VD or DV view was determined by dividing the thoracic cavity in thirds and determining where the center of the mass was located. Similarly, CMM location on the lateral view was determined by dividing the DV height of the thoracic cavity in thirds and determining where the center of the mass was located. Dorsal deviation of the trachea in the lateral view was recorded if the trachea was parallel or near-parallel to the thoracic spine. Carina location caudal to the level of the sixth thoracic vertebral body on a lateral view was recorded as caudal deviation. CMM were considered circular if the DV dimension of the mass was within 25% of the craniocaudal dimension as measured in the lateral view. Discrete sternal lymphomegaly was considered present if, in a lateral view, a broad-based soft tissue opacity contacting the sternum was distinguishable from the CMM. Tracheobronchial lymphomegaly was considered present if, in the lateral view, there was increased soft tissue opacity dorsal to the carina resulting in focal ventral displacement of the trachea and/or carina. These two lymph node variables were combined for statistical analysis. Pleural effusion was considered present if there was increased soft tissue opacity within the pleural space, rounding of the lung margins, or widening of pleural fissures in either the lateral or VD/DV views. Esophageal dilation was recorded if there was diffuse widening of the intrathoracic esophagus as a result of gas or fluid accumulation. For masses that extended caudally beyond the cranial margin of the cardiac

TABLE 1

Results of Assessments of Categorical Radiographic Variables for Cranial Mediastinal Masses in 62 Dogs and 28 Cats

Radiographic Variables	No. of Dogs with TETs Fulfilling the Criteria/Total No. of Dogs Fulfilling that Criteria (% of Canine Cases That Were TETs)		No. of Cats with TETs Fulfilling the Criteria/Total No. of Cats Fulfilling that Criteria (% of Feline Cases That Were TETs)	
Well-defined margins (lateral view)	Yes	16/25 (64.0)	Yes	2/7 (28.6)
	No	8/37 (21.6)	No	5/21 (23.8)
	$P < .001$			
Lateral cardiac silhouette displacement (VD/DV view)	Right	4/4 (100)	Right	2/2 (100)
	Left	0/1 (0)	Left	—
	None	20/57 (35.1)	None	5/26 (19.2)
	$P < .01$			
Lateral tracheal displacement (VD/DV view)	Right	6/9 (66.7)	Right	2/4 (50)
	Left	0/1 (0)	Left	—
	None	18/52 (34.6)	None	5/24 (20.8)
Location (VD/DV view)	Right	0/3 (0)	Right	—
	Left	10/17 (58.8)	Left	0/1 (0)
	Midline	14/42 (33.3)	Midline	7/27 (25.9)
Location (lateral view)	Dorsal	0/1 (0)	Dorsal	—
	Ventral	11/24 (45.8)	Ventral	4/9 (44.4)
	Middle	13/37 (35.1)	Middle	3/19 (15.8)
Sternal contact (lateral view)	Yes	19/42 (45.2)	Yes	7/24 (29.2)
	No	4/10 (40)	No	0/2 (0)
	Not evaluated	1/10 (10)	Not evaluated	0/2 (0)
Cardiac silhouette contact (lateral view)	Yes	17/36 (47.2)	Yes	6/22 (27.3)
	No	6/22 (27.2)	No	1/6 (16.7)
	Not Evaluated	1/4 (25)	Not Evaluated	—
Dorsal tracheal deviation (lateral view)	Yes	8/21 (38.1)	Yes	3/16 (18.8)
	No	16/41 (39.0)	No	4/12 (33.3)
Caudal carinal deviation (lateral view)	Yes	5/13 (38.5)	Yes	4/14 (28.6)
	No	19/49 (38.8)	No	3/14 (21.4)
Circular shape (lateral view)	Yes	14/31 (45.2)	Round	1/7 (14.3)
	No	8/26 (30.8)	Other	5/18 (27.8)
	Not evaluated	2/5 (40)	Not evaluated	1/3 (33.3)

TABLE 1 (Continued)

Radiographic Variables	No. of Dogs with TETs Fulfilling the Criteria/Total No. of Dogs Fulfilling that Criteria (% of Canine Cases That Were TETs)		No. of Cats with TETs Fulfilling the Criteria/Total No. of Cats Fulfilling that Criteria (% of Feline Cases That Were TETs)	
Sternal or tracheobronchial lymphadenopathy (lateral view)	Yes	0/7 (0)	Yes	0/2 (0)
	No	24/55 (43.6)	No	7/26 (26.9)
Pleural effusion (either view)	Yes	7/19 (36.8)	Yes	2/13 (15.4)
	No	17/43 (39.5)	No	5/15 (33.3)
Esophageal dilation (lateral view)	Yes	4/7 (57.1)	Yes	—
	No	20/55 (36.4)	No	7/28 (25.0)
Amount of extension beyond the cranial margin of the cardiac silhouette (VD/DV view)	0	8/27 (29.6)	0	1/6 (16.7)
	≤25%	8/20 (40)	≤25%	3/15 (20)
	25-50%	3/9 (33.3)	25-50%	3/6 (50)
	≥50%	5/6 (83.3)	≥50%	0/1 (0)
Side of extension beyond the cranial margin of the cardiac silhouette (VD/DV)	Left	11/21 (52.4)	Left	3/8 (37.5)
	Right	—	Right	0/2 (0)
	Midline	5/14 (35.7)	Midline	3/12 (25)

The numbers and percentages of dogs and cats that had TETs are shown for each category.
The — represents 0/0 (i.e., no cases had left lateral displacement at all).
DV, dorsoventral; TET, thymic epithelial tumor; VD, ventrodorsal.

silhouette in the VD/DV views, the amount of extension was categorized as ≤25, 25–50, or ≥50% of the length of the cardiac silhouette, and the side of the extension was noted. Ratios of CMM mass size (width and height) to thoracic cavity size (width and height) were calculated from the lateral and the VD/DV views. When a variable could not be evaluated because of either a large mass size resulting in border summation with adjacent structures or the presence of pleural effusion causing border effacement, a value for that variable was not recorded.

Statistical Analysis

Multivariable logistic regression analysis was performed to examine associations between radiographic variables and mass type. Dogs and cats were analyzed separately. To reduce the likelihood that type I

TABLE 2

Results of Assessments of Continuous Radiographic Variables for Cranial Mediastinal Masses in 62 Dogs and 28 Cats

Radiographic Variables	Means in Dogs	Means in Cats
Ratio of mass width:thoracic cavity width (VD/DV view)	Dogs with TETs = 0.593	Cats with TETs = 0.581
	Dogs with lymphoma = 0.599	Cats with lymphoma = 0.636
Ratio of mass height:thoracic cavity height (lateral view)	Dogs with TETs = 0.654	Cats with TETs = 0.825
	Dogs with lymphoma = 0.653	Cats with lymphoma = 0.763

For each variable, mean values for dogs and cats with TETs and lymphomas are shown. The data shown does not include imputed values.
DV, dorsoventral; TET, thymic epithelial tumor; VD, ventrodorsal.

errors would result from the large number of variables considered, $P < .01$ was considered significant. A standard open-source statistical software program[c] was used to perform forward variable selection. After a multivariable model was defined, backward selection analysis was performed to confirm that all variables included significantly improved the model.

Three continuous radiographic variables had missing values as a result of large mass size or presence of pleural effusion. To examine the effect of missing data, two data sets were generated: one in which missing data was not considered and one in which values were imputed as follows. In one dog and one cat, the ratio of the maximum mass height to the thoracic height at the same level could not be determined because of large mass size, and the maximum value for the variable from the existing species data set (0.938 and 0.896, respectively) was imputed. In four dogs and two cats, the same variable could not be determined as a result of border effacement secondary to pleural effusion, and the mean value for the variable from the existing species data set (0.596 and 0.623, respectively) was imputed. Finally, in three dogs and two cats, the ratio of the maximum mass width to thoracic width at the same level could not be determined because of pleural effusion, and the mean value for the variable from the existing species data set (0.653 and 0.775, respectively) was imputed.

The model development process was performed both for the data set with missing values and for the data set with imputed values.

Results

Dogs

Of a total of 62 dogs that met the inclusion criteria, 38 (61.3%) had lymphoma and 24 (38.7%) had a TET. The diagnoses of lymphoma were based on cytology of the CMM (n = 5), a peripheral lymph node (n = 13), pleural fluid (n = 6), or bone marrow (n = 1); histology of the CMM (n = 8) or a peripheral lymph node (n = 1); or polymerase chain reaction for antigen receptor rearrangements of a peripheral lymph node (n = 3) or an unspecified site (n = 1). Of the 25 lymphomas diagnosed by cytology, 21 diagnoses were confirmed by slide review, and cytologic preparations were unavailable for 4. Of the nine lymphomas diagnosed by histology, eight diagnoses were confirmed by slide review, and histological preparations were unavailable for one. The diagnoses of TET were based on cytology (n = 4) or histology (n = 20) of the CMM. Of the four TETs diagnosed by cytology, three were confirmed by slide review, and cytologic preparations were unavailable for one. All TETs diagnosed by histology were confirmed by slide review.

Breeds represented were Labrador retrievers (12); boxers (7); golden retrievers (5); English bulldogs (4); German shepherd dogs (2); shih tzu (2); Shetland sheepdogs (2); 1 each of Airedale terrier, Australian shepherd, beagle, Chihuahua, collie, dachshund, Doberman pinscher, French bulldog, German pinscher, goldendoodle, Great Dane, Jack Russell terrier, Lhasa apso, Rhodesian ridgeback, rottweiler, schnauzer, St. Bernard, Tibetan terrier, vizsla, and Weimaraner; and 8 mixed-breed dogs. There were 3 male, 29 neutered male, 2 female, and 28 spayed female dogs. The mean age at the time of diagnosis was 8.5 yr (range 1.0–16.2 yr).

Two- and three-view thoracic studies were available for 10 and 52/62 dogs, respectively. Images evaluated included 37 right and 25 left lateral views as well as 14 VD and 48 DV views. Results of variable assessments for both dogs and cats are shown in Tables 1 and 2.

In dogs, the final model without imputed values included two significant variables: the presence of two or more well-defined margins on a lateral view ($P < .001$) and rightward cardiac displacement on a VD/DV view ($P < .01$) were each associated with TETs. Examples of these findings are shown in **Figures 1 and 2**. These variables were also significant when missing values were imputed ($P < .001$ and $P < .01$, respectively). Among CMMs that had well-defined margins, 16/25 (64.0%) were TETs, and among masses without well-defined margins, only 8/37 (21.6%) were TETs. Four CMMs, all of them TETs, displaced the cardiac silhouette to the right on the VD/DV view.

Cats

Of a total of 28 cats who met the inclusion criteria, 21 (75.0%) had lymphoma and 7 (25.0%) had a TET. Diagnoses of lymphoma were based on cytology of the CMM (n = 9), pleural fluid (n = 6), spleen (n = 2), peripheral lymph node (n = 1), or an unspecified site (n = 1); or histology of the CMM (n = 2). Of the 19 lymphomas

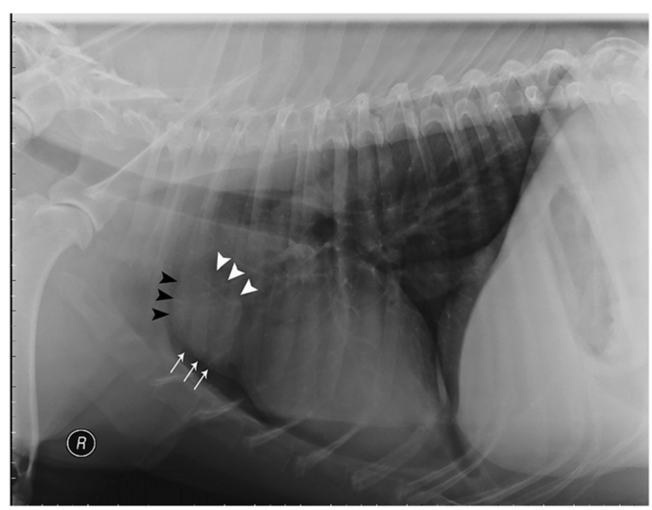

FIGURE 1 *Left lateral thoracic radiograph of a dog with a well-defined thymic epithelial tumor. The mass has discrete cranial (*black arrowheads*), dorsal (*white arrowheads*), and ventral (*white arrows*) margins.*

diagnosed by cytology, 16 were confirmed by slide review, and cytologic preparations were unavailable for 3. Of the lymphomas diagnosed by histology, one was confirmed by slide review, and histologic preparations were unavailable for one. Diagnoses of TETs were based on cytology (n = 2) or histology (n = 5) of the CMMs. All of these diagnoses were confirmed by slide review.

Breeds represented were domestic short-haired (16), domestic long-haired (5), Siamese (3), and 1 each of Bengal, Persian, Maine coon, and Tonkinese. There were 23 neutered male and 5 spayed female cats. The mean age at diagnosis was 8.2 yr (range 1.1–17.7 yr).

Two- and three-view studies were available for 15 and 13/28 cats, respectively. Images evaluated included 18 right and 10 left lateral views as well as 5 VD and 23 DV views. No radiographic variables were significantly associated with tumor type in cats.

Discussion

The present study showed that in dogs, the presence of two or more well-defined margins in a lateral radiograph and rightward displacement of the cardiac silhouette in a VD/DV radiograph were significantly associated with the presence of a TET. Clinicians should recognize that these radiographic parameters do not allow a definitive diagnosis of either lymphoma or TETs and do not obviate the need for fine needle aspiration or biopsy of a CMM. However, evaluation of these parameters may provide evidence of tumor type and may be useful to clinicians in providing clients with preliminary information regarding the staging and therapeutic measures that may be recommended once the tumor type is definitively established through cytology or histopathology.

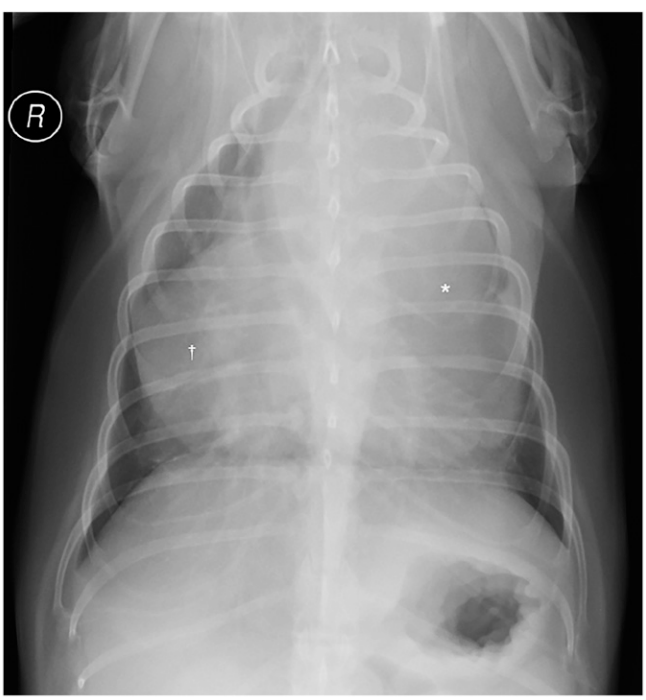

FIGURE 2 *Dorsoventral thoracic radiograph of a dog with a very large, left-sided thymic epithelial tumor (*) that is displacing the cardiac silhouette (†) to the right.*

Although investigation of the morphologic features of lymphomas and TETs that underlie their varying degrees of radiographic margination was beyond the scope of the study, the finding that TETs commonly had well-defined margins is consistent with the observation that they are often well circumscribed at surgery and are commonly encapsulated histologically.[12] It is possible that lymphoma may involve multiple mediastinal lymph nodes, resulting in radiographic summation of margins and contributing to the tumor's tendency to appear poorly marginated.[12] A limitation of the study was that variable degrees of superimposition of the foreleg musculature over the CMM may have reduced the proportion of margins considered to be well defined. The availability of only a single lateral view or a somewhat malpositioned lateral view in some cases may have had a similar effect. Because the degree of margination may vary in different regions of a given CMM, we elected not to consider masses to have well-defined margins unless the finding was present in at least two regions of a mass on a lateral view, and the same criterion should be used when the parameter is evaluated in clinical patients.

The finding that rightward displacement of the cardiac silhouette was associated with TETs likely reflects the anatomy of the normal canine thymus.[13] The organ is divided near the midline into right and left lobes; the right lobe typically abuts and terminates at the cranial surface of the pericardial sac, whereas the left lobe extends to approximately the level of the left ventricle. TETs arising in the left lobe may be ideally positioned to cause rightward displacement of the heart.

The most important limitation of the present study was the relatively small sample size, which likely limited the study's potential for identifying predictive parameters in both dogs and cats. Assessment of many of the radiographic parameters considered in the study is somewhat subjective, and prone to intra- or interobserver variability. In addition to margination, other parameters may have been significantly influenced by variability in patient positioning and radiographic technique at the time of image acquisition. Assessments of CMM size may have been influenced by variability in the radiographic views selected for individual patients, as there could be magnification of a left-sided mass in a right lateral view and vice versa. Finally, although lymphoma and TETs are by far the most common CMMs in both dogs and cats, less common CMMs, including benign mediastinal cysts, may resemble these tumors radiographically, increasing the importance of tissue sampling in establishing a definitive diagnosis.

Conclusion

In dogs, CMMs with at least two well-defined radiographic margins on a lateral view and CMMs causing rightward shift of the cardiac silhouette on a VD or DV view are significantly more likely to be TETs than lymphomas. No predictive radiographic variables were identified in cats, although this should be interpreted with caution as the cat sample size was limited.

FOOTNOTES

[a] Computed radiography; Carestream Health, Inc, Rochester, New York
[b] Carestream Health, Inc, Rochester, New York
[c] R: A language and environment for statistical computing. R Foundation for Statistical Computing; R Core Team, Vienna, Austria

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