COMPUTED TOMOGRAPHIC FINDINGS IN 24 DOGS WITH LIPOSARCOMA

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Computed tomography (CT) continues to become more widely available for assessment of tumors in dogs, yet there are no studies describing the CT appearance of canine liposarcomas. In this retrospective, multicenter study, CT images of dogs with histologically confirmed liposarcomas were reviewed for size, location, attenuation, contrast enhancement, border definition, internal homogeneity, local infiltration, and mineralization. A total of 24 dogs with 26 liposarcomas were sampled. Mean attenuation was +15.2 (SD = 22.3) Hounsfield units (HU) with a range of –36 to +47.5 HU based on representative regions of interest. Twenty tumors (77%) contained focal areas of fat attenuation. All masses enhanced with contrast medium administration, which is distinct from what has been reported previously in infiltrative lipomas. Other CT features associated with canine liposarcomas included heterogeneous internal attenuation (81%) and lack of a clearly defined capsule (38%) suggesting infiltration of local structures. Six tumors (23%) had foci of mineralization. Findings from the current study indicated that liposarcoma should be considered as a differential diagnosis for mixed-attenuation, contrast-enhancing masses in dogs that contain at least one focus of fat attenuation on precontrast images; however, presence of foci of fat attenuation was not a necessary finding for the diagnosis of canine liposarcoma.

Key words: Attenuation, canine, CT, liposarcoma.

Introduction

LIPOSARCOMAS ARE UNCOMMON MALIGNANT FATTY tumors in dogs that typically arise from subcutaneous sites and often occur at axial or appendicular locations.[1,2] Liposarcomas are further characterized histologically, according to the World Health Organization (WHO) grading for soft tissue sarcomas, as well differentiated, round cell, myxoid, dedifferentiated, or pleomorphic.[1,3–5] In human studies, well-differentiated tumors are most common, whereas in veterinary studies pleomorphic (77%) and grade 1 (54%) tumors have each been reported as most common.[2,6,7] The study reporting grade 1 disease used a numerical grading scheme separate from the WHO scheme mentioned above, with grade 1 corresponding to a low-grade sarcoma. Within the veterinary literature, few reports comparing the biologic behavior of the various histologic subclassifications of canine liposarcomas exist, but a retrospective study did not find prognostic differences between well differentiated, myxoid, or pleomorphic types.[2,8] Surgical resection with wide margins carries a dramatically better mean survival time (MST) than either marginal excision or incisional biopsy; MST for each procedure is 1188, 649, and 183 days, respectively.[1] Prognosis is considered good following proper surgical resection of liposarcomas and this differs from the recommended marginal excision of lipomas, which is considered curative.[1] Metastatic lesions in dogs, although rare, are most commonly found in the lung, abdominal organs, and bone.[1,2]

CT is commonly used in humans to evaluate liposarcomas. Numerous reports exist in the human literature that describe the CT appearance of fatty tumors.[4,9–15] Human studies have gone further to describe characteristic findings on CT that can aid in the differentiation between benign and malignant fatty tumors, and between histologic subtypes of liposarcoma.[4,9,10,12,16,17] Some studies have shown that using CT in conjunction with MRI increases the ability to differentiate between lipomas and liposarcomas.[12–15] CT findings in humans suggestive of a more malignant fatty abdominal tumor include inhomogeneity, infiltration, or poor margination, Hounsfield Units (HU) greater than the patient's normal fat, or contrast enhancement.[10]

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With the increasing widespread availability of CT, identification of imaging findings typical of liposarcoma in dogs could increase clinical suspicion and potentially spare more invasive techniques for diagnosis. The aim of this study was to describe the CT appearance of histologically confirmed liposarcomas in a group of dogs.

Materials and Methods

Dogs with a histologically confirmed liposarcoma that had undergone a CT examination were recruited by emailing American College of Veterinary Radiology diplomates. Inclusion criteria were a CT scan of the mass and a histopathologic diagnosis of liposarcoma based on excisional, incisional, or needle biopsy. Dogs with only a cytologic diagnosis of liposarcoma were excluded from the study. Breed, age, gender, history, clinical signs, and diagnostic methods were extracted from medical records when available. Computed tomography scans were performed according to each institution's own protocol and information regarding kVp, mAs, reconstruction algorithm, slice thickness, and patient positioning were not available for all cases. Intravenous contrast medium was given to all dogs, but data regarding contrast medium dose and timing of the postcontrast scans relative to contrast administration were not available for most cases.

All CT studies were reviewed by the primary author (J.A.F.) and two board-certified veterinary radiologists (J.K.R. and D.S.), and findings were recorded based on consensus. Images were evaluated using a dedicated DICOM viewing software (eFilm v3.3, Merge Healthcare, Hartland, WI) using a soft-tissue window (width: 350; level: 40). If bone involvement was suspected, images were further reviewed in a bone window (width: 2000, level: 600). Mass size in three dimensions, clear encapsulation vs. nonencapsulation (nonencapsulation suggesting infiltration of surrounding structures), internal precontrast homogeneity (hetero- vs. homogeneous), presence of mineralization, presence of contrast-medium enhancement, and regional lymph node symmetry were analyzed. Tumors were considered to be nonencapsulated if margins were poorly defined; tumors were considered encapsulated if there was a sharp distinction between tumor and surrounding tissues. Internal homogeneity was considered heterogeneous if attenuation subjectively varied and it was considered homogeneous if subjectively of uniform appearance. A representative region of interest (ROI) was obtained to calculate mean HU pre- and postcontrast medium administration; the largest possible ROI that subjectively represented the overall mass architecture was selected, areas of mineral attenuation and tumor margins were avoided. Also, to establish intratumoral attenuation ranges, focal minimum and maximum HU measurements pre- and postcontrast were recorded.

Results

A total of 28 dogs with liposarcomas imaged with CT were identified from eight institutions during the period 2004–2015. Two dogs were excluded due to only having a cytologic diagnosis and two dogs were excluded due to the CT scans being acquired after surgical mass excision. This left 24 dogs included in the study comprising a total of 26 tumors (one dog presented with three separate liposarcomas). Breeds included Labrador Retriever (6), unspecified (3), and one each of Dalmatian, Bernese Mountain Dog, Siberian Husky, Bassett Hound, Lhasa Apso,

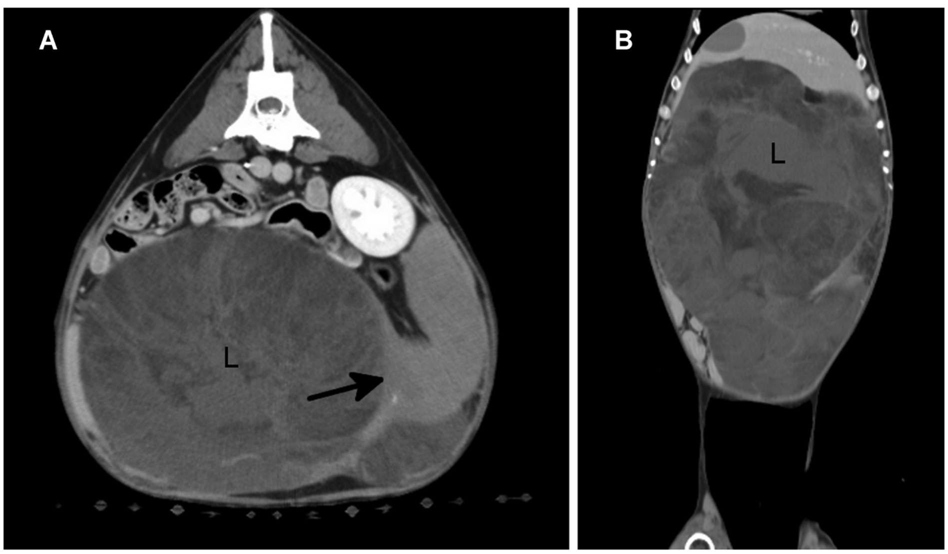

FIG. 1. Transverse (A) and dorsal (B) postcontrast CT images (W:350, L:40) of a dog with an omental liposarcoma (L). In the transverse image, the margins between the mass and the spleen are poorly defined, and splenic infiltration was suspected on CT (arrow), but no invasion of the splenic capsule was identified on histopathology.

TABLE 1. CT Scanners Used Across Eight Institutions

Name	Manufacturer	Location	Slices
Sensation 16	Siemens Medical Solutions	Hoffman Estates, IL	16
Sensation 64	Siemens Medical Solutions	Hoffman Estates, IL	64
Aquilion 16	Toshiba American Medical Systems, Inc.	Tustin, CA	16
GE HiSpeed CT/i	GE Healthcare	Pewaukee, WI	1
GE LightSpeed QX/i	GE Healthcare	Pewaukee, WI	4
GE BrightSpeed	GE Healthcare	Pewaukee, WI	16
Sytec Sri	GE Healthcare	Pewaukee, WI	1
Gemini TF Big Bore	Philips	Andover, MA	16
PQ 5000	Picker	Highland Heights, OH	1

TABLE 2. Computed Tomographic Findings in 26 Liposarcomas ($n = 24$ Dogs)

CT Parameter	Value
Mean (SD) length (cm)	9.3 (7.0)
Mean (SD) width (cm)	6.3 (4.8)
Mean (SD) height (cm)	6.9 (4.2)
Mean (SD) precontrast HU	15.2 (22.3)
Mean (SD) postcontrast HU	42.3 (29.3)
Contrast enhancement	26 (100%)
Precontrast ROI attenuation >0 HU	18 (69%)
Encapsulated	16 (62%)
Nonencapsulated	10 (38%)
Heterogeneous appearance*	21 (81%)
Homogeneous appearance*	5 (19%)
Mineral attenuation	6 (23%)

SD, standard deviation, HU, Hounsfield Units, ROI, region of interest.
*Subjective homo- vs. heterogeneous appearance did not change appreciably with the addition of contrast, although mean HU did increase.

German Shepherd Dog, Chinese Crested, Shetland Sheepdog, Beagle, Rottweiler, Chihuahua, Manchester Terrier, Bichon Frise, Poodle mix, and Terrier mix. The dogs ranged in age from 4 to 15 years with a mean of 11 years. There were 12 neutered males (50%), four intact males (17%), and eight spayed females (33%). Twenty-one dogs (81%) presented for a noticeable/palpable mass; of these, 18 (75%) had no other clinical signs. Other clinical signs, when present, included lameness (4), decreased appetite (3), lethargy (2), pain (2), enlarged lymph node (2), vomiting (1), weight loss (1), cough (1), dyspnea (1), muffled heart sounds (1), and dysphagia (1). One of the dogs that presented for decreased appetite had an omental liposarcoma, which was only identified following physical examination (Fig. 1). The dog that presented with coughing and dyspnea had a mediastinal liposarcoma; there was no appreciable mass on physical examination and the mass was discovered on thoracic radiographs. The dog that presented with dysphagia presented initially for periodontal cleaning and had three lingual liposarcomas identified during oral examination while under general anesthesia.

Eighteen masses (69%) were surgically excised and submitted for histopathology, with eight masses (31%) sampled via punch or needle biopsies. Mass location included the thoracic limb (5), thoracic wall (5), neck (4), axillary region (3), tongue (3), pelvic limb (2), omentum (1), mediastinum (1), shoulder (1), and hip (1). Pathology reports varied with respect to histologic grading of the liposarcoma, with some histopathology reports providing no further classification beyond liposarcoma. For this reason, comparisons among histologic subtype classifications were not possible. The histopathological report and CT images of the dog with three lingual masses did not identify any interconnection between the masses and they were included in this study as three separate masses.

Computed tomography images were acquired using various helical scanners across eight institutions (Table 1) and results of CT interpretations are summarized in Table 2. Mean maximal length, width, and height (SD; range) of the masses, in centimeters, were 9.3 (7.0; 2.0–31.3), 6.3 (4.8; 1.1–23.1), and 6.9 (4.2; 1.5–15.5), respectively. Of the 26 tumors, 6 (23%) had mineral-attenuating areas (Fig. 2). Sixteen tumors (62%) were considered encapsulated. Internal homogeneity was highly variable with 21 (81%) heterogeneous in appearance and 5 (19%) homogeneous. The mean precontrast attenuation (SD; range) of the ROI for each

FIG. 2. Precontrast transverse CT image (W: 350, L:40) of a dog with a liposarcoma in the left thoracic limb (L). Mineral attenuation (arrow) can be seen in the periphery of the mass.

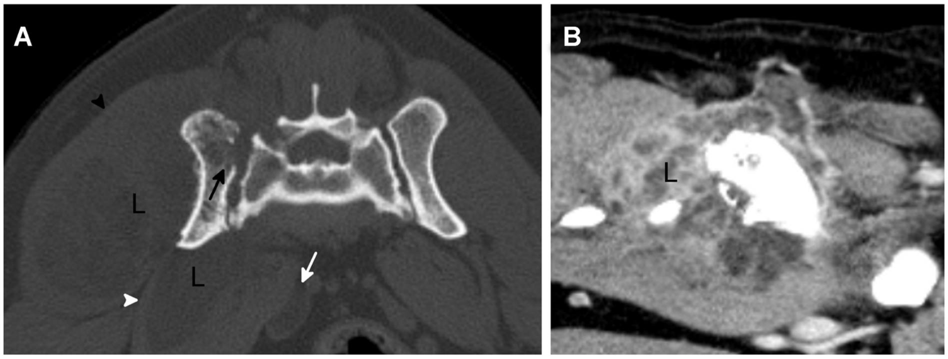

FIG. 3. Precontrast transverse (A) and postcontrast sagittal (B) CT images in a bone window (W:2000, L:600) and soft tissue window (W:350, L:40), respectively. A liposarcoma (L) is infiltrating the right gluteus medius (black arrowhead), iliopsoas (white arrowhead), and related muscles. Local infiltration into the right ilium (black arrow) is present with some regional periosteal reaction. The tumor also passes through the pelvic canal (not pictured) and can be seen invading the right external iliac vein (white arrow).

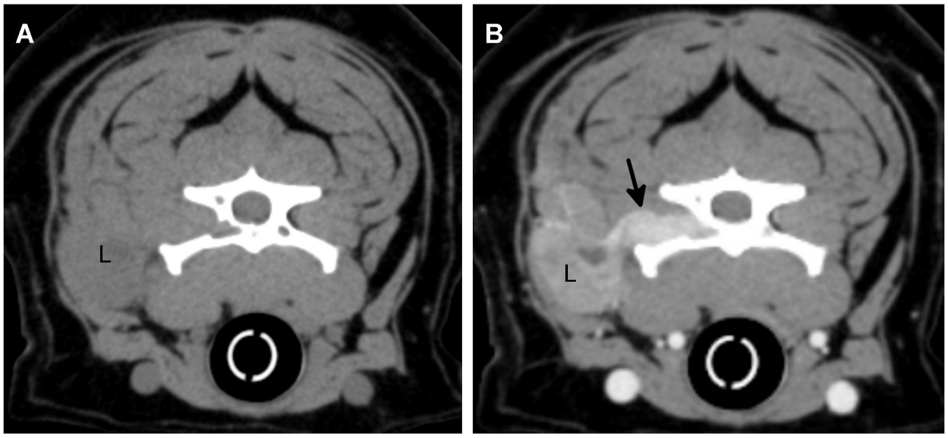

FIG. 4. Precontrast (A) and postcontrast (B) CT images (W: 350, L:40) of a dog with a cervical liposarcoma (L) showing local infiltration of the fifth cervical spinal nerve (arrow). Infiltration is not readily distinguished on the precontrast image.

mass was +15.2 (22.3; –36 to +47.5) HU and the mean postcontrast attenuation was +42.3 (29.3; –9.5 to +105) HU. The range of focal attenuations for all masses on precontrast images was –140 to +600 HU; this changed slightly on postcontrast images, which had a range of –133 to + 600 HU. Eighteen masses (69%) had a precontrast mean ROI attenuation greater than 0 HU; however, 12 of these had foci of fat attenuation. Twenty masses (77%) had a focus of fat attenuation and 6 (23%) had no identifiable fat attenuation on precontrast images. Following contrast medium administration, the focal minimum and mean ROI attenuations of all masses increased, resulting in the elimination of any fat attenuating values in five of the 20 masses that had foci of fat attenuation (25%).

Nonencapsulated masses with local infiltration on CT were observed in 10 dogs (38%) and included regional musculature (9), bone (2), fifth cervical spinal nerve (1), larynx (1), and spleen (1) (Figs. 3 and 4). The mass with suspected

TABLE 3. Computed Tomographic Findings in Seven of 26 Liposarcomas That Were Subclassified ($n = 24$ Dogs).*

Histopathologic subclassification	Attenuation mean (HU)	Attenuation range (HU)	Internal homogeneity	Presence of infiltration
Well differentiated	−11	–48–34	Heterogeneous	No
Well differentiated	41.5	9–48	Heterogeneous	Yes (muscle)
Grade 1	–6.1	–76–32	Heterogeneous	Yes (muscle)
Grade 1	31.3	10–45	Homogeneous	No
Grade 1	42.5	–12–45	Heterogeneous	No
Grade 2	–16.2	–90–83	Heterogeneous	Yes (muscle)
Grade 2	16.3	–33–67	Heterogeneous	Yes (muscle, connective tissue)

HU, Hounsfield units.
*Only two of these tumors followed the classification scheme proposed by the World Health Organization for liposarcomas.

splenic infiltration on CT did not breach the splenic capsule when examined histologically and was proven to not actually infiltrate the splenic parenchyma despite CT findings. The dog with the mediastinal liposarcoma also had numerous contrast-enhancing masses that appeared to arise from the pleura; histopathology reports were not available for these additional masses to confirm extension or metastasis. Regional lymph nodes were thought to be asymmetric in size in five dogs (19%), but there was no information available in the medical records regarding the lymph nodes in these cases. Seven tumors were further classified: two were reported as well differentiated, three as grade 1, and 2 as grade 2 (Table 3). Due to the small number of tumors classified according to WHO guidelines, correlation with imaging characteristics was not performed.

Discussion

The most common clinical sign in this study was a noticeable mass, which is consistent with prior human and veterinary studies.[2,11] Liposarcomas in this study frequently exhibited soft-tissue attenuation or had mixed attenuation of both fat and soft tissue, with all tumors having a precontrast mean ROI attenuation between –50 and +50 HU. Additionally, 69% of tumors had precontrast mean ROI attenuations greater than 0. It is important to note, however, that despite all masses having a mean ROI attenuation between fat and soft tissue, a majority of tumors in this study (77%) still contained at least some foci of fat attenuation. With these findings, it is the authors' recommendation that liposarcoma should be included as a differential diagnosis for any soft-tissue attenuating mass that contains foci of fat attenuation. As the representative ROI of each mass was selected subjectively, it is possible that the ROI attenuations obtained did not accurately reflect the average attenuation of the masses. It is possible that the ROIs may have included small, mineralized areas despite efforts to avoid them, and this could have resulted in overestimation. Authors also acknowledge that attenuation values could have been affected by the widely varying scanners and technical protocols.

The finding of a mean precontrast attenuation greater than fat is similar to a human study investigating attenuation of fatty tumors where five liposarcomas were found to have attenuations spanning from –80 HU to +60 HU,[10] although the maximum attenuation in our study was far greater due to the presence of highly mineralized areas in some tumors that were not present in the human report. It is interesting to note that the presence of mineralization within retroperitoneal liposarcomas in people has been shown to be a poor prognostic indicator.[18] In our study, five of the six mineralized masses were considered encapsulated with no discernable local infiltration, which, according to human studies, would suggest more benign disease.

In human studies, well-differentiated liposarcomas are predominantly fat attenuating.[14,19] In our study, only eight of 26 masses had a negative precontrast mean ROI attenuation. Because masses were not further classified, it is possible that our population contained a higher proportion of poorly differentiated masses since other human studies found that myxoid, pleomorphic, and dedifferentiated types typically show attenuation above 0.[14,19] Even though veterinary reports disagree regarding what is the most common histologic type of canine liposarcoma, this would corroborate those reports that well-differentiated disease is not the most commonly encountered. These findings, however, may represent a selection bias as dogs with more extensive morbidity or aggressive disease are more likely to undergo diagnostics.

Contrast medium enhancement occurred in all masses included in this study. This is distinct from lipomas as a canine CT study of dogs with infiltrative lipomas found no enhancement after administration of contrast medium to 11 dogs.[20] The presence of contrast medium enhancement is thus potentially an important CT marker between liposarcomas and lipomas and is likely due to the larger soft tissue component of liposarcomas. Furthermore, that same study reported canine lipomas to be fully fat attenuating,[20] whereas every tumor in this review contained tissue with attenuation higher than fat. These two distinct characteristics can therefore be used to aid in the differentiation between liposarcomas and lipomas on CT. The reason why liposarcomas enhance with contrast medium while lipomas fail to do so is unknown, but could be related to the higher perfusion or angiogenesis in these more aggressive tumors. Despite contrast enhancement occurring in all cases, over half of the masses retained foci of fat attenuation.

Nearly half of the masses studied were considered nonencapsulated, which is similar to previous reports.[1,10] The omental liposarcoma with suspected splenic invasion on CT was proven to not breach the splenic capsule histologically, thus suggesting that CT may overestimate the extent of local invasion and may be limited in its ability to differentiate between invasion and intimate association; however, imaging parameters were not included in this study and could play a role. Depending on slice thickness, for example, volume averaging artifact could result in two distinct structures (in this case, the spleen and the omental tumor) appearing to blend as one causing the appearance of invasion on CT images. Previous human studies have documented that CT is not always able to accurately assess infiltration.[21] All 10 of the nonencapsulated masses extended into regional musculature. Although rare in this study, two masses invaded bone and one invaded into the laryngeal cartilage. The authors found a single case report documenting osseous invasion of liposarcoma in a dog with the invasion occurring in L5–7, the sacrum, and the ilium;[22] interestingly, the osseous structures involved in our study were vertebral bodies (both dogs) and the ilium (one dog). Neither of the masses that invaded osseous structures in this study was subclassified histologically, but both had indistinct borders and heterogeneous internal appearance, which, according to human studies, would suggest more aggressive disease.[10]

This study has several limitations. First, there is variability among the data given the retrospective and multi-institutional nature of the study. CT protocols were not standardized among the institutions. Histologic samples were reviewed by multiple pathologists and histopathologic classifications were not standardized. Also, internal control for HU was not performed that could affect the attenuations recorded in this study. Further studies with standardized imaging and contrast protocols, as well as standardized histologic classifications with a single pathologist would be needed for further evaluation. Comparison between histologic subtypes could potentially yield distinctive characteristic CT appearances that would allow more accurate diagnosis based on imaging alone. Also, comparing CT and MR images of canine liposarcomas, as has been done in humans, may potentially improve the likelihood of finding characteristic lesions.

This study identified contrast enhancement within all liposarcomas imaged, which is disparate from that described with lipomas. Also, despite a large range of attenuation values, internal heterogeneity, and encapsulation vs. nonencapsulation, the imaging characteristics of liposarcomas found in this study are distinct from previous descriptions of lipomas and confusion between the two mass types on CT is unlikely. The presence of fat attenuating regions in any soft-tissue mass on CT should cause the clinician to include liposarcoma as a possible differential diagnosis; however, CT cannot replace the role of histopathology for definitive diagnosis.

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Category 1

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(b) Acquisition of Data: Jean K. Reichle, David Szabo, Eli B. Cohen, David S. Biller, Justin M. Goggin, Anthony J. Fischetti, Susan E. Emerson, Stacie Aarsvold, John F. Griffin IV.
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Category 2

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Category 3

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