Retrospective Evaluation of Three Treatment Methods for Primary Hyperparathyroidism in Dogs

The medical records of 110 dogs treated for primary hyperparathyroidism were reviewed. Dogs were treated via parathyroidectomy (n=47), percutaneous ultrasound-guided ethanol ablation (n=15), or percutaneous ultrasound-guided heat ablation (n=48). Forty-five of 48 (94%) parathyroidectomies resulted in control of hypercalcemia for a median of 561 days. Thirteen of 18 (72%) ethanol ablation procedures resulted in control of hypercalcemia for a median of 540 days. Forty-four of 49 (90%) heat-ablation treatments resulted in control of hypercalcemia for a median of 581 days. J Am Anim Hosp Assoc 2007;43:70-77.

Introduction

In dogs with naturally occurring primary hyperparathyroidism, hypercalcemia develops secondary to autonomous production of parathyroid hormone (PTH).\textsuperscript{1,2} The condition is most commonly caused by a solitary parathyroid gland adenoma.\textsuperscript{3,4} Less commonly, the condition develops as a result of a parathyroid gland carcinoma or autonomously functioning hyperplastic parathyroid gland(s).\textsuperscript{5} About 10\% of afflicted dogs have two abnormal parathyroid glands, either simultaneously or sequentially.\textsuperscript{6,7}

Naturally occurring primary hyperparathyroidism is usually suspected in a dog with hypercalcemia, mild clinical signs, and a serum phosphorous concentration within or less than the reference range.\textsuperscript{8} Serum PTH concentrations within or above the reference range help confirm the diagnosis.\textsuperscript{9-11} In the past two decades, cervical ultrasonography has been used as a diagnostic aid for dogs with hypercalcemia.\textsuperscript{12} Dogs with primary hyperparathyroidism usually have a solitary round or oval hypoechoic mass in close association with one thyroid lobe.\textsuperscript{6,7,9,12,13} Abnormal parathyroid nodules usually measure 4 to 6 mm, but they can be as large as 20 mm in their greatest dimension.\textsuperscript{6,7,9,12,13} Once the condition has been confirmed, surgical removal of the abnormal parathyroid gland or glands has been a permanent treatment option. More recently, novel therapeutic strategies using ultrasound-guided alcohol or heat ablation have been described, but reports have had limited numbers of dogs and short follow-up times.\textsuperscript{14-16} The purposes of this study were to evaluate and compare the treatment of primary hyperparathyroidism via surgery, ethanol ablation, and chemical ablation in a larger group of dogs and to determine the long-term efficacy of the three treatments.

Materials and Methods

Medical records of dogs diagnosed with naturally occurring primary hyperparathyroidism between November 1997 (date of the first ultrasound-guided percutaneous treatment procedure) and March 2005 were reviewed. Diagnosis of primary hyperparathyroidism was based on physical examination, phosphorous concentration within or below the reference
range, repeatable hypercalcemia, PTH concentration within or above the reference range, and one or two parathyroid glands visualized on ultrasonography or at surgery. All dogs that had surgery had excised tissue evaluated histopathologically. All dogs entered in the study were treated for primary hyperparathyroidism and had calcium concentrations evaluated once daily for 6 days and at 90 days after treatment. Dogs were excluded from the study if metastasis was seen on thoracic radiography.

Medical records for dogs with primary hyperparathyroidism were reviewed for signalment, clinical signs, total serum calcium concentrations, plasma ionized calcium concentrations, PTH concentrations, diagnostic imaging, treatment method, date of treatment, and response to treatment. Routine methods were used to perform serum biochemical analyses, CBCs, and urinalyses. Serum total calcium concentration was determined by colorimetric evaluation. Serum ionized calcium concentration was determined by ion-selective electrode analysis. Serum PTH concentration was determined by use of a validated, two-site immunoradiometric method that recognizes amino- and carboxy-terminal ends of the intact molecule. All PTH assays were performed in the clinical chemistry laboratory at the University of California, Davis, or at the endocrine laboratory at Michigan State University. Ultrasonography of the neck was performed with a 10-MHz linear, phased-array transducer and a standard ultrasonography machine. Arbitrarily, dogs with a parathyroid mass >12 mm at its greatest dimension were treated with surgery. Other treatments were chosen by the primary clinician after discussions with the owners.

**Therapeutic Techniques**

Treatments employed for primary hyperparathyroidism associated with parathyroid mass(es) were surgical removal, ultrasound-guided alcohol ablation, or ultrasound-guided heat ablation, as previously described. Alcohol ablation was performed with the dog under general anesthesia. The parathyroid nodule was located with ultrasonography, and 96% ethanol was injected into the parathyroid gland via a 27-gauge needle until the entire gland was infiltrated. Heat ablation was performed in a similar manner, with the animal under anesthesia while the abnormal parathyroid tissue was visualized with ultrasonography. With the dog lying on a cautery ground pad, a 20-gauge, over-the-needle intravenous catheter was placed into the parathyroid gland, and radiofrequency energy was applied at 10 to 20 W until the entire gland became hyperchoic. The needle was occasionally redirected in both procedures to try to ablate the entire gland. The ultrasound procedures were performed by numerous radiology clinicians and residents.

Complications following treatment were recorded from the medical record. Treatment was considered successful if complete resolution of hypercalcemia was documented at 6 and 90 days after therapy. The dates, timing, and chronological order of the successful and unsuccessful treatments were reviewed. Follow-up examinations were performed by the local veterinarian or by the primary clinician and always included measurement of a serum calcium concentration.

**Statistical Analysis**

Data are reported as means ± standard deviation (SD). Two-tailed t-tests were used to compare results between dogs in the different treatment groups. Laboratory data included serum calcium, ionized calcium, and PTH concentrations, as well as the length of time required for the calcium to fall within reference range after treatment. Fisher’s exact tests were used to compare the outcomes of the treatment groups. All analyses were performed with standard statistical software. A P value <0.05 was considered significant.

**Results**

A total of 110 dogs were included in the study, and the signalment data are presented in Table 1. The most commonly affected breed was the keeshond (n=21), followed by the mixed-breed dog (n=18), Labrador retriever (n=9), German shepherd dog (n=7), golden retriever (n=6), miniature poodle (n=6), shih tzu (n=5), Australian shepherd (n=4), Rhodesian ridgeback (n=3), and American cocker spaniel (n=3). The remaining 28 dogs comprised 18 other breeds. Each treatment group was composed of numerous breeds. The most common clinical signs reported in the dogs are presented in Table 2. Hypercalcemia was an incidental finding on routine geriatric or preanesthetic laboratory screenings in 42 of the 110 dogs. The pertinent laboratory findings are presented in Table 3.

Cervical ultrasonography was performed on all 110 dogs, and all dogs had one (n=96) or two (n=14) masses visualized that were consistent with abnormally enlarged parathyroid glands. Of the 14 dogs with two parathyroid nodules identified, nine had bilateral masses and five had two ipsilateral masses. Twelve dogs had a parathyroid mass that measured >12 mm. Forty-seven dogs were treated with parathyroidectomy, 15 dogs were treated with ethanol ablation, and 48 dogs were treated with heat ablation. The 47 dogs treated with surgery had 56 nodules based on ultrasonography. Thirty-eight dogs had a single nodule, and nine dogs had two nodules (bilateral n=7, ipsilateral n=2). The 15 dogs treated with ethanol ablation all had a single nodule. The 48 dogs treated with heat ablation had 53 nodules; 43 dogs had a single nodule, and five dogs had two nodules (bilateral n=3, ipsilateral n=2). The number of successful and failed treatments and follow-up times after therapy are presented in Table 4. Fisher’s exact tests showed no significant differences in the outcomes between parathyroidectomy and heat ablation (P=0.71) and between heat ablation and ethanol ablation (P=0.12). A significant difference in outcomes was found between parathyroidectomy and ethanol ablation (P=0.03).

Hypercalcemia resolved in 44 of the 47 dogs treated with one surgery within 1 to 6 days (mean 1.6±1.1 days). Either serum total or ionized calcium concentration returned to normal within 48 hours in 29 dogs. Hypercalcemia resolved in 3 to 4 days in 13 dogs and in 4 to 6 days in two dogs.
Hypercalcemia failed to resolve after parathyroidectomy in three dogs. Two of these three dogs were not treated again, and one had a second parathyroidectomy 30 days later, with complete resolution of the hypercalcemia within 48 hours. The two dogs not treated again had no parathyroid tissue identified in histopathological samples. Based on pathology of the 54 surgically excised glands from 45 dogs, parathyroid adenoma was the most common lesion (n=42), followed by glandular hyperplasia (n=9) and adenocarcinomas (n=3).

Twelve of 15 dogs were treated successfully with one ethanol ablation, with hypercalcemia resolving in 1 to 4 days (mean 1.9±1.4 days). Either serum total or ionized calcium concentrations decreased to the reference range values within 48 hours in 10 dogs. Hypercalcemia resolved in 3 days in one dog and in 4 days in one dog. One dog remained hypercalcemic after an initial ethanol ablation, but it responded to a second ablation procedure, and the calcium concentration returned to normal within 48 hours. Two other dogs remained hypercalcemic after two separate percutaneous ethanol injections. A total of 18 ablation procedures were performed in the 15 dogs, with five considered to be failures.

Forty-three of 48 dogs treated with percutaneous ultrasound-guided heat ablation had resolution of hypercalcemia after one treatment, and one dog responded after a second treatment. Two dogs had ipsilateral masses, and both masses were ablated at the same time, with resolution of the hypercalcemia. Three dogs had bilateral masses. Two of these dogs had one nodule ablated initially, and the second nodule was ablated 30 days later. The procedures were staged in order to minimize the risk of bilateral laryngeal paralysis. Hypercalcemia resolved after the second gland

<table>
<thead>
<tr>
<th>Treatment Group*</th>
<th>Age Range (y) (mean ± SD)</th>
<th>Gender‡</th>
<th>Weight Range (kg) (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery (n=47)</td>
<td>6.6-14 (10.7±2.7)</td>
<td>M=3</td>
<td>11-58.8 (25.2±14.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CM=23</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>F=0</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>SF=21</td>
<td></td>
</tr>
<tr>
<td>Ethanol ablation (n=15)</td>
<td>6-15.75 (10.1±3.6)</td>
<td>M=1</td>
<td>5.2-52.2 (26.8±15.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CM=8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>F=0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SF=6</td>
<td></td>
</tr>
<tr>
<td>Heat ablation (n=48)</td>
<td>8.33-16 (11.5±2.9)</td>
<td>M=0</td>
<td>2.8-45 (20.8±14.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CM=23</td>
<td></td>
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<tr>
<td></td>
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<td>F=0</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>SF=25</td>
<td></td>
</tr>
<tr>
<td>Total study population (n=110)</td>
<td>6-16 (11.1±3.0)</td>
<td>M=4</td>
<td>2.8-58.8 (22.4±15.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CM=54</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>F=0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SF=52</td>
<td></td>
</tr>
</tbody>
</table>

* n=number of dogs
† SD=standard deviation
‡ M=male; CM=castrated male; F=female; SF=spayed female
was treated in both dogs, and these dogs were treated as single treatment successes. The third dog had complete resolution of hypercalcemia after an ablation procedure was performed on the larger of the two parathyroid masses. The smaller gland, therefore, was not treated, and hypercalcemia did not recur.

A total of 43 dogs were treated successfully with one heat ablation treatment, with hypercalcemia resolving in 1 to 6 days (mean 2.3±1.3 days). Mean time to resolution was significantly longer than that for the surgically treated dogs (P=0.001) and the ethanol-treated dogs (P=0.004). Either serum total or ionized calcium concentration decreased to reference range values within 48 hours in 32 dogs, while six dogs required 2 to 4 days, and six dogs required 4 to 6 days. Hypercalcemia failed to resolve in one dog after the initial treatment, but it resolved after a second treatment. The calcium concentration returned to normal within 48 hours of the second treatment. Four other dogs failed to respond to one percutaneous heat treatment, and they were not treated a second time. A total of 49 treatments were performed, with five considered to be failures.

It was interesting to note that in the heat ablation treatment group, three of the four treatment failures were among the first 24 procedures performed. If the dogs are separated into three groups of 16 based on chronology of treatment, the first group had three treatment failures, the second group had one, and the third group had none. If the dogs treated with ethanol ablation are added to those treated with heat ablation (63 dogs total), there were six treatment failures among the first 31 dogs treated and one treatment failure among the second 32 dogs treated.

Hypocalcemia was the most common complication noted after treatment in all three treatment groups. Other complications were few and are presented in Table 5. Delayed recurrence of hypercalcemia was noted in two dogs treated with surgery. Hypercalcemia recurred in one dog 305 days after surgery and at 687 days after surgery in the other dog. Both dogs underwent a second surgery for a parathyroid gland adenoma contralateral to the initial mass. Hypercalcemia resolved in both dogs after the second procedure. Relapse of hypercalcemia also occurred in one dog 477 days after ultrasound-guided heat ablation treatment. This dog underwent a second successful heat ablation treatment of a contralateral parathyroid gland.

Discussion

Overall, the responses to all three treatment modalities for primary hyperparathyroidism were good. There was no statistical significance between the success rates for parathyroidectomy and heat ablation, but there was a statistical significance between the success rates for parathyroidectomy and ethanol ablation. There was no statistical significance between the success rates for heat ablation and ethanol ablation. The total number of dogs in the ethanol ablation group was less than the total number of dogs in the surgery and heat ablation groups, which may have affected the statistical outcome between the groups. Dogs treated with heat ablation had similar outcomes to dogs treated with parathyroidectomy.

Surgery (i.e., parathyroidectomy) has been used as a treatment for primary hyperparathyroidism for decades. Previous studies have not reported any failures. In the current study, three surgeries failed to control hypercalcemia, and no parathyroid tissue was detected on histopathology of these cases. These surgical failures arose from an inability to locate the abnormal parathyroid tissue. Despite ultrasonographic identification of a mass, the ultrasound may not have correctly identified the abnormal gland.

Ethanol ablation for dogs with primary hyperparathyroidism was first described in 1999. In the original study, a total of nine treatments were performed in eight dogs, and seven treatments were successful. Six dogs were evaluated 6 months after therapy, and all had normal calcium concentrations. A more recent study in 2005 discussed five dogs treated with ethanol ablation; two dogs had a decline in calcium concentrations, but all dogs continued to have hypercalcemia and were considered failures. These two studies had very different outcomes. The dogs in the earlier study had similar outcomes to the dogs in the study reported here. The current study contained a larger number of dogs treated with ethanol ablation, with longer follow-up times. Needle insertion into a parathyroid tumor using ultrasound guidance is a relatively new approach. It is often necessary to redirect the needle several times during either ethanol or heat ablation when attempting to ablate all abnormal tissue. In the study reported here, the incidence of ethanol treatment failure may have been minimized, in part, by having an experienced radiologist involved with each procedure.

One previous report exists on the use of heat ablation for primary hyperparathyroidism in dogs. In that study, nine

### Table 2

**Clinical Signs of 110 Dogs With Primary Hyperparathyroidism**

<table>
<thead>
<tr>
<th>Clinical Signs</th>
<th>No. of Dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyuria, polydipsia</td>
<td>47</td>
</tr>
<tr>
<td>Weakness</td>
<td>46</td>
</tr>
<tr>
<td>Lethargy</td>
<td>42</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>35</td>
</tr>
<tr>
<td>Weight loss or muscle wasting</td>
<td>21</td>
</tr>
<tr>
<td>Vomiting</td>
<td>11</td>
</tr>
<tr>
<td>Shivering or trembling</td>
<td>7</td>
</tr>
</tbody>
</table>

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Table 3
Clinicopathological Data Prior to Treatment in 110 Dogs With Primary Hyperparathyroidism

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>Reference Range</th>
<th>Mean ± SD&lt;sup&gt;*&lt;/sup&gt; for All Dogs</th>
<th>Mean ± SD for Surgery Group</th>
<th>Mean ± SD for Ethanol Ablation Group</th>
<th>Mean ± SD for Heat Ablation Group</th>
<th>P Value&lt;sup&gt;†&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total serum calcium (mg/dL)</td>
<td>9.9-11.4</td>
<td>14.3±1.7</td>
<td>14.5±1.48</td>
<td>13.9±1.55</td>
<td>14.3±1.38</td>
<td>0.12</td>
</tr>
<tr>
<td>Plasma ionized calcium (mm/L)</td>
<td>1.1-1.4</td>
<td>1.79±0.21</td>
<td>1.82±0.25</td>
<td>1.77±0.25</td>
<td>1.76±0.23</td>
<td>0.18</td>
</tr>
<tr>
<td>PTH&lt;sup&gt;‡&lt;/sup&gt; (pmol/L)</td>
<td>2-13</td>
<td>12.7±8.3</td>
<td>12.3±7.7</td>
<td>12.8±8.55</td>
<td>12.9±9.38</td>
<td>0.14</td>
</tr>
</tbody>
</table>

<sup>⁎</sup> SD=standard deviation

<sup>†</sup> P value <0.05 is significant; parameters from each treatment group were compared to the other two treatment groups using student t tests.

<sup>‡</sup> PTH=parathyroid hormone
Table 4
Treatments and Outcomes for 110 Dogs Diagnosed With Primary Hyperparathyroidism

<table>
<thead>
<tr>
<th>Treatment Type</th>
<th>No. of Dogs Treated</th>
<th>No. of Procedures Performed</th>
<th>No. of Successful Procedures (%)</th>
<th>No. of Dogs Successfully Treated (%)</th>
<th>Length of Follow-up (d)</th>
<th>Median ± SD* Follow-up (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical parathyroidectomy</td>
<td>47</td>
<td>48</td>
<td>45 (94%)</td>
<td>45 (96%)</td>
<td>90-1857</td>
<td>561±367</td>
</tr>
<tr>
<td>Ethanol ablation</td>
<td>15</td>
<td>18</td>
<td>13 (72%)</td>
<td>13 (87%)</td>
<td>120-1477</td>
<td>540±406</td>
</tr>
<tr>
<td>Heat ablation</td>
<td>48</td>
<td>49</td>
<td>44 (90%)</td>
<td>44 (92%)</td>
<td>100-1165</td>
<td>581±388</td>
</tr>
<tr>
<td>Total study population</td>
<td>110</td>
<td>115</td>
<td>102 (89%)</td>
<td>102 (93%)</td>
<td>90-1857</td>
<td>566±386</td>
</tr>
</tbody>
</table>

* SD=standard deviation
dogs had a total of 12 treatments, and eight were successful.15 These dogs were followed for 3 to 8 months.15 The dogs in the current study had similar outcomes, and there were more dogs in the current study, with longer follow-up times. When ultrasound-guided heat ablation was used to treat hyperthyroidism in cats, the procedure controlled the disease for a mean of 4 months.17 It was important, therefore, in the current study to evaluate long-term efficacy of all treatments. The median follow-up time for all of the dogs in the study reported here was 560 days. Both percutaneous ethanol and heat ablation procedures provided long-term control of the hypercalcemia in the majority of cases. The decrease in treatment failures with the ultrasound-guided procedures over time may have indicated that improved skill gained from experience had a positive impact on outcome.

All dogs that had a successful procedure performed, regardless of type, had calcium concentrations within the reference range within 6 days after the therapy. In previous studies of dogs treated for primary hyperparathyroidism with surgery, ethanol ablation, or heat ablation, the majority of dogs had resolution of hypercalcemia within 48 hours of therapy, which is similar to the dogs reported in this study.14-16 In the current study, calcium took a significantly longer time to return to normal after heat ablation when compared to times after surgery and ethanol treatment. The statistical difference may have occurred because of the pathophysiology of heat ablation.18

Thermal necrosis causes cell death that can continue to occur after the heat ablation procedure is terminated. The effects of parathyroidectomy are immediate, because the tissue is excised. The time difference between heat ablation and chemical ablation may have arisen from differences between thermal necrosis and coagulation necrosis.15 More tissue may be affected more rapidly with ethanol ablation compared to heat ablation. The end points for both heat ablation and ethanol ablation are subjective, and this could also affect the amount of tissue treated.

Biocchemical hypocalcemia was fairly common after all three treatment modalities (n=41; 37%); however, clinical signs of hypocalcemia were rare (n=12; 11%). In a previous study on dogs with primary hyperparathyroidism treated with surgery, 11 of 19 dogs had laboratory hypocalcemia, nine dogs had clinical hypocalcemia, and one died of tetany.3 These findings may have prompted closer monitoring for hypocalcemia and more aggressive treatment with vitamin D and calcium. In previous studies, four of eight dogs treated with ethanol ablation and five of eight dogs treated with heat ablation had hypocalcemia.14,15

In the current study, complications other than hypocalcemia were infrequent. There were no observed side effects noted in any dogs after parathyroidectomy. Other mild complications occurred in a small number of dogs after both types of ultrasound-guided treatment modalities. Leakage of the ethanol or extension of thermal necrosis from the parathyroid gland may have extended into the surrounding

<table>
<thead>
<tr>
<th>Treatment Groups (No. of dogs)</th>
<th>No. of Dogs With Laboratory Hypocalcemia</th>
<th>No. of Dogs With Clinical Signs of Hypocalcemia</th>
<th>No. of Dogs With Other Complications</th>
<th>Other Complications (No. of dogs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical parathyroidectomy (n=47)</td>
<td>18</td>
<td>5</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>Ethanol ablation (n=15)</td>
<td>7</td>
<td>2</td>
<td>3</td>
<td>Cough (n=2) Change in bark (n=1)</td>
</tr>
<tr>
<td>Heat ablation (n=48)</td>
<td>16</td>
<td>5</td>
<td>3</td>
<td>Cough (n=1) Change in bark (n=2) Horner’s syndrome (n=1)</td>
</tr>
<tr>
<td>Totals</td>
<td>41</td>
<td>12</td>
<td>6</td>
<td>Cough (n=3) Change in bark (n=3) Horner’s syndrome (n=1)</td>
</tr>
</tbody>
</table>
tissues and caused damage to structures, such as the recurrent laryngeal nerve and vagosympathetic trunk. Laryngeal examinations were not performed, so laryngeal paralysis was not documented in any dogs that were coughing or had changes in bark. In previous studies, two of eight dogs had dysphonia after ethanol ablation, and one of nine dogs had dysphonia after heat ablation. Previous studies did not document Horner’s syndrome or coughing, unlike the current report.

There were several limitations to this retrospective study. Numerous primary clinicians, radiologists, and surgeons were involved in all of the cases, so each case was managed differently. No cytological or histopathological samples were submitted from dogs treated with ethanol or heat ablation. Recheck examinations were often performed by local veterinarians, and total calcium concentrations were used to monitor the response to therapy in most cases. Ionized calcium concentrations were not commonly measured as part of the follow-up process.

Conclusion

Dogs with primary hyperparathyroidism were treated with one of three treatment methods. Parathyroidectomy was the most successful treatment, with no complications other than hypocalcemia. Percutaneous ultrasound-guided ethanol ablation was the least successful treatment and had the most side effects. This study showed that heat ablation is an effective alternative to surgery, as there was no statistical significance between the outcomes in these two groups of dogs. There were more treatment failures in the first group of dogs treated with ethanol and heat ablation compared to the third group of dogs, suggesting that there is a learning curve with these two ultrasound-guided procedures.

References

Ultrasonographic Visualization of the Adrenal Glands of Healthy Ferrets and Ferrets With Hyperadrenocorticism

A protocol was developed to compare the ultrasonographic characteristics of the adrenal glands of 21 healthy ferrets and 37 ferrets with hyperadrenocorticism. By using specific landmarks, the adrenal glands were imaged in 97% of the cases. The adrenal glands of ferrets with hyperadrenocorticism had a significantly increased thickness, with changes in shape, structure, and echogenicity compared to the adrenal glands of healthy ferrets. Based on the findings of the study, adrenal glands may be classified as abnormal when they have a rounded appearance, increased size of the cranial/caudal pole (thickness >3.9 mm), a heterogeneous structure, increased echogenicity, and/or signs of mineralization.


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Introduction

Hyperadrenocorticism is a common disease in ferrets, which differs from the disease seen in humans, dogs, and cats. In the latter species, a high concentration of cortisol is responsible for the clinical signs, while in ferrets signs are caused by high concentrations of sex-related steroids.1-4 Over 70% of the cases of hyperadrenocorticism in humans, dogs, and cats are caused by a pituitary tumor; in ferrets, the primary cause of the disease is always a uni- or bilateral abnormality of the adrenal gland.1-7 The most prominent clinical signs of hyperadrenocorticism in ferrets are symmetrical alopecia, vulvar swelling in spayed female ferrets (jills), nonparasitic or nonfungal-related pruritus, stranguria in castrated male ferrets (hobs), and the return of sexual behavior despite ovarioectomy or castration.8-10

It has been reported that the diagnosis of hyperadrenocorticism in ferrets can be based on clinical signs, plasma hormone concentrations (i.e., androstenedione, 17α-hydroxy-progesterone, dehydroepiandrosterone sulfate, estradiol), an elevated urinary corticoid to creatinine ratio, and an enlarged adrenal gland seen during ultrasonography.1,2,4,9,11-18 Measurement of hormone concentrations, however, does not allow differentiation between hyperadrenocorticism and functional ovarian remnant tissue, nor does it provide information as to whether the left or right adrenal gland is affected.2,4,11,12 Ultrasonography has been used to identify affected adrenal glands and to assess their size, shape, structure, and possible vascular invasion.1,9,13-18 In addition, abnormalities of other abdominal organs, such as remnant ovarian tissue, may be found with ultrasonography.

Since the introduction of medical treatment of hyperadrenocorticism with the gonadotropin-releasing hormone (GnRH) agonist, leuprolide acetate,4 adrenalectomies are less frequently performed, which seemingly makes the need for localizing affected adrenal gland(s) less important. By administering a GnRH agonist, the production and release of gonadotropins are suppressed, resulting in a decreased production of adrenocortical hormones and a reduction of the clinical signs in affected
ferrets.12 In ferrets and in at least one woman with hyperadrenocorticism treated with leuprolide acetate, the affected adrenal gland did not decrease in size and actually increased in size after the treatment.12,19 The actual effect of leuprolide acetate on altered adrenal glands in ferrets is poorly understood, so evaluation of the adrenal glands via ultrasonography during leuprolide treatment would be useful.

The ultrasonographic size and appearance of adrenal lesions of ferrets with hyperadrenocorticism have been described.1,15-17 These reports did not describe the exact method of visualization of the adrenal glands, and the accuracy with which adrenal glands were identified varied considerably (50% to 100%).1,9,15-18 The lower detection rates have led some authors to suggest that ultrasonography may be of little value in diagnosing hyperadrenocorticism in ferrets.3 The purposes of the present study were to assess a protocol for visualizing adrenal glands in ferrets using ultrasonography and to document the size, shape, and structure of the adrenal glands in both healthy ferrets and ferrets with hyperadrenocorticism.

Materials and Methods
Selection of Cases
The medical records of ferrets that were presented to the Division of Avian and Exotic Animal Medicine of the Faculty of Veterinary Medicine in Utrecht, the Netherlands, with signs of hyperadrenocorticism between April 1999 and April 2005 were reviewed. Only ferrets with at least one clinical sign of hyperadrenocorticism (e.g., symmetrical alopecia, nonparasitic or nonfungal-related pruritus, return of sexual behavior despite ovariectomy or castration, vulvar swelling in jills, stranguria in hobs) that experienced resolution of their clinical sign(s) with therapy (i.e., adrenalectomy, leuprolide or deslorelin administration) were included in the study. Thirty-seven ferrets met the criteria for inclusion. Signalment (i.e., age, gender) and clinical signs for these ferrets were recorded.

For comparison, the adrenal glands of 21 healthy research ferrets (based on a young age [<2 years], normal history and physical examination findings) were examined ultrasonographically, with the approval of the Ethics Committee of the Faculty of Veterinary Medicine, Utrecht, the Netherlands.20 These ferrets were individually housed at the Division of Avian and Exotic Animal Medicine in outdoor, suspended cages with a closed sleeping area. Water and ferret pellets were available ad libitum.

Anatomy
The adrenal glands are located cranio medial to the cranial pole of the kidneys. The left adrenal gland is located ventrolateral to the aorta at the level of and/or immediately caudal to the origin of the cranial mesenteric artery. The right adrenal gland is located more cranial than the left, and it is attached to the dorsal and dorsolateral surface of the caudal vena cava at the level of and/or immediately cranial to the origin of the cranial mesenteric artery, and it lies adjacent to the caudomedial aspect of the caudate process of the caudate liver lobe.17,21-23

The ultrasonographic cranio caudal (length) and ven dors al (thickness) dimensions of normal ferret adrenal glands are 5.4 to 9.8 mm and 2.3 to 3.6 mm, respectively, for the left gland and 5.8 to 10.5 mm and 2.2 to 3.8 mm, respectively, for the right gland.17,18 The normal shape of the adrenal gland varies from oblong to ovoid, slightly bilobed, or rectangular.1,17,18

Ultrasonography Protocol
Food was withheld from all ferrets for at least 4 hours prior to ultrasonography. Anesthesia was induced by mask inhalation of 4% isoflurane in oxygen and was maintained with 2% isoflurane. Ultrasonography was performed with a high-definition ultrasound system equipped with a 38-mm long, 10- to 5-MHz, broadband, linear-array transducer (lateral resolution of 1.1 mm and axial resolution of 0.9 mm at a depth of 2 cm). The ferrets were placed in dorsal recumbency, and the transducer was gently placed on the abdominal wall to avoid compression or distortion of the abdominal organs and/or blood vessels.

Scanning along a longitudinal plane through the ventral abdominal wall, the left kidney was identified. With the cranial edge of the kidney approximately in the center of the image, the transducer was angled, orienting the soundbeam gradually from a vertical to a more horizontal plane. The ultrasonic beam traversed the aorta from dorsal to ventral and then across the celiac and cranial mesenteric arteries. The left adrenal gland was then located. When necessary, the transducer was slightly rotated to obtain a maximal longitudinal image of the left adrenal gland [Figure 1]. From this position, the transducer was rotated 90° to obtain transverse images.

Scanning along a longitudinal plane to the right of the midline, the right adrenal gland was found dorsal to the caudal vena cava, just where it enters the liver. When this technique was not immediately successful, the liver was examined in a transverse direction, and the aorta, caudal vena cava, and portal vein were identified. By slightly angling the transducer in a craniocaudal direction and moving the transducer gradually in a caudal direction along the caudal vena cava, and using the liver as an acoustic window as much as possible, the right adrenal gland was then located. The caudal pole of the right adrenal gland may be more lateral than dorsal to the caudal vena cava.

When this technique failed, a right lateral approach was used, with the animal in left lateral recumbency. Transverse and longitudinal scans through the last intercostal spaces and the right flank were used to identify the aorta and caudal vena cava. In the area where the caudal vena cava enters the liver, at the level of and/or immediately cranial to the origin of the cranial mesenteric artery, the right adrenal gland lies dorsal to the caudal vena cava. Once the right adrenal gland was identified using any of these three approaches (i.e., midline longitudinal, midline traverse, right lateral longitudinal), the transducer was rotated slightly until a longitudinal image of the right adrenal gland was obtained [Figure 2A]. From this position, the transducer...
was rotated 90° to obtain transverse images [Figure 2B].

During the ultrasonographic examination, color-flow Doppler was used to assess blood flow in the aorta, celiac and cranial mesenteric arteries, and caudal vena cava. These vessels were used as landmarks.

From the ultrasound images, the craniocaudal (length) and ventrodorsal (thickness) dimensions of the adrenal glands were measured using cursors and the ultrasound system’s software. The shape, structure (e.g., homogeneous, heterogeneous, cystic, mineralized), and overall echogenicity (as compared to the surrounding fat) were assessed visually. Differentiation between normal and abnormal adrenal glands in the ferrets with hyperadrenocorticism was made subjectively on the basis of the size, shape, and structure. Adrenal glands were classified as being abnormal when they were increased in size (as compared to the contralateral gland and/or the reference values for healthy ferrets), had an abnormal shape (e.g., rounded, asymmetry of the cranial and caudal pole), or had an altered structure.17,18

Statistical Analysis

A Mann-Whitney U test was used to determine significant differences between the sizes of the adrenal glands in

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**Figure 1**—A longitudinal sonogram of a left adrenal gland (between the arrows) in a 3.5-year-old, spayed female ferret with hyperadrenocorticism. The cranial pole is enlarged. Adrenal length is 10.4 mm, and thickness is 6.4 mm. Histopathological diagnosis was adrenocortical hyperplasia. Note the location of the adrenal gland ventrolateral to the aorta (A). The top of the image is ventral, Cr=cranial, Cd=caudal.

**Figures 2A, 2B**—Longitudinal (A) and transverse (B) sonograms of the right adrenal gland (between the arrows) in a 6.5-year-old, castrated male ferret with hyperadrenocorticism. The adrenal gland is hyperechoic, heterogeneous, and contains mineralizations (hyperechoic spots). The adrenal gland length is 15.6 mm, and thickness is 5.5 mm. The right adrenal gland is located dorsolateral to the vena cava (VC). The top of the image is ventral, A=aorta, VP=vena porta, R=right, L=left, Cr=cranial, Cd=caudal.
healthy ferrets and the sizes of both normal and affected adrenal glands in ferrets with hyperadrenocorticism. Values of P<0.01 were considered statistically significant.

Reference ranges for adrenal gland size in the healthy ferrets and the normal adrenal glands in the ferrets with hyperadrenocorticism were calculated using the formula: mean ± (r x standard deviation [SD]).24,25 The positive and negative predictive values of these results in the healthy ferrets were also assessed. The adrenal gland sizes of the affected ferrets were log transformed (to base e) to meet the assumption of normality; then, using the transformed data, a reference range was calculated, which was converted back to the original scale by taking the antilogarithm.25

Results

Clinical Data

Thirty-seven privately owned ferrets with hyperadrenocorticism were included in the study. They ranged in age from 2 to 7.5 years (mean 5.0±1.2 years). The ferrets consisted of 16 castrated males and 21 spayed females (male to female ratio=0.76). The most common presenting clinical signs were asymmetrical alopecia (n=34), pruritus (n=11), vulvar swelling (n=12 females), fatigue (n=8), weight loss (n=7), the return of sexual behavior despite ovarioectomy or castration (n=6), and stranguria (n=2 males). Twelve ferrets were treated by adrenalectomy, 18 ferrets received leuprolide acetate injections, and seven ferrets were treated with a 9.5-mg GnRH implant.

Twenty-one research ferrets were used as normal controls, and they ranged in age from 8 to 23 months. The normal ferrets consisted of 10 females, eight males, and three spayed females. All the research ferrets were kept for at least 4 years after completing the study, and none developed clinical signs of hyperadrenocorticism.

Adrenal Glands of Healthy Ferrets

In the 21 normal ferrets, 41 adrenal glands were identified (accuracy 98%). One right adrenal gland could not be identified ultrasonographically. The adrenal glands were oblong to oval in shape, uniformly structured, and hypoechoic to the surrounding fat. The mean dimensions of the left adrenal glands were 6.1±1.0 mm (range 4.5 to 8.3 mm; reference range 4.0 to 8.1 mm) for length and 2.9±0.5 mm (range 1.8 to 3.7 mm; reference range 1.8 to 3.9 mm) for thickness. The positive and negative predictive values of these dimensions were 93% and 57%, respectively, for length and 100% and 78%, respectively, for thickness. The mean dimensions of the right adrenal glands were 7.8±1.4 mm (range 4.6 to 9.8 mm; reference range 4.9 to 10.6 mm) for length and 2.5±0.6 mm (range 1.4 to 3.6 mm; reference range 1.3 to 3.7 mm) for thickness. The positive and negative predictive values of these dimensions were 100% and 56%, respectively, for length and 100% and 77%, respectively, for thickness [see Table].

Adrenal Glands of Affected Ferrets

Both adrenal glands were identified by ultrasonography in 35 of the 37 affected ferrets (accuracy 97%). In two ferrets, the right adrenal gland could not be identified. Based on the dimensions, structure, and echogenicity of the 72 adrenal glands that were identified, 48 were classified as abnormal (28 left, 20 right), and 24 were classified as normal. Bilateral lesions were found in 11 (30%) ferrets. The mean dimensions of the 28 abnormal left adrenal glands were 9.2±3.2 mm (range 5.0 to 19.5 mm; reference range 4.6 to 16.6 mm) for length and 6.3±3.0 mm (range 2.4 to 15.1 mm; reference range 2.4 to 13.8 mm) for thickness. The dimensions of 19 abnormal right adrenal glands were 8.5±2.5 mm (range 4.6 to 15.2 mm; reference range 4.5 to 14.9 mm) for length and 5.2±3.3 mm (range 2.2 to 17.6 mm; reference range 1.7 to 12.8 mm) for thickness. The abnormal adrenal glands in the ferrets with hyperadrenocorticism had a significant increase (P<0.01) in the length of the left adrenal gland and in the thickness of both adrenal glands [see Table] when compared to the dimensions of the normal adrenal glands.

All 28 abnormal left adrenal glands had an altered shape; 25 (89%) had a rounded appearance, and four (14%) had a large or rounded cranial pole. Seven (25%) of the 28 left adrenal glands had a heterogeneous structure, and six (21%) had increased echogenicity compared to the surrounding fat. The other 22 left adrenal glands had normal echogenicity (hypoechoic to the surrounding fat). Of the 20 abnormal right adrenal glands, 18 had an altered shape, 10 (56%) had a rounded appearance, four (22%) had a large or rounded cranial pole, and one (6%) had a large or rounded caudal pole. In seven (35%) of the 20 right adrenal glands, a heterogeneous structure (pattern) was found, and eight (40%) had increased echogenicity. In two of these eight adrenal glands, mineralization was detected. The other 12 right adrenal glands had normal echogenicity.

Histology was performed in the 12 affected adrenal glands that were surgically removed (all left adrenal glands). The histopathological diagnoses included cortical hyperplasia (n=5), adenoma (n=2), adenocarcinoma (n=2), carcinoma (n=1), and an unspecified adrenal tumor (n=2). There was no significant difference in size between the surgically removed and nonoperated abnormal adrenal glands (Mann-Whitney U test, P=0.15).

Twenty-four adrenal glands of ferrets with hyperadrenocorticism were classified as being normal (nine left, 15 right). The mean dimensions of the left adrenal glands were 6.3±0.9 mm (range 5.1 to 7.7 mm; reference range 4.2 to 8.4 mm) for length and 2.5±0.6 mm (range 1.4 to 3.4 mm; reference range 1.2 to 3.8 mm) for thickness. The mean dimensions of the right adrenal glands were 6.0±1.7 mm (range 3.7 to 9.2 mm; reference range 2.3 to 9.6 mm) for length and 2.1±0.6 mm (range 1.3 to 3.7 mm; reference range 0.8 to 3.5 mm) for thickness [see Table]. There were no statistical differences between the dimensions of the normal adrenal glands of affected ferrets and those of normal ferrets with regard to length of the left adrenal gland (P=0.48), thickness of the left adrenal gland (P=0.06), and thickness of the right adrenal gland (P=0.07). The length of the right adrenal gland of affected ferrets was statistically smaller (P=0.004) than that of the normal ferrets.
### Table

Ultrasonographic Dimensions of the Adrenal Glands of Healthy Ferrets and Ferrets With Hyperadrenocorticism

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<td>Thickness (mm)</td>
<td>1.2-3.8</td>
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* SD=standard deviation
† n=number of ferrets; one right adrenal gland was not identified, and length could not be measured in one right adrenal gland
‡ n=number of ferrets; two right adrenal glands were not identified
§ Length could not be measured in one right adrenal gland, and thickness could not be measured in one right adrenal gland
\ Length could not be measured in one right adrenal gland
¶ Values were significantly (P<0.01) larger compared to values for healthy ferrets, using the Mann-Whitney U test
# Value was significantly smaller (P=0.004) compared to values for healthy ferrets, using the Mann-Whitney U test
Discussion

The ultrasonographic protocol used in this study allowed identification of 98% of the adrenal glands in the healthy ferrets and 97% of the adrenal glands in the affected ferrets, which was higher than several previous reports. Detection rates may have been lower in earlier reports because of the presence of large lymph nodes in the abdomen of ferrets. These lymph nodes have a round or oval shape, are usually hypoechoic compared to surrounding fat, and resemble adrenal glands. By using the anatomical landmarks (e.g., the right adrenal gland is attached to the dorsolateral surface of the caudal vena cava; the left adrenal gland is located ventrolateral to the aorta, just caudal to the origin of the cranial mesenteric artery), differentiation between lymph nodes and adrenal glands is relatively easy.

In the study reported here, abnormal adrenal glands in the ferrets with hyperadrenocorticism had a significant increase in thickness. A greater length was found in abnormal left adrenal glands, but not in abnormal right adrenal glands, which may be explained by the fact that the cranial pole of the right adrenal gland lies dorsal to the caudal vena cava, and the caudal pole is usually dorsolateral or lateral to the caudal vena cava, making it difficult to obtain a longitudinal image that contains the whole adrenal gland. Similar to the findings in other studies, the abnormal adrenal glands were fairly rounded in shape or had a large cranial and/or caudal pole. It is hypothesized that early in the disease, thickness increases rather than the length, which results in a round gland or increased size of one pole. Eventually, the entire gland is affected and the internal architecture is disrupted.

The adrenal gland size in the 21 healthy ferrets was in accordance with previous studies. The size of the normal adrenal glands in the healthy animals resembled the size of the normal adrenal glands of the affected ferrets, except for the length of the right adrenal gland. Again, difficulties in accurately measuring the length of right adrenal glands may have affected these results.

The control group consisted of a large number of intact ferrets (n=18), unlike the group of affected ferrets (none of which were intact). Since hyperadrenocorticism is predominantly found in neutered ferrets, it was believed that the adrenal size in intact ferrets was a correct representation of normal size.

Adrenal neoplasms can also be identified ultrasonographically by a change in adrenal shape and structure. In 14 (29%) of the 48 abnormal adrenal glands, the structure was heterogeneous, and 14 (29%) had increased echogenicity. In previous studies, echogenicity of abnormal adrenal glands has been described as mixed or hyperechoic, but the ultrasonographic technique used and the number of affected glands imaged were not reported. An affected adrenal gland can also have a normal structure and echogenicity. In the current study, 28 (58%) of 48 abnormal adrenal glands had a normal structure and were hypoechoic; however, they were all increased in size and/or had a rounded appearance. Only two (4%) of the 48 abnormal adrenal glands contained mineralized areas, similar to previous reports in which mineralization is rarely described.

The lesions found in this study involved 28 left and 20 right adrenal glands, which contradicted the historical impression that adrenal gland lesions mostly affect the left adrenal gland. Bilateral lesions were found in 11 (30%) ferrets; this percentage was greater than that previously described (16% to 19%). This latter difference may be explained by the subjective element involved in the differentiation of normal versus abnormal adrenal glands, which can lead to the under-interpretation of minor changes in an adrenal gland after obvious abnormalities have been found in the contralateral adrenal gland. The findings of equal distribution of adrenal lesions of the left and right adrenal glands and a high percentage of bilateral lesions are in accordance with the suggested pathogenesis of hyperadrenocorticism, which is overstimulation of the adrenal glands by luteinizing hormone following neutering.

Normal adrenal glands in the ferret are oblong to oval in shape, uniformly structured, and hypoechoic to the surrounding fat. Increased echogenicity was found during ultrasonographic examination in two of the adrenal glands in the healthy ferrets (both intact males), possibly because they contained more fat. These two male ferrets had the highest body weights of all the healthy ferrets examined, and they may have stored more fat in their adrenal glands.

Since ultrasonography is relatively inexpensive and non-invasive, it is the most practical method for imaging the adrenal glands. Ultrasonography can also detect the presence of an intact female genital tract or an ovarian remnant (the two most important differential diagnoses for hyperadrenocorticism in young [<2 years of age], female ferrets), and it may be used to monitor changes in adrenal gland size and structure during the course of hormonal therapy. Ultrasonography permits evaluation of all abdominal organs for secondary effects, may identify an adrenal gland tumor, and also facilitates percutaneous-guided biopsy.

Based on the results of this study, adrenal glands should be classified as abnormal when they have a rounded appearance, have an enlarged cranial and/or caudal pole (thickness >3.9 mm), a heterogeneous structure, increased echogenicity, and/or contain mineralizations. By using the specific landmarks described in the protocol, the accuracy of an ultrasonographic examination increased to such extent that almost all adrenal glands were imaged. For each of the 12 ferrets in the present study in which the affected adrenal gland was removed surgically, the clinical signs of hyperadrenocorticism resolved within 1 month following surgery, indicating that the adrenal gland considered normal on ultrasonographic examination was functionally normal. A normal shape, structure, and echogenicity of a ferret’s adrenal gland, however, does not rule out a functional adrenal lesion.
Conclusion

Ultrasonography was very accurate in identifying abnormal adrenal glands in 37 ferrets with signs of hyperadrenocorticism, after specific landmarks were identified. Adrenal glands were classified as abnormal when they had a rounded appearance, an enlarged cranial and/or caudal pole, a heterogeneous structure, increased echogenicity, and/or contained mineralization.

References

Reevaluation of the University of Wisconsin 2-Year Protocol for Treating Canine Lymphosarcoma

This retrospective study investigated a population of 96 dogs with newly diagnosed malignant lymphosarcoma that were treated with the commonly used University of Wisconsin-Madison (UW-M) chemotherapy protocol. Pretreatment characteristics were analyzed to determine prognostic factors. Dogs with higher World Health Organization (WHO) stages (including stage IV) and dogs with hypercalcemia were at significantly higher risk of relapse ($P=0.018$ and $P=0.016$, respectively). Dose reduction, treatment delays, and prior therapy with corticosteroids were not associated with clinical outcome. First remission duration of 270 days was similar to historically reported data. Overall survival time of 218 days was much shorter than historical data. J Am Anim Hosp Assoc 2007;43:85-92.

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Introduction
Lymphosarcoma, neoplasia arising from lymphoreticular cells, is one of the malignancies most likely to respond to chemotherapy, and it is also one of the most common neoplasms of the dog. Various chemotherapeutic regimens have been used and usually consist of multiple drugs. Response rates of 80% to 90% with median survival times of 250 to 300 days have been reported. Numerous studies have been undertaken to identify prognostic factors relating to response to treatment, length of remission, and survival times. Results from these studies have varied.

One common treatment regimen used for canine lymphosarcoma is the University of Wisconsin-Madison (UW-M) 2-year chemotherapy protocol. Studies with limited numbers of dogs have investigated survival times of dogs treated with this protocol.

The objective of this retrospective study was to evaluate signalment, prognosis, and prognostic factors in a previously unreported canine population that underwent treatment with the UW-M chemotherapy protocol for lymphosarcoma.

Materials and Methods
Case Selection
Medical records from April 1996 to December 2002 were searched at the Small Animal Clinic, Veterinary School, University of Zurich, for dogs with definitive cytological or histopathological diagnosis of lymphosarcoma that had received no chemotherapy except corticosteroids before being treated with the UW-M 2-year chemotherapy protocol. Diagnosis of lymphosarcoma was made on the basis of cytological examination of needle aspirates and/or histological examination of surgically excised lymph nodes or other tissue samples. If any question concerning the accuracy of a cytological diagnosis arose, histological examination of a tissue specimen was performed.

Staging was done using the modified World Health Organization (WHO) staging system for canine lymphosarcoma and consisted of a complete blood count (CBC), a serum biochemical profile, urinalysis,
and thoracic radiography. Whenever the physical examination and/or the serum biochemical profile suggested visceral involvement, abdominal ultrasonography (n=27) or radiography (n=31) was performed. Leukemia was diagnosed based on bone marrow evaluation (n=6) or cytological examination of blood smears (n=11). The WHO staging system was modified as described in a previous study, so that extranodal lymphosarcomas were considered a separate stage. Stage VI was created based on the fact that extranodal lymphosarcomas do not clinically behave like stage V lymphosarcomas [Table 1].

The dogs were further divided into substage a (without clinical signs) and substage b (with clinical signs of illness). Factors that were investigated included age, gender, breed, weight, clinical stage and substage, anatomical location, presence of hypercalcemia (reference range 9.6 to 11.2 mg/dL) or hyperbilirubinemia (reference range 0.145 to 0.44 mg/dL), hematocrit, hemoglobin, presence of neurological signs, prior treatments, time between onset of signs until first treatment, toxicities associated with chemotherapy, dose reductions and alterations in therapy, and therapy instituted at relapse. Month of presentation and month of relapse were also noted in order to evaluate for seasonality, a factor anecdotaly reported in dogs. Because absolute thrombocyte counts were not available in most cases (i.e., platelet numbers were indicated as sufficient, high, or low), this parameter was not evaluated. Immunophenotyping was not routinely performed, owing to cost concerns.

Treatment Protocol

The doses and frequency of drugs used in the UW-M protocol are shown in Table 2. In 22 dogs, the first dose of vincristine was reduced to 0.5 mg/m² because of concerns of increased toxicity in the first week of therapy when L-asparaginase and vincristine were combined.

Side Effects

Toxicity was assessed based on the National Cancer Institute (NCI) toxicity grading system for hematological and gastrointestinal toxicities [Table 3]. Owners were questioned as to whether the dog had any signs of gastrointestinal toxicity (e.g., anorexia, vomiting, or diarrhea) and whether the dog’s demeanor had changed. In cases of myelosuppression (i.e., a neutrophil count <3000/µL), treatment was delayed for a week, and subsequent doses of that drug were reduced. If severe drug-induced gastrointestinal toxicosis developed, therapy was withheld, and the dosage of the agent thought to be the cause of toxicosis was reduced. Only treatment delays resulting from toxicity were statistically evaluated.

Responses and Outcomes

Complete remission was defined as the disappearance of all clinical evidence of disease on physical examination, radiography, ultrasonography, CBC, and/or biochemical analyses. A partial response was defined as a decrease in tumor volume ≥50%, with no new lesions. Stable disease was defined as no change in tumor burden or <50% decrease in tumor volume. Progressive disease was defined as appearance of new lesions and/or tumor growth.

The first remission duration was defined as the time between recognition of a complete remission until evidence of relapse. Overall survival time was defined as the time from the first chemotherapy treatment until death from lymphosarcoma or treatment. Survival time was determined by review of the medical record or by contact with the referring veterinarian or owner.

Statistical Analysis

All dogs entering the study were included in analysis for overall survival time (n=96). Dogs that received only one treatment and were euthanized or died were evaluated, despite not completing the induction protocol. Only dogs that achieved remission were included in remission duration calculations (n=76). Discrete factors evaluated for significance included gender, breed, clinical stage and substage, anatomical location, presence of hypercalcemia, presence of neurological signs, prior treatments, toxicities experienced, dose reductions, alterations in therapy, and therapy at relapse. Continuous factors included age, body weight, hyperbilirubinemia, hematocrit, hemoglobin, time between onset of disease until treatment, and toxicities experienced. Univariate analysis to assess the prognostic values of the different discrete cofactors was performed by the Kaplan-Meier method, together with the logrank or “Breslow” test. The associations between two discrete covariates were evaluated by
In order to compare means of a continuous variable with respect to a factor with only two levels, the Mann-Whitney U test was applied.\textsuperscript{16} For two continuous covariates, Pearson’s correlation coefficient was computed with a 95% confidence interval.\textsuperscript{16} Month of presentation and month of relapse were evaluated by the goodness of fit chi-square ($\chi^2$) test.\textsuperscript{17} Variables that were identified to be significant in univariate analysis were included in a multivariate Cox proportional hazards model regression analysis with a forward and backward step selection for both survival and remission.\textsuperscript{16} Results were considered to be significant with $P$ values <0.05.

\begin{table}
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\begin{tabular}{|l|l|l|}
\hline
\textbf{Treatment Cycles} & \textbf{Drug} & \textbf{Dosage}^* \\
\hline
\textbf{Cycle 1 (Induction)} & & \\
Wk 1 & Vincristine & 0.7 mg/m$^2$ IV\textsuperscript{†} \\
Wk 1 & L-asparaginase & 400 IU/kg SC \\
Wk 1 & Prednisone & 2 mg/kg PO \\
Wks 2, 7 & Cyclophosphamide & 200 mg/m$^2$ IV/PO \\
Wk 2 & Prednisone & 1.5 mg/kg PO \\
Wks 3, 6, 8 & Vincristine & 0.7 mg/m$^2$ IV \\
Wk 3 & Prednisone & 1.0 mg/kg PO \\
Wks 4, 9 & Doxorubicin & 30 mg/m$^2$ IV\textsuperscript{‡} \\
Wk 4 & Prednisone & 0.5 mg/kg PO \\
\hline
\textbf{Cycle 2 (Maintenance)} & & \\
Wks 11, 15, 19, 23 & Vincristine & 0.7 mg/m$^2$ IV \\
Wks 13, 21 & Chlorambucil & 1.4 mg/kg PO \\
Wk 17 & Methotrexate & 0.8 mg/kg IV \\
Wk 25 & Doxorubicin & 30 mg/m$^2$ IV\textsuperscript{‡} \\
\hline
\textbf{Cycle 3 (Maintenance)} & & \\
Wks 28, 34, 40, 46, 52, 58 & Vincristine & 0.7 mg/m$^2$ IV \\
Wks 31, 43, 55 & Chlorambucil & 1.4 mg/kg PO \\
Wks 37, 61 & Methotrexate & 0.8 mg/kg IV \\
Wk 49 & Doxorubicin & 30 mg/m$^2$ IV\textsuperscript{‡} \\
\hline
\textbf{Cycle 4 (Maintenance)} & & \\
Wks 65, 73, 81, 89, 97, 105, 121 & Vincristine & 0.7 mg/m$^2$ IV \\
Wks 69, 85, 101, 117 & Chlorambucil & 1.4 mg/kg PO \\
Wks 77, 93, 109 & Methotrexate & 0.8 mg/kg IV \\
\hline
\end{tabular}
\caption{University of Wisconsin 2-Year Chemotherapy Protocol for Canine Lymphosarcoma\textsuperscript{12}}
\end{table}

* IV=intravenous; SC=subcutaneous; PO=orally
\textsuperscript{†} Initiated therapy at 0.5 mg/m$^2$ if dog had a large tumor burden or was clinically ill
\textsuperscript{‡} Delivered in 0.9% saline solution over 1 h; 1 mg/kg dose for dogs <10 kg
Dogs were censored in analysis of remission duration if they were in remission at the end of the study, were lost to follow-up, or had died from other causes while in remission. Dogs were censored in analysis of survival if they were lost to follow-up, died from causes unrelated to lymphosarcoma or chemotherapy, or were alive at the end of the study period.

Results

Case Data

Ninety-six dogs met the inclusion criteria for the study. The median age at diagnosis was 7.7 years (range 0.5 to 14 years; mean 7.63±0.3 years). Forty-six dogs were females (32 spayed), and 50 were males (18 castrated). The most common breeds included the Bernese mountain dog (n=11), rottweiler (n=5), German shepherd dog (n=5), Doberman pinscher (n=4), and Labrador retriever (n=4). Forty-seven (49%) dogs were composed of 30 additional breeds, and 20 (21%) animals were mixed-breed dogs. The median weight was 31 kg (range 4 to 78 kg; mean 30.0±1.5 kg). Stage distribution is shown in Table 4.

Seventeen (18%) dogs were leukemic, 17 (18%) had cranial mediastinal involvement, and six (6%) had pulmonic involvement. The sites of involvement of the nine stage-VI dogs were gastrointestinal (n=3), ocular (n=3), nasal (n=1), and spinal (n=2). Fifteen (16%) dogs had hypercalcemia (median 14.8 mg/dL, range 12.5 to 18.8 mg/dL), eight of which had mediastinal involvement (i.e., stage I, mediastinum only [n=1]; stage II [n=1]; stage III [n=4]; and stage IV [n=2]). Hypercalcemic dogs without mediastinal involvement were staged as III (n=5) and IV (n=2). Nine dogs had hyperbilirubinemia. The median bilirubin level of all dogs measured was 0.19 mg/dL (range 0.005 to 14.15 mg/dL). The median hematocrit was 42.0%±0.8% (range 18% to 61%), and the median hemoglobin was 14.4±0.3 g/dL (range 3.8 to 21 g/dL). Three dogs were presented with neurological signs. Correlations were found between WHO stage and age (P=0.0002), WHO stage and hypercalcemia (P=0.0227), and WHO stage and age and weight (P=0.021). Hypercalcemia was found in younger dogs in lower stages. Higher WHO stages were associated with greater age and smaller body weights.

Fifty-four dogs received prior treatments that consisted of antibiotics (n=24), corticosteroids (n=14), antibiotics and corticosteroids (n=11), or alternative medications, such as mistletoe or immunomodulatory drugs (n=5). Median duration of pretreatment was 13.5±2.4 days (range 1 to 81 days). Median time from appearance of first clinical signs until treatment was 18±2.8 days (range 4 to 165 days). The initial

<table>
<thead>
<tr>
<th>Type of Toxicity</th>
<th>Abnormalities</th>
<th>Score</th>
</tr>
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<tbody>
<tr>
<td>Bone marrow</td>
<td>WBC &lt;3000 N &lt;1500</td>
<td>H1</td>
</tr>
<tr>
<td></td>
<td>WBC &lt;2000 N &lt;1000</td>
<td>H2</td>
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<tr>
<td></td>
<td>WBC &lt;1500 N &lt;800</td>
<td>H3</td>
</tr>
<tr>
<td></td>
<td>WBC &lt;1000 N &lt;500</td>
<td>H4</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, anorexia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vomiting 1 to 5 times per d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diarrhea 5 to 7 times per d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;5% weight loss</td>
<td>G2</td>
</tr>
<tr>
<td></td>
<td>Vomiting 6 to 10 times per d</td>
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</tr>
<tr>
<td></td>
<td>Diarrhea &gt;7 times per d</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5% to 10% weight loss</td>
<td>G3</td>
</tr>
<tr>
<td></td>
<td>&gt;10% weight loss</td>
<td>G4</td>
</tr>
</tbody>
</table>

* WBC=peripheral white blood cells/µL; N=peripheral neutrophils/µL
† H=hematological; G=gastrointestinal
diagnoses were highest in the months of July (n=10), August (n=10), November (n=15), and December (n=10), but this pattern was not statistically significant (χ² test=16.05; P=0.1393). A higher tendency of relapse was detected in the months of May (n=8), June (n=7), July (n=7), September (n=9), and October (n=7) (χ² test=15.75; P=0.1507). In the years from 1996 until the end of the study in 2004, not one dog relapsed in the month of April.

Side Effects

Side effects and dosage reductions are summarized in Tables 5 and 6. Side effects were most frequently experienced after the first week of treatment. The five dogs that died after their first treatment were all substage b in stage III (n=2), stage IV (n=2), or stage VI (n=1). Twelve dogs suffered bone marrow toxicity after week 1, and 26 dogs had gastrointestinal toxicities; some dogs suffered concurrently from both. Sixteen dogs had to be hospitalized (mean duration 2.9±0.7 days, range 1 to 11 days) for drug-induced toxicity. Six (6.2%) hospitalizations occurred after week 1. Eleven dogs were hospitalized once, and five dogs were hospitalized more than once (two to three times). The drug that most frequently caused side effects (in 66 dogs) was vincristine. Thirteen dogs exhibited gastrointestinal toxicity after the first doxorubicin treatment in week 4. In one case, vincristine-induced neuropathy was strongly suspected, and vincristine was discontinued at week 15 of the protocol.

Treatment delays owing to toxicity usually occurred during the induction phase (n=39). Remission duration was not significantly associated with dosage reductions (n=43; P=0.248) or treatment delays (n=35; P=0.233). Specifically for the 22 dogs that received vincristine at 0.5 mg/m² in week 1, there was no statistically significant influence on remission duration (n=19; P=0.10), and toxicities in week 1 for this group of dogs included gastrointestinal (n=6, 27%), bone marrow (n=3, 14%), hospitalizations (n=2, 9%), and death (n=1, 4%).

Treatment Response

Seventy-six (79%) dogs experienced a complete remission. Dogs that did not achieve a complete response had various stages of disease, namely stage II (n=1), stage III (n=6), stage IV (n=6), stage V (n=4), and stage VI (n=3). The median duration of the first remission was 270±20.3 days.
Breed and gender status had no statistical influence on remission. Univariate variables that significantly increased the likelihood of relapse were hypercalcemia ($P=0.017$) and higher initial stage classification (stages IV, V, and VI as opposed to stages I, II, and III; $P=0.018$).

Of the 15 dogs that were hypercalcemic, 11 had a complete response. The median duration of the first remission for the 11 dogs was only 139±26.3 days, as opposed to 296±31.2 days for dogs that were normocalcemic. Hypercalcemia did not influence the likelihood of achieving remission. In univariate analysis, the presence of leukemia resulted in shorter remission duration. Leukemic dogs had a median remission duration of 172±9 days, as opposed to 296±30.5 days for nonleukemic dogs ($P=0.02$). A tendency for longer remission duration was seen in dogs classified as substage a (308±43.7 days) versus substage b (176±55.3 days), but substage alone was not statistically significant ($P=0.16$). Being classified as substage a was not a significant predictor of the likelihood of remission ($P=0.21$). The time period between onset of the disease and the first chemotherapeutic administration was not associated with achievement or duration of remission ($P=0.90$). Of the 19 dogs pretreated with corticosteroids, remission duration was not significantly impacted ($P=0.70$).

Evaluation of multiple Cox regression by the backward search procedure revealed only two factors that remained statistically significant, namely elevated calcium ($P=0.037$; Figure 1) and higher WHO classification of stage ($P=0.016$; Figure 2). Forward stepwise analysis revealed leukemia as a negative prognostic marker ($P=0.011$), together with hypercalcemia ($P=0.007$).

### Table 6

<table>
<thead>
<tr>
<th>Drugs Requiring Dosage Reductions</th>
<th>No. Dogs</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate</td>
<td>7</td>
<td>7.3</td>
</tr>
<tr>
<td>Vincristine &lt;0.7 mg/m²*</td>
<td>15</td>
<td>15.6</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Combined (vincristine, doxorubicin and cyclophosphamide)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

* Excluding dogs with reduced dosages at wk 1

In 34 dogs, a second remission was attempted with either the same protocol (n=17) or with lomustine (60 mg/m² per os q 3 weeks; n=17). A number of dogs received other rescue therapies, such as mitoxantrone (n=1), actinomycin (n=1), melphalan (n=1), or no treatment (n=16), but they were not included in the second remission analysis because of low numbers in each treatment group. Eighteen (53%) of 34 dogs achieved a second remission; 11 of these 18 received the same protocol, and seven received lomustine. A significant difference in the length of second remission duration was detected between those treated with the same protocol and those treated with lomustine: dogs that were reinduced with the same protocol had a significantly longer overall survival time than the latter group ($P=0.008$; Figure 3).
have reported no significance of hypercalcemia as a univariate analysis in some studies, whereas other studies analyses. This finding has been reported previously using significant prognostic factor in univariate and multivariate hospitals. A comparison of affected dogs with the overall hospital population was not performed, however. The median age and weight of the dogs were 443±136.1 days; the median overall survival time for dogs that had the full dose, so it may be useful to consider a dose reduction in all dogs at week 1, or at least in those that are considered to be at greater risk for toxicity) were selected to receive a reduced dose of vincristine at week 1. Avoiding toxicity at week 1 allowed subsequent administration of full dosages of vincristine for the remainder of the protocol (i.e., a permanent dose reduction was not made, based on the dog having had a toxic reaction to the vincristine at week 1). Remission duration for dogs that received vincristine at 0.5 mg/m² in week 1 was not shorter than the remission duration for the group that had the full dose, per os q 3 weeks) to dogs treated with the University of Wisconsin-Madison 2-year chemotherapy protocol at relapse. The median survival time for dogs in substages a and b was 136±77.3 days. Median overall survival time for dogs that achieved a complete remission was 322±68.6 days.

Discussion

Many findings of this study were similar to previously published results. The median age and weight of the dogs were similar to other studies. The high number of intact females in this study may have been related to regional differences, because in North American studies, intact females are typically underrepresented. In the present study, clinical courses experienced by intact females were similar to courses for spayed females and males. One new finding was the high percentage of Bernese mountain dogs, which might indicate a susceptibility to lymphosarcoma in this breed. A comparison of affected dogs with the overall hospital population was not performed, however.

The current study identified hypercalcemia as a significant prognostic factor in univariate and multivariate analyses. This finding has been reported previously using univariate analysis in some studies, whereas other studies have reported no significance of hypercalcemia as a prognostic indicator. The study reported here further identified a negative correlation between hypercalcemia and age and a positive association between hypercalcemia and lower WHO stages (a finding not previously reported). One European study found a WHO classification of stage IV to be a positive prognostic indicator for complete remission rates, whereas the present study identified stages IV, V, and VI as negative prognostic indicators.

Dogs that received prednisone before starting the protocol were not at a disadvantage; this finding was similar to a former study. Other studies have reported that delays in therapy and dosage adjustments were most frequently associated with vincristine, a finding that was confirmed in this study. Lowering the vincristine dose at week 1 did appear to decrease toxicity, because only 14% of the dogs in this study experienced bone marrow toxicity, versus 40% in a study by Northrup et al. In the present study, significant toxicity did occur in dogs given a reduced dose of vincristine in week 1, at a level similar to previous reports on this protocol. This finding supported the contention that it is the combination of vincristine and L-asparaginase, more than the dose of vincristine alone, that causes bone marrow suppression. Evaluation of vincristine toxicity in week 1 of the present study was skewed, however, in that certain dogs (often those with substage b or higher tumor burdens and considered to be at greater risk for toxicity) were selected to receive a reduced dose of vincristine at week 1. Avoiding toxicity at week 1 allowed subsequent administration of full dosages of vincristine for the remainder of the protocol (i.e., a permanent dose reduction was not made, based on the dog having had a toxic reaction to the vincristine at week 1). Remission duration for dogs that received vincristine at 0.5 mg/m² in week 1 was not shorter than the remission duration for the group that had the full dose, so it may be useful to consider a dose reduction in all dogs at week 1, or at least in those that are considered to be at the highest risk for side effects during initial induction.

The complete response rate of 79% was lower in this study than the rate previously reported (84% to 87%) using the same protocol. One European study also observed a similar 77% complete response rate. The median duration of the first remission was comparable to other studies. The overall survival time was lower at 218 days than the previously reported survival time of 357 days. The lower survival time may have been a real survival disadvantage, or it may have arisen from cultural differences, with European clients less likely to try multiple rescue protocols or choosing euthanasia earlier.

The current study contained several limitations; besides its retrospective nature, the study had a lack of control dogs, and differences existed in diagnostic testing procedures, ancillary treatments, and methods of evaluation and follow-up. The large number of dogs in this study helped to minimize some of these problems. Another important point was the possibility of some degree of backward stage migration, as low numbers of dogs placed in stages I to III (n=43) had

![Image](per os q 3 weeks)

**Figure 3**—Kaplan-Meier median second remission duration data comparing dogs treated with lomustine (60 mg/m² per os q 3 weeks) to dogs treated with the University of Wisconsin-Madison 2-year chemotherapy protocol at relapse. Median second remission durations were 29±15.1 days and 60±8.7 days, respectively (P=0.008).
abdominal ultrasonography (n=7) or radiography (n=10) performed. As many as 26 dogs may have been staged lower than they actually were. When these 26 dogs were experimentally classified as stage IV to VI, there was no longer a statistically significant difference between dogs in stages I to III (n=17) and dogs in stages IV to VI (n=79; P=0.32).

Additional factors may also have influenced treatment outcomes in the dogs of this study. Immunophenotyping has been used to identify prognostic differences between the cellular subtypes of canine lymphosarcoma, but it was not performed in the study reported here.21

Conclusion

Medical records for 96 dogs with lymphosarcoma treated with the UW-M 2-year chemotherapeutic protocol were reviewed. Hypercalcemia and higher stage of disease were confirmed as negative prognostic indicators independent of other variables. Treatment with corticosteroids prior to starting the chemotherapy protocol did not affect remission or survival. A correlation was found between young dogs, hypercalcemia, and low-stage disease. A trend was seen for dogs being presented more often in winter (November and December) and summer (July and August). Dose reduction of vincristine in week 1 appeared to decrease toxicity without affecting remission length or survival, and this should be considered as a viable modification of the protocol, particularly for dogs that are substage b.

References

A novel technique was developed to estimate the caudal medial tibial plateau landmark in the face of osteophytosis to improve accuracy in tibial plateau angle measurements. Using this technique, tibial plateau angles were evaluated in 31 normal dogs before and 8 months after right cranial cruciate ligament transection. There was no significant difference in mean tibial plateau angle before or after induction of osteophytosis. Additionally, it was determined that 90% of dogs had a difference of ≤2˚ between right and left tibial plateau angles, which was considered symmetrical. 


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Introduction

The tibial plateau leveling osteotomy (TPLO) was developed to dynamically stabilize the cranial cruciate ligament (CCL)-deficient stifle during the weight-bearing phase of ambulation. This stabilization is accomplished by decreasing the tibial plateau slope, which directs the tibial thrust from a cranial to caudal direction.1-4 The clinical recommendation of a 5˚ postoperative tibial plateau angle is consistent with the experimentally established, optimal postoperative tibial plateau angle of 6.5˚, which achieves cranial stability and minimizes stress on the caudal cruciate ligament.4,5

Determination of the tibial plateau angle is critical prior to performing a TPLO.2,4 Although under-rotation of the osteotomized tibial plateau may result in continued cranial instability and cranial tibial translation, over-rotation results in increased stress on the caudal cruciate ligament and caudal tibial translation.1-3,6 An accurate preoperative measurement of the tibial plateau angle is imperative in determining the appropriate magnitude of the tibial plateau rotation.

To achieve consistency in tibial plateau angle measurement, anatomical landmarks must be identified. The tibial plateau landmarks are the cranial medial aspect of the CCL insertion site (the most cranial point of the medial tibial plateau) and the most caudal aspect of the medial tibial plateau adjacent to the insertion of the caudal cruciate ligament.3,4,7 The landmarks of the functional tibial axis on a lateral radiograph centered on the stifle (including the tibiotarsal joint) are the intersection point of the medial and lateral tibial intercondylar eminences and the middle of the talus.1,3,4 Accurate and consistent identification of these landmarks is paramount to reliably determining preoperative and postoperative tibial plateau angle.

Accurate tibial plateau angle measurements can be difficult to obtain in clinical cases because of osteoarthritis, which commonly occurs following CCL rupture.8 In particular, the presence of osteophytosis in the stifle at the level of the proximal tibia can obscure anatomical landmarks, making it a challenge to preoperatively determine the tibial plateau
A clinical study evaluating tibial plateau angle variability in dogs with CCL rupture showed that osteoarthritis at the level of the caudal tibial plateau was the only factor that significantly affected tibial plateau angle measurements between observers. Similarly, greater variability in tibial plateau angle was present when using a line tangential to the medial tibial plateau instead of using the anatomical landmarks described above.

Inaccurate tibial plateau angle measurements resulting from tibial plateau osteophytosis could lead to inappropriate tibial plateau rotation and subsequent clinical failure. Dogs with CCL rupture and severe tibial plateau osteophytosis may have no or minimal osteophytosis in the contralateral tibial plateau. Assuming anatomical consistency between the right and left tibial plateaus, the measurement of the contralateral tibial plateau angle could be used instead of the measurement of the affected stifle.

Tibial plateau symmetry in dogs has not been defined. Although several studies have evaluated the mean tibial plateau angle between right and left stifles and found no statistical differences, standard deviations were not reported, thus limiting the usefulness of this information within individual animals. No study to date has evaluated the tibial plateau angle symmetry or the ability to reliably predict the contralateral tibial plateau angle in dogs. A human study evaluating radiographic tibial plateau slope measurements using both knees in normal individuals concluded that within an individual, tibial plateau slope measurement of one knee was unreliable in predicting tibial plateau slope of the contralateral knee; however, clinical experience has shown a high degree of similarity between tibial plateau angles of the right and left stifles in dogs.

The purpose of this study was to evaluate the effect of osteophytosis on the measured tibial plateau angle in mongrel dogs, as well as to determine tibial plateau angle consistency between the right and left stifles. The null hypotheses were that no differences exist: (1) between the right and left tibial plateau angles in normal stifles; (2) in tibial plateau angles before and after induction of tibial plateau osteophytosis; (3) between tibial plateau angles after induction of osteophytosis and the normal contralateral tibial plateau angle; and that (4) the changes in tibial plateau angle values before and 8 months after CCL transection are not related to the severity of osteophytosis.

Materials and Methods

This study was part of a comprehensive drug evaluation and was conducted under a protocol approved by the Institutional Animal Use and Care Committee. Animals were obtained through the University Laboratory Animal Resources facility at Michigan State University. Thirty-one mongrel dogs that were free of pelvic limb orthopedic disease according to radiographic and physical examinations were included in the study.

Radiographic Procedure

Standard mediolateral and craniocaudal radiographs of the right and left stifles at time 0 and of the right stifle 8 months after CCL transection were taken under acepromazine maleate (0.04 mg/kg intravenously [IV]) and butorphanol tartrate (0.2 to 0.4 mg/kg IV). The radiographic beam was centered on the joint space between the femoral and tibial condyles and included the tibiotarsal joint. The stifle and tibiotarsal joint were positioned at approximately 90° of flexion for the radiographs. Lateral radiographs were accepted once superimposition of the tibial condyles was achieved.

Surgical Procedure

The right stifle was arbitrarily chosen to undergo an arthroscopic modification of the Pond Nuki model for CCL transection to induce osteoarthritis. Thorough exploration of the intra-articular structures was conducted in a routine manner to confirm absence of joint pathology. The CCL was sharply transected at its midpoint using a specialized forward-cutting blade [Figures 1A, 1B, 1C]. Complete transection of the CCL was ascertained by intraoperative visualization and confirmed by direct and indirect cranial drawer examinations during surgery. Each animal was then housed in a 4 × 12-ft run for the duration of the study and allowed unrestricted activity. No bandage was applied postoperatively.
Radiographic Evaluation

Tibial plateau angles were measured to the nearest 0.5° using landmarks previously described [Figure 2]. For cases with severe tibial plateau osteophytosis, a technique was developed that estimated the caudal medial tibial plateau landmark. This technique, referred to as the extension technique, was used to determine the caudal medial tibial plateau landmark by drawing a distal to proximal line along the caudal cortex of the medial tibial ridge, just beyond the medial articular surface. A second line was then drawn following the articular surface of the medial tibial plateau, extending caudally until it intersected with the first line [Figure 3]. The intersection of those lines represented the landmark for the medial caudal tibial plateau. The cranial tibial plateau landmark was determined by identifying the most cranial aspect of the articular surface of the medial plateau. This landmark was identifiable even in the presence of osteophytosis. Tibial plateau angles were measured in one sitting and were done in random order with respect to time and sides. An extra fine-point permanent marker was used to identify landmarks on acetate sheets overlying the radiograph. A board-certified radiologist (masked to the tibial plateau angle measurements) evaluated the lateral radiographs in order to grade tibial plateau osteophytosis.

Osteophytosis scores were assigned to the cranial and caudal medial tibial plateau regions, based on osteophyte severity. Osteophyte scores were 0=none, 1=mild, 2=moderate, and 3=severe [Figures 4A, 4B, 4C, 4D, respectively]. The scores for the cranial and caudal tibial plateaus were combined for a maximum score of 6.

Statistical Analysis

Results are reported as means ± standard deviations. Comparisons between two sets of angles were done with a paired t-test. Linear correlation was used to test for an association between osteophytosis scores and changes in right tibial plateau angles over time. Statistical significance was defined as a nominal type I error rate of <5% (P<0.05). Statistical power calculations were made with a commercial software package.
Results

The 31 mongrel dogs used in the study ranged in weight from 26.6 to 36.0 kg (mean 30.4±2.6 kg). All dogs were radiographically skeletally mature and <5 years of age. Twenty-three dogs were male, and eight were female.

At time 0, no significant differences were found between the right tibial plateau angle (24.6˚±1.9˚, range 20˚ to 30˚) and the left tibial plateau angle (24.3˚±2.3˚, range 18˚ to 31˚) (P=0.25). The mean difference between the right and left tibial plateau angles at time 0 was 0.3˚±1.8˚ (range 0˚ to 4.5˚), and 90% of the dogs had an absolute difference of ≤2˚ between the right and left sides [Figure 5].

The mean right tibial plateau angle at 8 months postoperatively (25.1˚±2.4˚, range 17.5˚ to 29.5˚) was statistically similar to the right (P=0.36) and left (P=0.17) preoperative tibial plateau angles. The mean right tibial plateau angle change over the 8 months after surgery was 0.5˚±2.8˚ (range 0˚ to 6.5˚).

Severity of osteophytosis did not have a significant effect on the differences between tibial plateau angles. Tibial plateau angle differences between time 0 and 8 months were not related linearly to osteophytosis severity based on either a composite score (P=0.86) or separate cranial and caudal location scores (P=0.34, P=0.24, respectively). The mean osteophyte composite score was 0.0 prior to CCL transection and was 3.97±1.12 at 8 months after CCL transection. Seven dogs had severe osteophytosis (composite score 5 to 6); 20 dogs had moderate osteophytosis (composite score 3 to 4), and four dogs had mild osteophytosis (composite score 1 to 2). The mean caudal tibial plateau osteophytosis score (2.2±0.79) was significantly higher than the mean.

Figure 5—Graph illustrating the probability of finding any given difference in tibial plateau angle between the right and left stifles prior to cranial cruciate ligament transection in a group of 31 normal mongrel dogs. These data indicate a high probability (88%) of finding a difference of ≤2˚ (intersection of dashed lines). TPA=tibial plateau angle.

Figures 4A-4D—Lateral radiographs of the right stifle of four different adult dogs, taken at 2 weeks (A) and 8 months (B, C, D) after cranial cruciate ligament transection, illustrating the osteophytosis grading scheme. The white circles in Figure 4A represent the osteophytosis grading locations on the cranial and caudal tibial plateaus. Osteophytosis of the two regions were scored as (A) none (0/0), (B) mild (1/1), (C) moderate (2/2), and (D) severe (3/3). A cumulative score ranging from 0 to 6 was used for statistical comparisons. For simplicity, the radiographs presented here show identical cranial and caudal scores. However, the majority of dogs had different scores for these two locations, with the caudal scores significantly higher (P=0.01).
osteoophyosis score of the cranial tibial plateau (1.7±0.75, \( P=0.01 \)) at 8 months after CCL transection.

In this study, no statistically significant differences were found between the right and left tibial plateau angles preoperatively and the right tibial plateau angle before and after osteophyte induction. Statistical power analysis revealed that 31 animals was an adequate number to identify a significant time-related difference of ≥1.5˚, with a type II error rate of <0.2 (power ≥0.8).

**Discussion**

Accurate determination of the tibial plateau angle is critical prior to and after performance of a TPLO. Osteophytosis present on the proximal tibia can make accurate landmark identification difficult, because normal anatomical structures can be obscured. This may lead to an inaccurate tibial plateau angle measurement, with subsequent inappropriate tibial plateau rotation.\(^4\)\(^,\)\(^8\) Induction of tibial plateau osteoophytosis 8 months after CCL transection did not significantly alter the tibial plateau angle measurement compared to preoperative values in this group of mongrel dogs. This finding was unexpected in animals with severe osteoophytosis because of the difficulty in identifying proper radiographic landmarks to determine tibial plateau slope. Fettig \textit{et al.} described significant variability associated with osteoophytosis on the caudal tibial plateau landmark.\(^8\)\(^,\)\(^9\)

Results of the study reported here may be related to use of the extension technique. This technique was developed to provide a consistent estimate of the medial caudal tibial plateau landmark, which can be completely obscured in cases of severe osteoophytosis. The extension technique proved to be very useful in these dogs. The osteophytosis present in the region of the cranial tibial landmark did not significantly alter identification of this point. These osteophytes likely originated at the insertion of the CCL, which is typically distal and cranial to the radiographic landmark.\(^17\) The cranial tibial plateau region was also significantly less affected with osteophytosis compared to the caudal tibial plateau region, which facilitated landmark identification. Previous studies have demonstrated consistent osteophytosis production in the region of joint capsule attachment, which could explain the increase in cranial versus cranial tibial plateau osteoophytosis.\(^18\)\(^,\)\(^19\) The difference in severity of osteophytosis may also have resulted from the body’s response to an amplified stress experienced at the cranial tibial plateau during weight bearing while the tibia was subluxated cranially.

Although osteophytosis did not significantly alter tibial plateau angle measurements in this study, the standard deviation of angle differences increased after induction of osteoophytosis. That increase was likely a reflection of variability in landmark identification resulting from osteophytosis deposition that obscured normal anatomy.

The ability to use the radiographic tibial plateau angle of a normal contralateral stifle may be beneficial in situations where severe osteoophytosis decreases the ability to achieve an accurate angle measurement. While previous studies have compared tibial plateau angles in both right and left stifles and found no statistical difference in the mean of those angles (i.e., no reported standard deviation), symmetry was not defined on an individual basis.\(^9\)\(^,\)\(^10\)\(^,\)\(^20\) Symmetry could be defined as a difference in tibial plateau angle of ≤2˚. The 2˚ threshold for symmetry was based upon the precision of the measurement technique (i.e., marker tip size, straight edge and protractor placement). Tibial plateau angle measurement variability based on two points can be geometrically calculated using the mean diameter of the identification mark and the distance between these points. As an example, by connecting the top of one mark to the bottom of the other mark on the medial tibial plateau, a difference of nearly 2˚ is generated in the measurement of the tibial plateau angle. In contrast, considering the distance between the tibial axis landmarks, the potential error in the tibial plateau angle measurement would only be approximately 0.2˚. Accordingly, a difference of 2˚ could be introduced to the tibial plateau angle simply as a result of the measurement technique, even with exact landmark identification.

In a radiographic study evaluating symmetry of the human tibial plateau slope in 33 normal individuals, it was found that regardless of radiographic technique, the majority (55%) of patients had a tibial plateau slope difference of ≥3˚ between knees.\(^11\) Considering that the human plateau slope is approximately 10˚, this small discrepancy corresponds to a 30% difference in tibial plateau slope between knees.\(^11\)\(^,\)\(^21\)\(^-\)\(^24\) That study concluded that the tibial plateau slope in a healthy knee in any given patient should not be used to predict the contralateral tibial plateau slope.\(^11\)\(^,\)\(^21\)\(^-\)\(^24\) Conversely, in a canine kinematics study, symmetry was defined as up to an 8% difference in peak vertical force.\(^25\) The average tibial plateau angle of dogs in this study was 24.4˚, which was similar to previously reported results.\(^4\)\(^,\)\(^7\)\(^,\)\(^9\)\(^,\)\(^26\)\(^,\)\(^27\) Interestingly, 2˚ also represents an 8% difference between tibial plateau angles, which further supports the concept that symmetry in tibial plateau angles could be considered ≤2˚.

When comparing right and left tibial plateau angles prior to induction of osteoophytosis, subtle differences were noted between angles in individual dogs. Of these differences, 90% were ≤2˚; 10% of the dogs had a difference of 2˚ to 4.5˚ [Figure 5]. Differences >2˚ could be the result of true asymmetry between stifles, but they were more likely caused by a combination of measurement technique imprecision, landmark placement error, and performing the landmark identification in a masked fashion (unable to compare landmark location). Interestingly, based on Slocum’s TPLO rotation chart\(^4\) for a 30-mm saw blade, a 1-mm error in placement of the osteotomy alignment marks would result in a 2˚ discrepancy between theoretical and actual tibial plateau correction. This error is similar to the difference between the right and left tibial plateau angles that was seen in the current study.

Considering the numerous sources of error when measuring tibial plateau angle (e.g., radiographic and measurement technique, osteoophytosis, tibial axis shift after TPLO
correction, and geometric arc calculation), it seems that consistent rather than accurate landmark identification may be more important in the evaluation of a postoperative TPLO. Based on the study reported here, using the extension technique may help to reduce variability in tibial plateau angle measurement in cases of severe osteophytosis, and symmetry between the two stifles may allow use of the contralateral tibial plateau angle (if there is minimal or no osteophytosis) for preoperative planning.

Conclusion
Osteophytosis did not significantly alter the measured angle of the tibial plateau when using the extension technique in 31 normal mongrel dogs. Tibial plateau angle symmetry (i.e., a difference of \( \pm 2^\circ \)) was present in 90% of dogs. Based on symmetry, the unaffected limb can be used as a guide to predict the angle of the affected limb in cases where landmark identification is difficult because of severe osteophytosis.

References
Computed Tomographic Diagnosis of Nongastrointestinal Foreign Bodies in Dogs

Clinical data and computed tomography (CT) studies were reviewed for 13 dogs with confirmed nongastrointestinal foreign bodies. Locations of foreign bodies were the nasal cavity, thoracic wall, retropharyngeal region, and cerebellum. Types of foreign bodies included small plant components, blades of grass, wooden sticks, cloth fibers, and a needle. Foreign bodies in five dogs were not identified on CT, and secondary reactions resembled neoplastic or fungal disease. In eight dogs, foreign bodies were recognized by their shape and/or internal architecture. In two dogs, three-dimensional reformatting helped demonstrate foreign bodies in relation to palpable bony landmarks. J Am Anim Hosp Assoc 2007;43:99-111.

Introduction

Foreign bodies are an important cause of recurrent abscesses, draining tracts, or pyogranulomas in dogs. Types of nongastrointestinal foreign bodies include wood, plant material, microchips, retained surgical sponge, bone, needles, and hooks. The prognosis for affected dogs is good if the foreign bodies can be accurately localized and completely removed. In dogs, the initial diagnostic imaging tests most commonly recommended for localizing superficial foreign bodies are radiography, ultrasonography, and sinography.

In humans, computed tomography (CT) is recommended for treatment planning when foreign bodies are in complex anatomical regions and/or when they are surrounded by air or bone. Computed tomography is a noninvasive imaging technique that uses X-rays and computers to create sectional images of structures. One advantage of CT over radiography is the ability to remove superimposition of overlying bony structures. Because images are acquired digitally, they can be displayed using various settings (windows) to best demonstrate the structure of interest. Reformatting software programs also allow creation of three-dimensional images that can be rotated in space. Tissue densities can be measured using numerical values called Hounsfield units, which are units of density relative to water. Only a few individual case reports could be found describing CT diagnosis of nongastrointestinal foreign bodies in dogs. The purpose of this retrospective study is to describe the clinical and CT characteristics of confirmed foreign bodies in dogs.

Materials and Methods

Medical records were searched from January 1, 1995 to December 31, 2005 for dogs that had a final diagnosis of a nongastrointestinal foreign body and were examined with CT. Cases with a diagnosis of foreign body confirmed by direct visualization and/or histopathology were included in the study. Clinical characteristics retrieved from medical records included age, breed, sex, clinical signs, location of foreign body, method of final diagnosis, final diagnosis, and outcome. Complete digital CT image
files for each case were reloaded onto a reformatting workstation\(^4\) and reviewed jointly by two people. The evaluators were aware of the location and type of foreign body present. Technical parameters, such as type of CT scanner, slice thickness and interval, and type of contrast procedure (if available) were recorded for each case. A consensus opinion was reached for describing CT characteristics, such as foreign body size, shape, opacity, and margination; mean CT density of the foreign body; and the CT display setting that best demonstrated the foreign body. Other findings recorded were the appearance of secondary reactions, appearance of the foreign body in post-contrast images (if available), presence or absence of adjacent bony lysis or proliferation, and usefulness of three-dimensional reformating.

**Results**

Thirteen dogs met the criteria for inclusion in the study. Ages ranged from 1 to 13 years (median=4.9 years). Represented breeds were highly variable [Table 1]. Affected dogs included six males (two castrated) and seven females (four spayed). Dogs with nasal foreign bodies most commonly exhibited chronic nasal discharge (n=7). Other clinical signs included sneezing (n=3), pawing at the face (n=1), and stertor (n=1). Dogs with nonnasal foreign bodies had a localized soft-tissue swelling (n=2), chronic draining tract (n=1), and head tilt (n=1). Most foreign bodies were identified in the nasal cavity or nasopharynx (n=9). Other foreign bodies involved the thoracic wall (n=1), brain (n=1), and retropharyngeal region (n=2).

Most foreign bodies were of plant origin (n=10). Four dogs had small pieces of plant material confirmed primarily by histopathology. Large plant components were confirmed by surgery (n=1), blind nasal biopsy with forceps (n=1), or rhinoscopy (n=4) in the remaining six dogs. Three of the large plant foreign bodies were wooden sticks. Other large plant foreign bodies were grass blades (n=2) and evergreen sprigs (n=1). Nonplant foreign bodies were identified primarily by direct visualization (rhinoscopy or oropharyngeal examination), and these included toy stuffing material (n=1), tennis ball fibers (n=1), and a needle (n=1).

For those dogs with known outcomes (n=11), most had resolution of their clinical signs after treatment (n=8). One dog with a plant foreign body granuloma in the cerebellum was euthanized because of severe neurological deficits and a poor prognosis for recovery. One dog with a plant foreign body pyogranuloma of the thoracic wall suffered recurrent abscesses after surgical excision. After one abscess ruptured, a segment of juniper branch was found at the site. One dog with rhinitis secondary to a mixture of plant material, hair, and keratin was reexamined for nasal discharge 1 year after treatment. A second endoscopic examination and repeated nasal flushings did not yield any additional foreign material, and further outcome information was unavailable.

Computed tomography scans were performed with a fourth-generation scanner\(^5\) in eight dogs and a spiral scanner\(^6\) in five dogs. Slice thicknesses ranged from 2 to 5 mm, with intervals ranging from 1.5 to 5 mm. Intravenous contrast-enhanced CT was performed in three dogs, and CT sinography was performed in one dog. Small pieces of plant material were not identified on CT in four dogs with confirmed plant foreign bodies [Table 2]. The secondary reaction in these dogs appeared similar to fungal disease or neoplasia [Figures 1A-1C].\(^{32,33}\) Larger plant foreign bodies were distinguishable in six dogs, with recognition based primarily on shape and/or internal architecture. Most of the large plant foreign bodies were best seen with lung or soft-tissue window settings.\(^{31}\) In one dog (case no. 9), an intranasal wooden stick exhibited a “target” shape in the transverse plane and a tubular shape in the sagittal and dorsal planes [Figures 2A-2C]. In another dog (case no. 10), wooden stick foreign bodies in the retropharyngeal region exhibited a striated internal architecture [Figure 3A]. The locations of the foreign bodies and associated sinus tract, relative to palpable bony landmarks, were best delineated in three-dimensional, reformatted images [Figures 3B, 3C]. In case no. 12, cloth stuffing material appeared as a homogenous, nonenhancing, focal area of increased soft-tissue opacity and was similar to an area of fluid accumulation [Figure 4A].\(^{31}\) Tennis ball fibers in one dog (case no. 11) were visible as fusiform to oblong areas of air opacity within a region of soft-tissue opacity, and these were best seen with the lung window setting [Figure 4B].\(^ {31}\) Awareness of the final diagnoses and the unusual shapes helped to differentiate these foreign bodies from normal gas pockets. A retropharyngeal needle foreign body was clearly distinguishable in one dog (case no. 13). The linear shape of the needle was best appreciated with a wide, bone window setting [Figure 5A].\(^ {31}\) Radiating streak artifacts and the secondary soft-tissue swelling were best seen in a soft-tissue window setting [Figure 5B].\(^ {31}\) The orientation of the needle, relative to the hyoid bones and other palpable bony landmarks, was best appreciated in three-dimensional reformatted images [Figure 5C].

**Discussion**

The goal of this study was to gain a better understanding of the CT appearances of nongastrointestinal foreign bodies in dogs; therefore, the people evaluating the CT scans were aware of the final diagnoses. Even with this prior knowledge, however, foreign bodies were not distinguishable in five dogs, and the secondary reactions that occurred in four dogs were considered similar to neoplastic or fungal disease. These similarities to neoplastic or fungal disease were in agreement with previous reports in humans and dogs.\(^ {10,32,33}\) Petersen et al. reported that foreign body reactions in humans can exhibit a pseudotumor appearance.\(^ {32}\) Leskovar et al. described a suspected neoplasm that was ultimately diagnosed as a plant foreign body granuloma on the lateral margin of the medulla and cervical spinal cord of a dog.\(^ {10}\) Saunders et al. described the presence of nasal foreign bodies in two of 35 dogs with mycotic rhinitis.\(^ {33}\)

For those foreign bodies that were identified with CT, the use of multiple window settings was helpful. The observation that some foreign bodies were best seen with the lung window setting was consistent with previous case reports in humans, where wood was found to mimic focal gas pockets in soft tissues.\(^ {28,34-39}\) Identification of the wood foreign
bodies in these cases was based primarily on a linear shape or orientation along a plane that did not match a known anatomical structure. The characteristic architecture of wooden sticks in some dogs was best seen using soft-tissue window settings, which was also similar to previous reports in humans. In these human cases, wooden sticks appeared to have increased opacity because of their high inherent density or absorption of body fluids. Diagnoses were based primarily on the presence of internal striations or a "target" shape in transverse images. The target shape was believed to be caused by inflammatory tissue formation on the surface of the wood. Streak artifacts from a needle foreign body in one dog (case no. 13) obscured visualization of its shape in all but the widest available bone window setting. This finding was similar to a previous case series of known metal foreign bodies in the human chest.

For one dog (case no. 10) with chronic draining tracts from retropharyngeal wooden foreign bodies, the relationship of sinus tracts to palpable surgical landmarks was best demonstrated using CT sinography and three-dimensional reformatted images. These findings were consistent with a previous case report of a dog with a bronchoesophageal fistula. Authors of this case report concluded that CT sinography with three-dimensional reformatting assisted surgical planning by demonstrating the relationship between the subcutaneous neck abscess, left cranial lobar bronchus, adjacent cervical vertebrae, and thoracic wall.

Conclusion

Based on the 13 dogs in this study, some foreign bodies may not be distinguishable with CT. Secondary reactions from foreign bodies may also mimic neoplastic or fungal disease. Foreign bodies with a characteristic shape or architecture are more likely to be distinguished with CT, especially if images are viewed with soft-tissue, bone, or lung window settings. Three-dimensional CT reformatting was a useful tool for demonstrating the relationship between foreign bodies, related sinus tracts, and palpable bony landmarks.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (y)</th>
<th>Breed</th>
<th>Sex</th>
<th>Presenting Clinical Signs</th>
<th>Foreign Body Location</th>
<th>Method of Final Diagnosis</th>
<th>Final Diagnosis</th>
<th>Outcome†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>Doberman pinscher</td>
<td>M</td>
<td>Right thoracic wall mass for 5 mos</td>
<td>Right thoracic wall mass for 5 mos</td>
<td>Surgery, histopathology</td>
<td>Pyogranuloma with undetermined plant fibers</td>
<td>Recurrent abscesses at 1 y, 6 y, 7 y after mass removal</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>Mixed-breed dog</td>
<td>F</td>
<td>Severe head tilt (first to right, then to left) for 2 mos</td>
<td>Left cerebellum and pons</td>
<td>Necropsy, histopathology</td>
<td>Pyogranuloma with plant fibers, suspected plant awn</td>
<td>Euthanized</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>German shepherd dog</td>
<td>M</td>
<td>Bilateral epistaxis for 2 mos</td>
<td>Bilateral nasal cavity</td>
<td>Rhinoscopy, histopathology</td>
<td>Mixed foreign material (hair, plant, keratin) in mucosa</td>
<td>Recurrent nasal discharge 1 y later; no foreign material seen at second rhinoscopy</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>Toy poodle</td>
<td>SF</td>
<td>Nasal discharge for 4 mos</td>
<td>Right nasal cavity</td>
<td>Pharyngoscopy, rhinoscopy, histopathology</td>
<td>Plant fibers in mucosa</td>
<td>Signs resolved</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>Chow chow</td>
<td>M</td>
<td>Sneezing for 6 wks</td>
<td>Right nasal cavity</td>
<td>Rhinoscopy</td>
<td>Blade of grass (2.5-3 in)</td>
<td>Signs resolved</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>Norwich terrier</td>
<td>F</td>
<td>Mucopurulent right nasal discharge, stertorous breathing, sneezing</td>
<td>Right ventral meatus</td>
<td>Rhinoscopy, blind biopsy of nasal cavity with forceps, histopathology</td>
<td>Blade of grass (6 in), pyogranuloma with plant fibers</td>
<td>Signs resolved</td>
</tr>
<tr>
<td>7</td>
<td>6</td>
<td>Boxer</td>
<td>SF</td>
<td>Left nasal discharge for 7 mos</td>
<td>Caudal left nasal cavity</td>
<td>Rhinoscopy</td>
<td>Evergreen sprigs</td>
<td>NA</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>Shih tzu</td>
<td>F</td>
<td>Right nasal discharge for 2 y</td>
<td>Right nasal cavity</td>
<td>Rhinoscopy</td>
<td>Cedar stick (2.5 in)</td>
<td>NA</td>
</tr>
</tbody>
</table>

(Continued on next page)
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (y)</th>
<th>Breed</th>
<th>Sex</th>
<th>Presenting Clinical Signs</th>
<th>Foreign Body Location</th>
<th>Method of Final Diagnosis</th>
<th>Final Diagnosis</th>
<th>Outcome†</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>3</td>
<td>Blue heeler</td>
<td>F</td>
<td>Chronic right nasal discharge, sneezing, pawing at face</td>
<td>Right nasal cavity</td>
<td>Rhinoscopy</td>
<td>Wooden stick</td>
<td>Signs resolved</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td>German shorthaired pointer</td>
<td>SF</td>
<td>Draining tract in right maxillary region for 4 mos</td>
<td>Right retropharyngeal</td>
<td>Surgery</td>
<td>Wooden stick (3 in) with two fragments</td>
<td>Signs resolved</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>Jack Russell terrier</td>
<td>M</td>
<td>Chronic bilateral mucoid nasal discharge, congenital soft-palate defect</td>
<td>Bilateral nasal cavity</td>
<td>Rhinoscopy</td>
<td>Tennis ball fibers</td>
<td>Signs resolved</td>
</tr>
<tr>
<td>12</td>
<td>1</td>
<td>Dachshund</td>
<td>SF</td>
<td>Stertorous respiration after chewing stuffed animal 5 mos prior</td>
<td>Left nasal choana</td>
<td>Pharyngoscopy, histopathology</td>
<td>Cloth fibers consistent with toy stuffing</td>
<td>Signs resolved</td>
</tr>
<tr>
<td>13</td>
<td>13</td>
<td>Mixed-breed dog</td>
<td>CM</td>
<td>Coughing, neck swelling, dyspnea</td>
<td>Right retropharyngeal</td>
<td>Digital palpation and removal</td>
<td>Needle</td>
<td>Signs resolved</td>
</tr>
</tbody>
</table>

* M=male; F=female; SF=spayed female; CM=castrated male
† NA=not available
References

Figures 3A-3C—Computed tomographic images of wooden stick material in the right retropharyngeal region of a 3-year-old, spayed female, German shorthaired pointer (case no. 10). (A) Nonenhanced, transverse, soft-tissue window image at the level of the external ear canal (E), demonstrating a striated internal architecture of the largest wood fragment (arrow). The image is oriented with dorsal at the top and R=right. (B) Nonenhanced, ventrodorsal, three-dimensional CT image demonstrating the location of the largest wood fragment (arrow) relative to surrounding palpable bony landmarks, such as the wing of the atlas (W). The image is oriented with rostral at the top and R=right. (C) Post-sinography, ventrodorsal, three-dimensional CT image demonstrating the location and extent of the secondary sinus tract (arrow) relative to palpable bony landmarks, such as the wing of the atlas (W). Rostral is at the top and R=right.
Table 2
Computed Tomographic Characteristics of Nongastrointestinal Foreign Bodies in 13 Dogs

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Final Diagnosis</th>
<th>Size (mm) *</th>
<th>Shape</th>
<th>Opacity †</th>
<th>Margination</th>
<th>CT Density (HU) ‡</th>
<th>CT Display Settings for Best Visualization §</th>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pyogranuloma with undetermined plant fibers</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>Lysis of medial margin of right 10th rib; mass of mixed opacity involving subcutaneous tissue, pleura, thoracic wall muscles. Pseudotumor appearance. ³²</td>
</tr>
<tr>
<td>2</td>
<td>Pyogranuloma with plant fibers, suspected plant awn</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>Mass of mixed opacity in left cerebellopontine region; compression of fourth ventricle; heterogenous contrast enhancement. Pseudotumor appearance. ³²</td>
</tr>
<tr>
<td>3</td>
<td>Mixed foreign material (hair, plant, keratin) in mucosa</td>
<td>9 × 2 × 11</td>
<td>Linear</td>
<td>Increased</td>
<td>Sharp</td>
<td>+255</td>
<td>Lung</td>
<td>Increased soft-tissue opacity in both nasal cavities.</td>
</tr>
<tr>
<td>4</td>
<td>Plant fibers in mucosa</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>Soft-tissue mass in right nasal cavity with lysis of maxillary turbinates, ethmoid turbinates, hard palate, and lateral maxilla. Loose teeth. Pseudotumor appearance. ³²</td>
</tr>
<tr>
<td>5</td>
<td>Blade of grass (2.5-3 in)</td>
<td>45 × 2 × 7</td>
<td>Ribbon</td>
<td>Similar</td>
<td>Ill-defined</td>
<td>-76 to -163</td>
<td>Lung</td>
<td>Lysis of right maxillary turbinates.</td>
</tr>
</tbody>
</table>

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### Table 2 (cont’d)

Computed Tomographic Characteristics of Nongastrointestinal Foreign Bodies in 13 Dogs

<table>
<thead>
<tr>
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<th>Margination</th>
<th>CT Density (HU)‡</th>
<th>CT Display Settings for Best Visualization§</th>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Blade of grass (6 in), pyogranuloma with plant fibers</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>Soft-tissue mass in right nasal cavity, nasal choana, and nasopharynx with lysis of hard palate, maxillary turbinates, and nasal septum. Pseudotumor appearance.</td>
</tr>
<tr>
<td>7</td>
<td>Evergreen sprigs</td>
<td>1 × 3</td>
<td>Oblong</td>
<td>Decreased</td>
<td>Sharp</td>
<td>-278</td>
<td>Lung</td>
<td>Soft-tissue mass in left nasal cavity with lysis of hard palate, turbinates, left lateral maxilla. Knowledge of final diagnosis helped in recognition of unusually shaped lucencies.</td>
</tr>
<tr>
<td>8</td>
<td>Cedar stick (2.5 in)</td>
<td>4 × 2 × 14</td>
<td>Tubular</td>
<td>Increased</td>
<td>Sharp</td>
<td>+73 overall, -8 interior</td>
<td>Soft tissue</td>
<td>Increased soft-tissue opacity in right caudal nasal cavity and choana, with lysis of maxillary turbinates, nasal septum, hard palate.</td>
</tr>
<tr>
<td>9</td>
<td>Wooden stick</td>
<td>5 × 6 × 63</td>
<td>Tubular</td>
<td>Increased</td>
<td>Sharp</td>
<td>63</td>
<td>Lung</td>
<td>Lysis of maxillary turbinates; increased soft-tissue opacity in right ethmoid region.</td>
</tr>
</tbody>
</table>

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### Table 2 (cont’d)
Computed Tomographic Characteristics of Nongastrointestinal Foreign Bodies in 13 Dogs

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<th>Margination</th>
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<th>CT Display Settings for Best Visualization§</th>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Wooden stick (3 in) with two fragments</td>
<td>11 × 7 × 74, 3 × 2 × 31, 2 × 3 × 29</td>
<td>Cylindrical, irregular</td>
<td>Increased</td>
<td>Sharp</td>
<td>+163 to +205</td>
<td>Soft tissue, bone 1</td>
<td>Soft-tissue mass extending from ramus of mandible to third cervical vertebra, ventral to right ear. Periosteal proliferation on angular process of mandible, with obscured margins of mandibular and parotid salivary glands. Cylindrical filling defects in contrast sinogram. Relationship between foreign body, sinus tract, and palpable bony landmarks best seen in three-dimensional, reformatted images.</td>
</tr>
<tr>
<td>11</td>
<td>Tennis ball fibers</td>
<td>1 × 1 × 10</td>
<td>Oblong to filamentous</td>
<td>Decreased</td>
<td>Sharp</td>
<td>-253 to -278</td>
<td>Lung</td>
<td>Increased soft-tissue opacity in ventral nasal cavity and choana, with bilateral lysis of maxillary turbinates and nasal septum. Knowledge of final diagnosis helped in recognition of unusual shapes.</td>
</tr>
<tr>
<td>12</td>
<td>Cloth fibers consistent with toy stuffing</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>Nonenhancing mass in left nasal choana and nasopharynx; focal lysis of vomer, lysis of maxillary turbinates. Appearance similar to fungal disease.³³</td>
</tr>
</tbody>
</table>

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### Table 2 (cont’d)

Computed Tomographic Characteristics of Nongastrointestinal Foreign Bodies in 13 Dogs

<table>
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<th>Opacity†</th>
<th>Margination</th>
<th>CT Density (HU)‡</th>
<th>CT Display Settings for Best Visualization§</th>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>Needle</td>
<td>49 × 1</td>
<td>Linear</td>
<td>Increased</td>
<td>Sharp</td>
<td>+1990</td>
<td>Bone 2</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soft-tissue mass in right retropharyngeal region with swollen laryngeal mucosa. Relationship of needle to palpable bony landmarks best seen in three-dimensional reconstructions.</td>
</tr>
</tbody>
</table>

* mm=millimeters; ND=foreign body not distinguishable
† Computed tomographic opacity relative to adjacent soft tissue
‡ CT=computed tomography; HU=Hounsfield units
§ Bone 1=1600 width, 300 level; Bone 2=3200 width, 1900 level; soft tissue=375 width, 75 level; lung=1600 width, -300 level
Figure 5A-5C—Computed tomographic images demonstrating the appearance of a needle foreign body in the right retropharyngeal region of a 13-year-old, castrated male, mixed-breed dog (case no. 13). (A) Oblique transverse, wide bone window image at the level of the atlantooccipital joint (AO), demonstrating the linear shape of the needle (arrow). The image is oriented with dorsal at the top and R=right. (B) Transverse, soft-tissue window image at the level of the first cervical vertebra, demonstrating radiating streaks (density change artifacts) around the needle (arrow) and retropharyngeal/laryngeal soft-tissue swelling. Dorsal is at the top and R=right. (C) Ventrodorsal, three-dimensional image demonstrating the location of the needle (arrow) relative to palpable bony landmarks, such as the wing of the atlas (W). Rostral is at the top and R=right.
Ultrasound-Assisted Drainage and Alcoholization of Hepatic and Renal Cysts: 22 Cases

Twenty-two dogs and cats with symptomatic renal or hepatic cysts that had undergone ultrasound-assisted drainage and alcoholization were retrospectively evaluated. Common presenting complaints were anorexia, reluctance to move, and vomiting. Abdominal pain was observed in all cases. Systemic hypertension was identified in four dogs and four cats with renal cysts. Cyst drainage and alcoholization were achieved without complications in 19 animals, and all clinical signs resolved after the procedure. In three cases, transient bleeding was observed during alcoholization, and the procedure was interrupted. Blood pressure normalized in the four dogs with renal cysts, but it remained elevated in the four cats.


Introduction

Renal and hepatic cysts are epithelium-lined cavities filled with a liquid of differing composition, depending on the organ of origin and presence of complicating factors.1,2 The lesions may be single or multiple. Cysts can be classified as simple (i.e., the contents do not contain cells, bacteria, or fungi) or as complicated.1,2 The pathogenesis of the cysts is not well defined.3 The epithelial cells lining the cyst are metabolically active, and the dynamic activity of these cells is responsible for any progressive increase in volume of the cyst.3 In humans, the cysts can cause ischemia in the surrounding renal parenchyma, leading to renal failure and to activation of the renin-angiotensin-aldosterone system, with development of systemic hypertension.4-6 Renal cysts in humans can also cause urinary obstruction from compression of the renal papillary ducts or the renal pelvis.1,7 With regard to hepatic cysts in humans, obstruction of the biliary tree is the most important complication, although rare.8 In people, common complaints with either renal or hepatic cysts are pain, decreased physical activity, and decreased appetite.1,2,9,10 In most cases, cyst drainage and alcoholization improve renal hypertension, urinary and biliary obstruction, and clinical signs.2,6,9,11,12

In dogs and cats, renal cysts are commonly observed in breeds predisposed to polycystic kidney disease, where the cysts may cause renal failure.13,14 In animals, cysts can also be found secondary to chronic nephropathies. In these latter cases, the cysts usually occur as single lesions.15 Less frequently, solitary renal cysts have been recognized as incidental findings in clinically healthy dogs.16 Obstruction of the proximal ureter has been documented in one cat, and obstruction of the renal pelvis has been described in a dog.17,18 With renal cysts, clinical signs are generally related to kidney failure, and abdominal pain is not always recognized in dogs and cats.19,20 Systemic hypertension has been reported with renal cysts in cats, although its clinical relevance is debated.17,19,20 Hepatic cysts in cats and dogs are generally associated with liver tumors, polycystic kidney disease, liver hydatidosis, and congenital
hepatopathies. In these conditions, cysts do not always contribute to the clinical signs.

The aim of the present study was to characterize the clinical and laboratory features of dogs and cats with symptomatic renal and hepatic cysts. The ultrasonographic technique of cyst drainage and alcoholization, as well as the complications and short-term outcomes were also evaluated.

Materials and Methods

The clinical records of dogs and cats admitted between October 2002 and October 2004 with a diagnosis of symptomatic renal or hepatic cysts that were submitted to ultrasound-assisted cyst drainage and alcoholization were retrospectively evaluated. Animals were excluded if ultrasonographic follow-up was not available at 3 to 4 weeks following the procedure. From the clinical records, information was collected on signalment, major complaints and physical findings at presentation, results of laboratory tests, ultrasonographic findings, and systemic blood pressure measurements. Blood pressure was evaluated on admission, 24 to 48 hours following intervention, and 3 to 4 weeks after intervention.

To perform drainage and alcoholization of cysts, all animals were fasted for 12 hours prior to intervention. Tramadol (2.0 mg/kg intramuscularly [IM]) was administered 1 hour before induction of anesthesia, which was done with intravenous (IV) propofol (dogs, 6.5 mg/kg; cats, 8.0 mg/kg). Anesthesia was maintained by repeated IV boluses of propofol (1.0 mg/kg). The intervention was carried out in a single session using two consecutive alcoholizations of the cystic cavity. The cyst was drained using a spinal needle (22 or 23 gauge) introduced via an ultrasound-assisted, percutaneous approach. Once the needle was positioned in the cystic cavity, the stylet was removed and connected to a three-way valve. Drainage of the cystic fluid was slowly achieved by aspiration with a syringe. In each case, the syringe volume was never more than double the estimated cyst volume. To avoid excessive negative pressure when aspirating the cyst and to have better manual control during the procedure, larger syringes were not used. An aliquot of 0.5 mL of the cystic fluid was collected in sterile, buffered transport medium and kept at 4° to 8° C for aerobic bacterial culture. The remaining amount of liquid was used for cytology. Slides were stained with May-Grünwald Giemsa and were examined by the same person.

When drainage of the cyst was completed, a volume of 95% ethanol that was equivalent to half of the amount drained was injected through the same needle. The alcohol was left in the cyst cavity for 3 minutes and then slowly removed. The alcoholization was repeated with 2% lidocaine added to the alcohol (lidocaine to alcohol solution volume was 1:10). The mixture was left in place for 3 minutes and was again drained. Tramadol (2 mg/kg IM or per os at 12 hours) was stopped 24 hours after the procedure if pain was not identified with abdominal palpation.

Blood pressure was measured by Doppler sphygmomanometry in a quiet room after a 10- to 20-minute period of acclimatization. Five measurements were obtained with the animal in lateral recumbency, and they were repeated after 5 to 10 minutes. The mean blood pressure was calculated, excluding the highest and lowest values. For dogs and cats, cuffs that were 40% and 30% of the front limb circumference were used, respectively. Systemic hypertension was defined as systolic values >150 mm Hg in dogs and >170 mm Hg in cats.

Results

Clinical Findings

Renal cysts were diagnosed in 10 animals (five dogs, five cats), and hepatic cysts were diagnosed in 12 animals (three dogs, nine cats) (Figures 1, 2). Eight dogs and two cats were intact males, seven cats were castrated males, four cats were spayed females, and one cat was an intact female. Median age for dogs was 11 years (range 8 to 13 years), and for cats the median age was 7 years (range 3 to 12 years). One dog was a German shepherd dog, another was a West Highland white terrier, and the remaining were mixed-breed dogs. Ten cats were Persians, two were domestic shorthairs, and two were exotic shorthairs.

In the five cats with renal cysts, one large cyst was present in each case, and some smaller cysts were present in some cats. In these cases, drainage and alcoholization were performed only on the most prominent cyst. In four of the cats with hepatic cysts, some small cysts were also found in the kidneys. In the remaining animals, only single renal and hepatic cysts were present. The median sizes of the renal cysts were 35 mm (range 28 to 65 mm) in dogs and 25 mm (range 19 to 32 mm) in cats. For the hepatic cysts, median sizes were 38 mm (range 35 to 43 mm) in dogs and 20 mm (range 15 to 26 mm) in cats. Polycystic renal disease was found in the five cats with renal cysts and in four cats with hepatic cysts and small cysts in the kidneys. In five dogs with a renal cyst and in three dogs and five cats with hepatic cysts, the primary renal and hepatic disorder was not established. In these cases, ultrasonography of the kidney and liver parenchyma was normal, but biopsy was not pursued.

Complaints at presentation included anorexia in three dogs and two cats with renal cysts, and in all animals with hepatic cysts. Reduced physical activity was noted in all animals with renal cysts and in two dogs and eight cats with hepatic cysts. Vomiting was reported in three cats with renal cysts and in five cats with hepatic cysts. The major finding on physical examination was pain upon abdominal palpation, which was identified in all animals. An enlarged and irregular kidney was palpated in each of the five cats with renal cysts. An abdominal mass was palpated in a dog with a renal cyst.

Laboratory Results

Among the animals with renal cysts, one cat was mildly anemic (hematocrit 27%; reference range 30% to 45%). The same cat and two others had mild to moderate azotemia (average serum creatinine was 3.5 mg/dL; range 2.4 to 4.1 mg/dL; reference range <1.6 mg/dL). Two of the azotemic
cats also had low urine specific gravity (1.019 to 1.022; reference range 0.035 to 1.060). On urinalysis, microscopic hematuria was found in a dog and a cat.

Among the animals with hepatic cysts, anemia was identified in one dog (hematocrit 36%; reference range 42% to 55%) and a cat (hematocrit 21%). In each case, the anemia was nonregenerative. The anemic cat also had mildly elevated alanine aminotransferase (89 U/L; reference range <50 U/L) and elevated bilirubin (0.6 mg/dL; reference range 0.1 to 0.2 mg/dL). Liver enzymes were normal in all other animals. Increased serum creatinine was found in the dog (2.1 mg/dL; reference range <1.5 mg/dL) and cat with anemia, and in two other cats. Average serum creatinine in the three azotemic cats was 3.1 mg/dL (range 2.6 to 3.2 mg/dL). Polycystic renal disease was diagnosed in all three cats. Each of the azotemic animals had reduced urine specific gravity and proteinuria, with a quiet urine sediment. The protein-to-creatinine urinary ratio was 1.8 in the dog (normal value <0.7). In cats, the protein-to-creatinine urinary ratio varied from 0.7 to 3.3 (normal value <0.5). Cytology of the cystic fluid was compatible with a simple cyst in all (n=22) cases, and bacterial culture was negative in all (n=22) cases.

Other Findings

The renal cyst caused dilatation of the renal pelvis in one dog. Renal cysts were associated with systemic hypertension in all affected dogs and cats. Systolic blood pressure in dogs ranged from 160 to 190 mm Hg (median 175 mm Hg), and in cats it ranged from 180 to 195 mm Hg (median 190 mm Hg). With regard to animals with hepatic cysts, a 3-year-old exotic shorthair cat also had obstruction of the bile duct. On ultrasonography, the cyst was compressing the duct, which appeared dilated. This cat was the one with documented anemia, increased serum alanine aminotransferase, and increased bilirubin levels. Blood pressure was not determined in any of the animals with hepatic cysts.

Complications and Follow-up

Abdominal bleeding occurred with two renal cysts (in one dog and one cat) and one hepatic cyst (in one dog). In all three animals, bleeding started from the cyst when ethanol was introduced, and the procedure was interrupted in each case. Bleeding was mild, and additional treatment for hemorrhage was not required.

Following drainage and alcholization, the 19 animals that had no complications showed resolution of their abdominal pain within 24 hours. At 24 hours, abdominal discomfort was still present in the three cases that experienced bleeding during intervention, and oral tramadol was administered. Anorexia, vomiting, and physical activity improved within 3 to 4 weeks following the procedure in the 19 animals without complications. Within 24 to 48 hours, serum creatinine and alanine aminotransferase were normal in these 19 animals. At 3 weeks, serum creatinine was further increased from 3.1 to 3.9 mg/dL in one cat with a hepatic cyst and azotemia. In all other animals with initial laboratory abnormalities, reevaluation at 3 to 4 weeks showed normal renal and hepatic biochemical test results. Blood pressure was normal at 3 to 4 weeks in the four dogs with renal cysts but did not improve in the four cats. In the three animals with bleeding, ultrasonographic evaluation performed 24 to 48 hours after alcoholization showed the formation of a blood clot and/or the presence of echogenic contents in the cyst. On repeat ultrasonography at 3 to 4 weeks, none of the 19 animals that completed the procedure without complications had a recurrence of the cyst. At this time the site of the cystic lesion was replaced by a hyperechoic lesion with indistinct margins, and it was smaller than the original cyst in all cases. In the dog with a renal cyst causing urinary obstruction, the pelvis was no longer dilated. In the cat with bile duct compression, the bile duct remained dilated, even though the
hepatic cyst was not identified. In this cat, serum alanine aminotransferase and bilirubin levels did not improve.

Discussion

In humans, one of the most common complaints associated with renal and hepatic cysts is pain, as the lesions distend the innerved organ capsule and stimulate nociceptive fibers.1,2,9,10 In this report, all animals were presented for changes in their behavior that also suggested nociceptive stimulation.27,28 Based on laboratory data, it was unlikely these signs arose from other clinical renal and hepatic disorders. Pain was elicited upon abdominal palpation in all affected animals. Compared to previous reports, the cysts in the animals of the present study were quite large and presumably big enough to distend the organ capsule and elicit pain. In addition, 3 to 4 weeks following the procedure, evidence of pain had subsided, and activity and attitude had improved. Because of its retrospective nature, some bias may have occurred in the assessment of these animals, especially in the follow-up period.

In humans, it is widely accepted that the activation of the renin-angiotensin-aldosterone system is the principal factor causing hypertension with renal cysts.2,4,29 The role of endocrine activation is further demonstrated by the good therapeutic response to angiotensin-converting enzyme inhibitors and the resolution of hypertension after drainage of the cysts.5,6 In the present study, systolic arterial hypertension was found in all animals with renal cysts; however, the response of hypertension to cyst drainage and alcoholization was different in dogs and cats. Even though most cats with polycystic kidney disease are not hypertensive, it is possible that the cats in the present study had more advanced renal compromise and secondary hypertension from activation of the renin-angiotensin-aldosterone system.19,20,30 This possibility may also explain the reason for the different responses observed in dogs, because dogs with renal cysts and hypertension were never azotemic. Another possibility to justify the different response may be related to the number of cysts present. All dogs had a single cyst, while the cats had several cysts. It is possible that relief of renal compression provided by treating one single cyst in the cats was inadequate.

In humans, complications of aspiration of renal and hepatic cysts are uncommon, but abdominal bleeding is the most frequent, especially with cystic lesions of the kidney.31,32 In the present study, the bleeding observed in three animals may have been caused by inadvertent puncture of a vessel or by excessive changes in the internal pressure of the cyst cavity, generated by excessive negative pressure during drainage or overextension of the cyst during alcohol injection. Even though bleeding was observed in some cases, interruption of the procedure was sufficient to prevent further hemorrhage.

Other potential risks related to insertion of a needle in a cystic lesion are seeding of neoplasms and secondary infections.33,34 Tumor metastasis has been described in dogs following fine-needle aspirates of transitional cell carcinomas.33 If this risk also applies to hepatic and renal tumors, it may potentially be offset by the introduction of ethanol to decrease the viability of the tumor cells. Dissemination of bacteria should be of limited concern with proper technique. In fact, drainage and alcoholization have been successfully reported in dogs and cats with hepatic abscesses.34

Another concern is the possibility that renal cyst alcoholization might impair kidney function, but results of the study reported here showed that serum creatinine remained stable over the first 3 to 4 weeks, both in animals that had normal or elevated creatinine levels before the procedure. Even though renal function impairment was not identified in this study, more sensitive diagnostic tools were not utilized. In nonazotemic animals with unilateral renal impairment, further damage could go undetected by routine clinical tests of renal function (i.e., serum creatinine). Alcoholization also appeared to be safe for treating hepatic cysts, in that none of the animals had an increase in liver enzymes following the procedure. One cat’s azotemia worsened, and in this case it was possible that anesthesia and inadequate IV fluid administration during the procedure led to further renal compromise.

Even though the results of this retrospective study showed that drainage and alcoholization of cysts in dogs and cats ameliorated the associated clinical signs, it was not established whether the procedure would also suffice for long-term control. None of the animals were reevaluated with ultrasonography to verify the possibility of cyst recurrence beyond 3 to 4 weeks. Eleven owners were contacted between 4 and 15 months following the procedure, and in all cases the clinical signs had not recurred.

Conclusion

Ten renal cysts and 12 hepatic cysts were diagnosed in dogs and cats. Ultrasound-assisted drainage and alcoholization of the cysts controlled the clinical signs and secondary disorders in most animals. Normalization of blood pressure was not achieved in cats with renal cysts. Based on the minimal invasiveness of the procedure and low rate of complications in this study, the procedure is a valid option for both dogs and cats with renal and hepatic cysts.

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Two Cases of Planned Relaparotomy for Severe Peritonitis Secondary to Gastrointestinal Pathology

Planned relaparotomy is a technique in which two or more surgeries are planned before or during the initial surgery. Two dogs underwent planned relaparotomy for severe peritonitis secondary to gastric ulceration and linear foreign body. Both dogs had good outcomes, and unnecessary procedures that would likely have led to increased morbidity were avoided. This technique may be useful in avoiding unnecessary procedures as well as providing for better stabilization of the animal. J Am Anim Hosp Assoc 2007;43:117-121.

Introduction

Planned relaparotomy in humans was initially performed for uncontrollable bleeding following liver trauma. The abdomen was packed with laparotomy pads and temporarily closed in order to place continual pressure on the bleeding sites. Once the blood loss had stopped and the patient was stabilized, a second surgery was performed to remove the laparotomy pads, visualize the wounds, and perform further procedures if needed. Planned relaparotomy has also been used in other traumatic situations and in cases of secondary peritonitis, which is defined as peritonitis arising from diseases of the gastrointestinal tract. Indications for planned relaparotomy in humans currently include trauma, peritonitis, increased intra-abdominal pressure, patient destabilization, and coagulopathies. Planned relaparotomy is also used in patients requiring surgical stabilization prior to transfer to specialty centers for definitive treatment.

Severe secondary peritonitis carries a high mortality and morbidity. Frequent complications include the systemic inflammatory response syndrome, multiple organ dysfunction, and disseminated intravascular coagulation. Management of secondary peritonitis via one surgical procedure includes definitive repair of the gastrointestinal tract followed by primary closure, open abdominal drainage, or abdominal closure with closed suction drains. In cases of secondary peritonitis, planned relaparotomy can offer advantages over a single surgery. One of these advantages is the possible avoidance of unnecessary surgical procedures. Severe peritonitis changes the appearance of tissues and can obscure necrotic borders, making initial surgical decisions difficult. In such cases, the initial laparotomy is used to lavage the abdomen, close hollow viscous perforations, and establish drainage. During the second laparotomy, viable tissues may improve in their appearance, which allows for more accurate surgical decisions. Planned relaparotomy can also be used in cases of peritonitis if destabilization of the animal during the initial surgery causes the surgery to be aborted. Other possible indications for planned relaparotomy include allowing for transfer of the animal to a
specialist for a second surgery, if there is need for a procedure in which the doctor performing the initial surgery has not been trained.7,9,10 The purpose of this report is to demonstrate the use of planned relaparotomy in two dogs for the management of severe peritonitis secondary to gastrointestinal pathology.

Case Reports

Case No. 1

A 12-year-old, 24-kg, spayed female Belgian sheepdog was presented obtunded and laterally recumbent. The dog had a history of a poor appetite and diarrhea for 1 week, and she was currently on cephalixin for superficial pyoderma and deracoxib for osteoarthritis. Rectal temperature was 100.0°F, heart rate was 120 beats per minute, and the femoral pulses were weak and synchronous. The dog’s abdomen was distended and moderately painful upon palpation. Oxygen therapy and lactated Ringer’s solution were started. After a bolus of intravenous (IV) fluids, systolic blood pressure was 100 mm Hg. Purified hemoglobin (5 g/dL) was given as an IV transfusion. Fentanyl (5 µg/kg per minute IV) was given for analgesia and oxygen saturation measured via pulse oximetry (SpO2) was 86%, so unilateral nasal oxygen was also started. The nasogastric tube was suctioned every hour to keep the stomach decompressed. Because the packed cell volume (PCV) was low (26%; reference range 38% to 47%), and in order to maximize oxygen delivery to the tissues prior to the second surgery, a transfusion of 2 units of packed red blood cells was initiated. Blood pressure stabilized following the transfusion. Fentanyl (0.20 µg/kg per minute IV) was given for pain control. Intravenous ticarcillin-clavulanate and famotidine were continued.

Fifteen hours after the initial surgery, the abdomen was re-explored. Generalized peritonitis appeared significantly improved from the prior surgery. A large portion of the omentum was necrotic and was resected. The necrotic area of the stomach was well demarcated, and the temporary closure of the gastric wall was within the necrotic area, which encompassed approximately one-third of the stomach (including much of the body and part of the pyloric antrum). Resection of the necrotic portion of the stomach was accomplished using a stapling device.9,10 As the pylorus appeared viable, a Bilroth procedure was not performed. The abdomen was lavaged with warm, sterile saline; two closed-suction drains were placed; and the abdomen was routinely closed. The dog recovered smoothly from anesthesia and was continued on crystalloid solutions, fentanyl (5 µg/kg per hour IV), and ketastarch (20 mL/kg per day IV). One episode of vomiting occurred postoperatively and was treated with metoclopramide (0.56 mg/kg per hour IV). The suction drains initially collected a large amount of serous-guineous fluid, but they were removed 48 hours postoperatively when the amount of drainage decreased and cytology revealed no bacteria. The dog was started on small amounts of a bland diet 36 hours postoperatively and was switched to oral amoxicillin-clavulanic acid (375 mg q 12 hours), on all serosal surfaces. Three areas of gastric perforation were detected along the body and pyloric antrum. Partially adhered omentum appeared necrotic, and adjacent gastric tissue was friable and purple to black in color. Demarcation between necrotic and healthy tissues was unclear. The viability of the pyloric area was questionable, which indicated the possible need for a Bilroth procedure. Despite IV administration of lactated Ringer’s solution, fresh-frozen plasma (21 mL/kg), and ketastarch (1.25 mL/kg per hour), systolic blood pressure decreased to 80 mm Hg and did not respond to a ketastarch bolus (6 mL/kg) or dopamine IV. The decision was made to temporarily seal the gastric perforations and lavage the abdomen, with the intention of performing a second laparotomy 12 to 24 hours later. Gastric perforations were closed with 2-0 polydioxanone in a Lembert pattern, and the abdomen was lavaged with warm, sterile saline. The linea alba and skin were sutured with a loose simple continuous suture pattern that provided a 1-cm gap for fluid to drain. A sterile, absorbent bandage was placed around the abdomen, and a nasogastric tube was inserted.

Postoperatively, lactated Ringer’s solution, dextrose, potassium chloride, ketastarch, and dopamine were continued IV. Oxygen saturation measured via pulse oximetry (SpO2) was 86%, so unilateral nasal oxygen was also started. The nasogastric tube was suctioned every hour to keep the stomach decompressed. Because the packed cell volume (PCV) was low (26%; reference range 38% to 47%), and in order to maximize oxygen delivery to the tissues prior to the second surgery, a transfusion of 2 units of packed red blood cells was initiated. Blood pressure stabilized following the transfusion. Fentanyl (0.20 µg/kg per minute IV) was given for pain control. Intravenous ticarcillin-clavulanate and famotidine were continued.
famotidine (10 mg q 24 hours), sucralfate (1 g q 8 hours), and metoclopramide (5 mg q 8 hours) prior to discharge 4 days after the second surgery.

Case No. 2
A 9-year-old, 60-kg, castrated male bullmastiff with a history of foreign body ingestion was presented as an emergency after being found laterally recumbent and surrounded by vomitus. On presentation, the dog was obtunded and recumbent. Rectal temperature was 99.8˚F, heart rate was 160 beats per minute, and respiratory rate was 50 breaths per minute. Laboratory tests revealed elevations of PCV (64%; reference range 37% to 55%), total protein (11 g/dL; reference range 5.8 to 7.9 g/dL), platelets (566,000/µL; reference range 200,000 to 500,000/µL), blood lactate (14 mmol/L; reference range 0 to 2 mmol/L), albumin (4.6 g/dL; reference range 2.6 to 4.3 g/dL), alkaline phosphatase (266 U/L; reference range 23 to 212 U/L), creatinine (2.8 mg/dL; reference range 0.4 to 1.8 mg/dL), calcium (12.7 mg/dL; reference range 7.9 to 12 mg/dL), and cholesterol (460 mg/dL; reference range 110 to 320 mg/dL). Mild hypokalemia (3.04 mEq/L; reference range 4.0 to 5.6 mEq/L) was also found. Prothrombin time was slightly elevated (16 seconds; reference range 8 to 14 seconds), but APTT was within normal limits.

Initial therapy included IV lactated Ringer’s solution, hydromorphone (0.07 mg/kg IV), cefazolin (33 mg/kg IV q 8 hours), enrofloxacin (6.7 mg/kg IV q 24 hours), and chlorpromazine (0.8 mg/kg SC q 8 hours). Lateral and ventrodorsal abdominal radiographs revealed markedly dilated small intestines and loss of serosal detail in the cranial abdomen. Because of the radiographic findings and a historical suspicion of ingestion of a foreign body, an exploratory laparotomy was performed.

Anesthesia was induced with propofol (4.2 mg/kg IV) and maintained with isoflurane in oxygen. Abdominal exploration revealed multiple gastric foreign bodies and a linear jejunal foreign body that had caused plication from the duodenal flexure to the distal ileum. A diffuse peritonitis was also present. A gastrotomy and four enterotomies were performed to remove the foreign bodies. The viability of the entire small intestine was questionable [Figure 1]. The decision was made to perform a second celiotomy 24 hours later to assess the viability of the bowel, rather than risk short-bowel syndrome secondary to resection of most of the small intestine. The abdomen was lavaged with warm, sterile saline; the linea and skin were loosely apposed; and a bandage was applied as described for case no. 1.

Postoperatively, crystalloids, potassium chloride, and hetastarch were administered IV, as well as an IV infusion of morphine, lidocaine, and ketamine for pain control. Cefazolin, enrofloxacin, and chlorpromazine were continued as before, and metronidazole (20 mg/kg IV q 12 hours) was added. Twenty-four hours later, the abdomen was explored a second time. The small intestine, including the enterotomy sites, appeared viable, though a diffuse peritonitis was still present [Figure 2]. Omentum was placed over the most severely discolored serosal sites, and an elective circumcostal gastropexy was performed. The abdomen was lavaged with warm, sterile saline; a closed suction drain was placed; and the abdomen was closed routinely.

Drug administration continued with IV crystalloids; hetastarch; a continuous infusion of ketamine, morphine, and lidocaine; and cefazolin, enrofloxacin, and metronidazole. Serosanguineous fluid was evacuated from the drain until the drain was removed 2 days later, at which time fluid collection was minimal. Cytology of the abdominal drainage prior to drain removal revealed no infectious organisms. The dog was started on oral feedings 24 hours after the second surgery; but after an episode of vomiting, metoclopramide (0.05 mg/kg per hour IV) and famotidine (0.3 mg/kg per os PO q 12 hours) were given. The dog was discharged from the hospital 7 days after the second surgery,
with postoperative administration of amoxicillin \(^w\) (17 mg/kg PO q 12 hours), metronidazole (21 mg/kg PO q 12 hours), metoclopramide (0.25 mg/kg PO q 8 hours), and enrofloxacin \(^a\) (2.3 mg/kg PO q 12 hours). The dog recovered well and had no clinical signs until he was presented 4 months later with another gastric foreign body, which was removed via gastrotomy. During surgery, the intestines were normal in appearance.

**Discussion**

Numerous studies in people and animals have been published on the management of severe peritonitis.\(^{11-14,16-23}\) These studies have often been retrospective, uncontrolled clinical investigations of a single management option (i.e., open abdominal drainage or primary closure with or without closed suction drain placement), so interpretations have been limited. Consequently, the preferred management approach for severe peritonitis remains controversial. The cases reported here describe a method of surgical management that differs from previously described options. Planned relaparotomy is a specific technique that refers to the planning of one or more surgeries either before or during the initial surgery, as opposed to relaparotomy on demand, in which further surgeries are performed if indicated based on the patient's clinical condition.\(^{20}\) Planned relaparotomy can include any of the previously described management options between surgeries, and it allows for the first surgery to be used to assess and control damage rather than being used for definitive repair.\(^{8}\) It allows potentially unnecessary procedures to be avoided at the initial surgery, provides better stabilization of the animal, and allows time for transfer to a specialist if indicated.\(^{7-10}\)

Both dogs in this report were managed with open abdominal drainage between surgeries. Open drainage was chosen to allow for maximal drainage of inflammatory fluid and for ease of entry during second surgery. However, planned relaparotomy can also be performed after closure (with or without drainage) of the abdomen.\(^{4,5}\)

The decision to use planned relaparotomy in the first case reported here was made intraoperatively, based on the appearance of the tissues and hemodynamic deterioration of the patient during anesthesia. During the initial surgery, the necrotic tissue appeared to include the pylorus, in which case a Bilroth procedure would have been required. By giving the animal supportive care and time, the demarcation between healthy and diseased tissue became clearer, and in the end a less aggressive surgical procedure (i.e., a partial gastric resection) was appropriate. Performing the resection during a later, second procedure, when the demarcation of necrotic tissue borders was well defined, also ensured that necrotic tissue would not be inadvertently left behind and lead to ongoing inflammation and potential dehiscence.

In the second case, initially it appeared that a radical intestinal resection and anastomosis were required, which would have resulted in short-bowel syndrome. By performing a second laparotomy, the viability of the intestine was more accurately assessed, and an unnecessary surgical procedure that would have resulted in life-long consequences for the dog was prevented.

**Conclusion**

Two dogs underwent planned relaparotomy for severe peritonitis secondary to gastrointestinal pathology. The additional time and better stabilization between surgeries allowed for a more accurate assessment of the tissues during a second surgery, and this technique prevented the need for radical procedures first thought necessary. Planned relaparotomy should be considered in dogs when peritonitis or hemodynamic instability may cause an altered appearance to the tissues and make surgical decisions more difficult.

**Acknowledgments**

The authors thank Kate Hopper, DVM, Diplomate ACVECC for her assistance in manuscript preparation.

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\(^w\) Amoxi Tab; Pfizer Animal Health, New York, NY 10017
\(^x\) Baytril tablets; Bayer Corporation, Shawnee Mission, KS 60516
Giant Hypertrophic Gastritis (Ménétrier’s-like Disease) in an Old English Sheepdog

An 11-year-old, male Old English sheepdog was admitted for weight loss and intermittent vomiting of 1 month’s duration. A cranioventral abdominal mass, anemia, hypoproteinemia, and hypoalbuminemia were the prominent abnormal findings. Imaging studies identified a remarkably thickened gastric wall with multilobulated folds protruding into the gastric lumen. Gastrotomy revealed the presence of giant cerebriform rugal folds arising from the fundus and body of the stomach. Pronounced gastric glandular hyperplasia and lack of evidence of cellular atypia were suggestive of giant hypertrophic gastritis. The dog was treated with prednisolone, cimetidine, and hyoscine butylbromide, only to experience a short-term remission.


Introduction

Giant hypertrophic gastritis is a rare disease in the dog and is characterized by pronounced mucosal proliferation of the gastric body, which usually spares the pyloric antrum. Breed-associated giant hypertrophic gastritis includes the immunoproliferative enteropathy of basenji dogs, in which gastritis is invariably associated with lymphocytic-plasmacytic enteritis, and the familial stomatocytosis-hypertrophic gastritis of Drentse Patrijshond dogs. Only a single case of giant hypertrophic gastritis has been reported in breeds other than the basenji or Drentse Patrijshond. Hypertrophic gastritis has been compared to Ménétrier’s disease in humans, which is characterized by giant gastric folds, hypoalbuminemia, hypochlorhydria, and mucosal epithelial cell hyperplasia.

The present report describes a case of giant hypertrophic gastritis in an Old English sheepdog. The condition bore a strong resemblance to Ménétrier’s disease, especially with regard to the clinicopathological, imaging, gastroscopic, and histopathological findings.

Case Report

An 11-year-old, 28-kg, male Old English sheepdog was admitted for a 1-month duration of marked weight loss, anorexia, intermittent vomiting, and tarry stools. On physical examination, the only abnormalities detected were pale mucous membranes and a large, football-sized, nonpainful mass in the cranioventral abdomen.

A complete blood count (CBC) revealed a nonregenerative, normocytic, normochromic anemia [see Table]. No abnormal erythrocyte morphology was noted in Giemsa-stained peripheral blood smears, and a saline agglutination test was negative. Blood serum biochemical abnormalities included hypoproteinemia, hypoalbuminemia, and hypoglobulinemia [see Table]. Complete urinalysis and routine coagulation profile (i.e., prothrombin time, activated partial thromboplastin time) were unremarkable. The dog tested negative for *Leishmania infantum* antibodies and *Dirofilaria immitis* antigens.

Survey abdominal radiography revealed an opaque mass in the cranial part of the abdomen, caudal to the liver and displacing the intestinal loops.
caudodorsally. Thoracic radiographs appeared normal. Barium contrast radiography demonstrated mild enlargement of the stomach, absence of the normal pattern of gastric rugal folds, and multiple variably sized filling defects extending across the gastric body [Figure 1]. Abdominal ultrasonography revealed a remarkably thickened gastric wall that ranged between 10 and 60 mm (reference range 3 to 5 mm). Multilobulated, thickened gastric folds protruded into the gastric lumen [Figure 2]. No blood flow could be detected by color and pulsed Doppler ultrasonography in the multiple anechoic areas that appeared like cystic lesions within the thickened folds.

Gastroscopy with a flexible endoscope revealed a restricted gastric cavity from the presence of multiple giant folds throughout the fundus and the body [Figure 3]. The antrum was spared. Mucosal friability and a moderate amount of gastric fluid were also noted. A gastrotomy performed immediately following gastroscopy revealed giant cerebriform rugal folds protruding from the fundus and

<table>
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<th>Clinicopathological Finding</th>
<th>Reference Range</th>
<th>Day From Initial Admission*</th>
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<tr>
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<td>45</td>
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<td>Hematocrit (%)</td>
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<td>Mean cell hemoglobin concentration (g/dL)</td>
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<td>Mean cell volume (fL)</td>
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<td>Calcium (mg/dL)</td>
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* ND=not done
body but sparing the antrum [Figure 4]. No regional lymphadenopathy was observed, and no gross lesions of the liver, pancreas, duodenum, kidneys, or omentum were identified. Incisional wedge biopsies were obtained from the gastric fundus and body, along with a mesenteric lymph node, and they were submitted in 10% neutral-buffered formalin for histopathology.

Sections from the gastric fundus and body had similar histological appearances. The overlying epithelium was intact, with pronounced glandular hyperplasia [Figures 5A, 5B]. The mucosal tissue was markedly expanded and composed of a loosely packed connective tissue matrix with muscle fiber bundles, within which numerous variably sized and cystically dilated glandular elements were embedded. There was no evidence of cellular atypia. The glandular lumena contained no secretions. Low numbers of mixed mononuclear cells (i.e., plasma cells, lymphocytes, and macrophages) were scattered throughout the stromal tissue.
Lymph node histopathology and Giemsa-stained imprint smears from the gastric specimens were unremarkable.

During the 6-day hospitalization period, the dog was treated with intravenous (IV) crystalloid solutions and metoclopramide (0.5 mg/kg IV q 8 hours). A blood-typed and cross-matched whole blood transfusion was also given. A post-transfusion hematocrit was 34% (reference range ≥37%). Intermittent vomiting, hematemesis, hemorrhagic diarrhea, and melena continued through day 4 of hospitalization; but on day 6, the dog appeared much better. Its appetite was fully restored, and the vomiting, diarrhea, and melena had resolved. The dog was discharged on prednisolone (0.5 mg/kg per os [PO] q 12 hours), hyoscine butylbromide (0.25 mg/kg PO q 12 hours), and cimetidine (10 mg/kg PO q 12 hours); administration of these medications was intended to continue for the next 3 months.

Forty-five days after initial admission, the dog was still in clinical remission, and a CBC revealed a moderate non-regenerative, microcytic, and normochromic anemia, as well as a mature neutrophilia, lymphopenia, eosinopenia, and thrombocytosis [see Table]. Serum biochemical profile was unremarkable apart from slightly elevated alanine aminotransferase (ALT) and alkaline phosphatase (ALP) [see Table]. At the same time, ultrasonography revealed a decrease in the gastric wall thickness (10 to 30 mm), and gastroscopy revealed an approximate 30% reduction in the rugal folds. Histopathology of multiple endoscopic pinch biopsies obtained from the gastric body did not differ from that of the original biopsies. The dog was discharged on the original treatment protocol, with the addition of ferrous sulphate (300 mg PO q 24 hours for 3 months).

On day 105 after the initial admission, the general condition of the dog was very good, including a substantial increase in body weight (32 kg). Laboratory investigation showed a moderate nonregenerative normochromic/normocytic anemia, along with mature neutrophilia, thrombocytosis, and marginal hypoalbuminemia [see Table]. One month later (day 135 from the admission) and while still in remission, the dog unexpectedly died. Permission for necropsy was declined by the owner.

**Discussion**

The presence of giant gastric folds, hypoalbuminemia, and the unique histopathological lesions that constitute the major features of human Ménétrier’s disease were all met in the case reported here. Documentation of hypochlorhydria (another typical feature of Ménétrier’s disease) was not pursued in this case, but it has not been established as a component of giant hypertrophic gastritis in dogs. Importantly, Ménétrier’s disease is clearly distinguished from Zollinger-Ellison syndrome, because the enlarged gastric folds of the latter disease are gastrin-induced secondary to pancreatic gastrinoma. In Ménétrier’s disease, gastrin levels are generally normal. In the case reported here, a thorough surgical exploration of the pancreas and adjacent structures ruled out the possibility of gastrinoma. More than 85% of gastrinomas have evidence of metastasis to the liver at the time of diagnosis, and no such lesions were seen in this case.

The majority of dogs reported with giant hypertrophic gastritis have belonged to the Drentse Patrijshond and basenji breeds. No stomatocytosis, evidence of neurological deficits, hemolytic anemia, or liver disease were documented in the dog of this study, as opposed to a significant proportion of Drentse Patrijshond dogs with familial stomatocytosis-hypertrophic gastritis. Also, giant hypertrophic gastritis of basenji dogs is characterized by chronic intractable diarrhea secondary to severe lymphocytic-plasmacytic enteritis, and most affected dogs have consistent hypoalbuminemia and hyperglobulinemia. Although no intestinal biopsies were procured, the diarrhea exhibited by the dog in this report was transient and was accompanied by panhypoproteinemia rather than combined hypoalbuminemia and hyperglobulinemia.
Although the cause of giant hypertrophic gastritis/Ménétrier’s disease is poorly understood, overrepresentation of certain canine breeds and the occasional appearance of Ménétrier’s disease in human twins indicate potential influence of hereditary factors. Immune-mediated mechanisms have also been incriminated in both dogs and humans. An association between Helicobacter pylori infection and Ménétrier’s disease has been reported in man, and cytomegalovirus infection may be implicated in the juvenile form of Ménétrier’s disease. However, a familial occurrence was not documented in this dog, and no Helicobacter-like organisms were observed on either cytological or histopathological examination of the gastric mucosa.

Hypertrophic gastritis usually affects older male animals, as was the case in this dog. Chronic vomiting and weight loss are common historical and clinical manifestations of giant hypertrophic gastritis/Ménétrier’s disease, while melena is uncommon unless the friability of the gastric mucosa leads to spontaneous bleeding. Diarrhea is rarely observed in giant hypertrophic gastritis, unless concurrent lymphocytic/plasmacytic enteritis is present (e.g., in basenji dogs). Interestingly, in a case described by van der Gaag et al., the observed diarrhea was not associated with intestinal inflammation or biochemical abnormalities suggestive of systemic disease. Since full-thickness intestinal biopsies were not obtained in that case, the possibility of intestinal inflammation could not be excluded.

The nonregenerative anemia identified in the case reported here was attributed to the chronic nature of the disease process and possibly to iron deficiency following persistent gastrointestinal blood loss. The latter factor was supported by the microcytic, normochromic anemia documented during the follow-up period (day 45) and the response to iron supplementation (day 105). The changes that occurred in the differential leukocyte count (i.e., mature neutrophilic leukocytosis, lymphopenia, and eosinopenia) after treatment were most likely the result of glucocorticoid administration. Glucocorticoid therapy may have accounted for the thrombocytosis and the increased activity of liver enzymes. Since no proteinuria, liver insufficiency, or bleeding tendencies were documented in this dog, hypoalbuminemia and hypoglobulinemia were attributed to gastric bleeding. In Ménétrier’s disease, profuse protein losses from increased vascular permeability may explain the severe hypoproteinemia (protein-losing gastropathy). Increased gastrointestinal protein loss without concurrent bleeding was documented in another canine case reported in the literature.

Ultrasonography revealed diffuse thickening of the gastric wall with enlarged folds containing multiple cystic-like lesions that probably represented dilated mucosal glands. These findings were confirmed by gastroscopy and exploratory gastroscopy, which indicated that ultrasonography was a useful, noninvasive tool in the diagnosis of giant hypertrophic gastritis. Although neoplasia is a highly ranked differential diagnosis in humans with enlarged gastric folds, most gastric neoplasms in the dog produce localized or diffuse thickening and/or ulceration of the gastric wall, and occasionally a substantial decrease in the number of rugae on imaging and gastroscopy. Therefore, the diagnosis of gastric neoplasia in the dog should not be made upon the basis of the gross appearance of the lesions, as a variety of potentially treatable diseases (e.g., granulomatous gastropathy) may have a similar appearance.

Histopathology is crucial to ruling out neoplasia. Wedge and pinch biopsies were apparently of the same value in the present case, although surgical biopsies should be obtained whenever a significant thickening of the gastric wall is demonstrated by radiography and/or ultrasonography. The histopathological features that met the criteria of Ménétrier’s disease in this dog were the excessive hyperplasia and cystic dilatation of mucosal glands. The mononuclear cell infiltrate is also a common finding in Ménétrier’s disease. Other investigators have questioned the importance of this inflammatory infiltrate, suggesting that Ménétrier’s disease simply represents a noninflammatory gastropathy. The efficacy of therapeutic measures in giant hypertrophic gastritis is unclear because the condition is rare, controlled trials are lacking, and spontaneous remission occurs in some cases. The rationale for the treatment instituted in the present case was that histamine (H2) receptor antagonists and anticholinergic agents would decrease gastric protein loss by strengthening the intercellular tight junctions or by reducing hydrogen ion production and, hence, its potential damaging effect to the mucosa. The concurrent use of glucocorticoids was based on the assumption of an immune-mediated etiology. A significant reduction in the size of the gastric folds and an increase in serum protein concentration were documented approximately 40 days after the initiation of the treatment. The same response was also observed in a human patient following intensive treatment with propantheline bromide. Subtotal or total gastrectomy is reserved for refractory cases in humans.

The cause of death in the dog reported here remained elusive, since postmortem examination was denied by the owner. Massive gastric bleeding and thromboembolic disease secondary to protein-losing gastropathy are considered life-threatening complications in Ménétrier’s disease and may have developed in this dog.

Conclusion

An 11-year-old, Old English sheepdog demonstrated clinical, laboratory, and histopathological evidence of giant hypertrophic gastritis, a disease that is comparable to Ménétrier’s disease in humans. Giant gastric folds, low serum albumin concentration, and mucosal epithelial cell hyperplasia were the main features of the disease in this dog. A combination of glucocorticoids, a histamine-receptor antagonist, and an anticholinergic agent resulted in short-term clinical remission.
References
Surgical Correction of Colonic Duplication in a Cat

A 2-year-old, castrated male Manx cat was presented for anorexia, obstipation, and straining to defecate. Imaging tests revealed a cystic mass associated with the descending colon. Three surgical explorations over several years were performed before complete resection of the cystic mass was achieved. Histopathology of the mass revealed normal colonic structures consistent with colonic duplication. Complete resection of a noncommunicating duplicate colon may allow successful treatment of this condition and resolution of associated clinical signs. J Am Anim Hosp Assoc 2007;43:128-131.

Introduction
Colonic duplication is a rare condition that has been reported in humans, five dogs, and one horse.1-4 In three of the five reported cases of colonic duplication in dogs, additional serious congenital cecal, vertebral, and urinary anomalies were also noted.1-6 In two dogs, surgical correction was performed by removing the conjoined colonic duplicate via extension of a pre-existing communication between the colon and the colonic duplicate.2,3

Intestinal duplication can occur at any level of the intestinal tract. A recent report described a subclinical jejunal duplication in a cat.7 In humans, the jejunum and ileum are the most common sites of alimentary tract duplication, and colonic duplication is reported less frequently.8-10 In up to 80% of humans with colonic duplication, there is concurrent duplication of other organs.11

The embryological mechanisms leading to colonic duplication have not been clearly delineated. The embryonic origin of the alimentary tract is the yolk sac endoderm, and the hindgut segment develops into the distal colon, rectum, and urogenital tract.12 Potential causes for colonic duplication include interepithelial vacuolar persistence during intestinal development, duplicate formation of the early colon and rectum after cloacal division, and embryonic notochord division.5,13-15

The clinical signs associated with colonic duplication vary according to the anatomical location of the duplicated segment, its size, and the presence or absence of communications.8,10,11 The most common clinical signs reported in humans are nonspecific and include abdominal pain, abdominal distention, constipation, and vomiting.8,10,11 Complications of colonic duplication may lead to perforation, volvulus, intussusception, obstruction, infection, ulcerative hemorrhage, and malignant transformation.8,11,12,16

This report describes a challenging case of colonic duplication in a cat, a species in which the condition has not, until now, been reported.

Case Report
A 2-year-old, 4-kg, castrated male Manx cat was referred for anorexia, obstipation, and straining to defecate for 2 weeks. Referral radiographs
showed a soft-tissue mass dorsal to the colon in the region of the pelvis. The cat was medically managed with oral lactulose and enemas. On physical examination, the cat was extremely uncomfortable on abdominal palpation and rectal examination. A complete blood count (CBC) and biochemical panel were normal. Abdominal ultrasonography identified a homogenous, 3-cm diameter mass in the caudal abdomen that was most consistent with an abscess. An ultrasound-guided fine-needle aspirate of the mass was performed, but cytology of the thick fluid aspirated from the mass was nondiagnostic.

An exploratory laparotomy revealed an intramural cystic mass of the dorsal wall of the distal colon. Needle aspirate samples were obtained, and the lesion was drained and omentallized by placing omentum into the defect and securing it to the serosa with simple interrupted sutures. Obstipated feces were massaged through the colon and into the rectum. The cat recovered from anesthesia uneventfully. Cytology of the aspirate was again nondiagnostic, and there was no growth on aerobic and anaerobic bacterial cultures. Within 2 days after surgery, the cat’s obstipation and abdominal discomfort were markedly relieved by the procedure.

The cat was reexamined 44 months after surgery. The cat was able to defecate normally until 2 to 3 weeks prior to presentation, at which time tenesmus, anorexia, and lethargy recurred. Abdominal radiographs showed a soft-tissue density in the sublumbar region, causing ventral displacement and luminal narrowing of the colon. Abdominal ultrasonography showed a fluid-filled, cystic structure dorsal to and in contact with the colon at the level of the lumbosacral junction. Computed tomography (CT) revealed a mass arising dorsal to the colon, caudal to the internal iliac bifurcation just left of midline and extending caudally to the level of the obturator foramen, with marked ventral displacement of the colon [Figure 1]. The mass did not enhance after intravenous (IV) administration of 2.2 mL/kg iodinated contrast medium (iothalamate sodium, 400 mg iodine per mL). Because the mass was not contrast enhancing, it was concluded the lesion was most likely a cyst or abscess.

A second exploratory laparotomy revealed an intramural, cystic mass of the dorsal colonic area. The outer wall of the cyst was excised, and copious amounts of viscous, opaque, yellow fluid were removed. Omentalization of the cyst cavity was repeated in a fashion similar to the previous surgery. No growth occurred on aerobic and anaerobic bacterial cultures. Histopathology of the cyst wall was consistent with full-thickness sections of colon (i.e., mucosa, submucosa, and muscular wall) and mild, chronic inflammation. No evidence of a neoplastic process or an active infectious process was found. These findings were suggestive of congenital duplication of the colon or a colonic diverticulum.

The cat was again able to defecate normally after surgery. It was reexamined 17 months after the second surgery because of a 4-week history of obstipation and intermittent tenesmus. Upon physical examination, firm stool was palpable in the colon, and a firm, 1- to 2-cm, dorsally located mass was palpated 4 cm orad to the anus. No pain was noted during rectal examination. A CBC, biochemical panel, and urinalysis were normal. An abdominal ultrasound showed a poorly defined, 1-cm mass in the area of the dorsal colonic wall mass [Figure 2]. No evidence of colonic invasion or obstruction was detected.

A third exploratory laparotomy revealed a 1-cm cystic structure in the dorsal wall of the distal descending colon. The cyst extended from approximately 1 cm orad to the pubis into the pelvic canal. The cystic mass was dissected from the colon using a combination of blunt and sharp dissection. During dissection, the wall of the cyst ruptured, and a thick, green, mucoid discharge was retrieved for cytological analysis and aerobic and anaerobic bacterial cultures. After the cyst ruptured, it became evident that the structure extended approximately 3 cm caudally within the seromuscular layer of the colonic wall. The lumen of the cyst was lined with mucosa-like tissue, and no connection to the colonic lumen was identified. The cystic structure was dissected from the colon without penetration of the colonic lumen, and it was resected in its entirety. The seromuscular defect was sutured with 4-0 polydioxanone in a simple continuous pattern. Prior to closing the abdomen, an assistant performed a rectal palpation and confirmed that no mass was digitally palpable and that no stricture had been created. The abdomen was lavaged thoroughly with warm isotonic saline and was closed routinely.

The cat made an uneventful postoperative recovery. Intravenous oxymorphone (0.05 mg/kg) and cefotetan (30
mg/kg q 6 hours) were started, and lactulose (1.5 mL per os [PO] q 8 hours) was also administered. The day after surgery, the antibiotics were changed to amoxicillin/clavulanic acid (62.5 mg PO q 12 hours). A CBC performed 24 hours after surgery was normal. No signs of tenesmus or fecal incontinence were noted. Because of occasional liquid feces, the lactulose dose was decreased to 1 mL PO q 12 hours. The cat was discharged from the hospital 3 days after surgery.

Histopathological examination showed that the wall of the resected cystic mass was similar to normal colon [Figure 3]. The wall was lined by colonic mucosa, with slightly disorganized glands, submucosa, tunica muscularis, and serosa. The tunica muscularis was incomplete and consisted of dispersed, small bundles of smooth muscle. Small numbers of lymphocytes and plasma cells were scattered in the lamina propria. In the absence of a communication with the lumen of the colon, colonic duplication was the most appropriate diagnosis.

Two weeks after surgery, the cat was defecating normally and the lactulose therapy was discontinued. Five months after surgery, the cat was still defecating normally and had soft to formed stools, with no recurrence of constipation. Physical examination at this time revealed no significant abnormalities. An abdominal ultrasound showed a fibrotic area located at the distal colon, consistent with the site of surgery. No new masses were observed. Abdominal radiographs showed a moderate amount of fecal material present in the descending colon, but no dilatation or constriction of the distal descending colon was noted. In follow-up telephone conversations 12 and 18 months after surgery, the owners reported the cat was able to defecate normally and the feces had a normal consistency.

Discussion

The cat in this report was a Manx, and the development of colonic duplication may have been associated with the caudal vertebral anomalies found in this breed. A classification system for colonic duplication in humans has been developed. Type I is partial and limited to the colon and rectum, and type II is complete and usually concurrent with other anomalies, such as vertebral malformations and urogenital duplications. Type I colonic duplication is further subdivided into type IA (spherical, noncommunicating), type IB (tubular, noncommunicating), type IC (tubular, communicating), type ID (loop with separate blood supply), and type IE (multiple duplications). On the basis of the human classification system, the cat in this report had a tubular, noncommunicating type IB colonic duplication.

Clinical signs associated with colonic duplication in the dog have included tenesmus, constipation and fecal retention, increased frequency of defecation, and abdominal distention. Clinical signs exhibited by the cat in this report were similar. Diagnostic imaging modalities that have been used in the diagnosis of colonic duplication include plain and contrast radiography, abdominal ultrasonography, CT, and magnetic resonance imaging. In the case reported here, radiographs, ultrasonography, and CT showed the presence of a soft-tissue density dorsal to the colon; however, these modalities did not provide further information on the etiology of the mass. As in other reported cases, exploratory surgery with biopsies was ultimately required to characterize and diagnose colonic duplication.
Surgical excision of the duplicated colonic segment is the treatment of choice. The cat in this report experienced recurrence of clinical signs associated with reformation of the duplicate after incomplete excision and omentalization. Successful surgical resection was possible in this cat, because there were separate blood supplies to the colon and the duplicate segment, and there was no communication with the true colon. Although the cyst extended into the pelvic canal, it was completely excised by placing cranial traction on the colon during dissection, and the need for a pelvic osteotomy was eliminated.

Following excision, the resulting seromuscular defect was closed primarily. Potential complications of primary closure include stricture formation and obstruction from potential loss of serosal circumference. In this cat, a rectal examination was performed during surgery to verify adequate patency of the colon after seromuscular closure and to ensure there was no luminal obstruction. Alternative techniques for closure of the seromuscular defect include the application of a porcine small intestinal submucosal graft with an overlying omental flap, and serosal patching to reinforce primary repair of the seromuscular defect.

Colonic duplication should be differentiated from a colonic diverticulum, which is bulging of the mucosa from a weakened muscular tunic. The lack of communication with the lumen of the colon and the presence of all layers of the colonic wall within the cystic structure were diagnostic for colonic duplication in the case reported here.

**Conclusion**

Colonic duplication was diagnosed in a 2-year-old Manx cat with chronic, persistent tenesmus and constipation. In this case, omentalization of the cyst was an inadequate surgical treatment, and complete excision of the duplicate colon was required to alleviate the cat’s clinical signs.

**References**

Epidural Spinal Myelolipoma in a Dog

Epidural spinal myelolipoma was diagnosed in a 13-year-old, male Siberian husky that was referred for evaluation of progressive pelvic limb paresis and urinary incontinence. An epidural mass was detected by magnetic resonance imaging and computed tomography. The mass was removed and identified histopathologically as an epidural myelolipoma. Pelvic limb paresis improved after surgery, but urinary retention associated with neurological bladder dysfunction persisted. J Am Anim Hosp Assoc 2007;43:132-135.

Introduction

Myelolipoma is a benign, typically asymptomatic tumor consisting of fat, myeloid, and erythroid marrow elements. The tissues affected in cats and dogs by myelolipoma have included the spleen, adrenal glands, and liver. The etiology of myelolipoma is controversial. In humans, extraadrenal myelolipomas are usually single, well-circumscribed, encapsulated masses that are most commonly seen in middle-aged to elderly persons with a 2:1 female predominance. Approximately half of the tumors are located in the presacral region with mediastinal, perirenal, hepatic, and gastric sites occurring in decreasing frequency. Extraadrenal myelolipomas are postulated to arise from metaplasia of previously uncommitted mesenchymal cells or from hematopoietic stem cells carried to ectopic sites during fetal life. As such, it is unclear whether these masses represent hyperplasia, choristomas, or neoplasia.

An epidural myelolipoma has been previously reported in a dog that was euthanized without therapy. A thoracic spinal myelolipoma has also been reported in a man. A dorsal laminectomy and mass resection were performed in the man, and significant improvement was seen in his gait disturbance. The present report describes a case of epidural spinal myelolipoma in a dog. The diagnosis was supported by magnetic resonance imaging (MRI) and computed tomography (CT) and was confirmed by histopathology. The epidural myelolipoma was removed surgically, and the quality of life subsequently improved.

Case Report

A 13-year-old, male Siberian husky was presented with a 2-year history of progressive pelvic limb paresis and a 6-month history of urinary incontinence. Six months prior to evaluation, the dog had been examined by another veterinarian, and at this time a presumptive diagnosis of intervertebral disk disease was made and therapy was begun with prednisolone. The therapy was unsuccessful, however, and the medication was stopped. The dog was referred for further examination.
Upon presentation, general physical examination was normal except for moderate muscle atrophy in the pelvic limbs. A complete blood count and serum biochemical profile were normal. On neurological examination, mentation and cranial nerve function were normal. General proprioception was reduced in both pelvic limbs. Depression of the left patellar reflex and absence of the right patellar reflex were noted. Flexor reflexes were intact, and pain responses were normal. Spinal hyperesthesia was absent. The suspected anatomical location of the lesion was within the fourth lumbar to third sacral spinal cord segments. Magnetic resonance imaging and myelography were advised, and the owner agreed to an MRI.

The MRI of the lumbar portion of the vertebral column was done using a 1.5 tesla MRI scanner. Sagittal plane T1-weighted and T2-weighted images showed a lesion of increased signal intensity that compressed the spinal cord from the area of the 13th thoracic to the third lumbar vertebrae. Additionally, both T1-weighted and T2-weighted images showed that the elongated mass had multiple focal and serpiginous areas of low signal intensity [Figures 1A, 1B]. Differential diagnosis was spinal arteriovenous malformation or epidural lipoma based on the MRI findings. In humans, selective spinal arteriography is performed to establish the diagnosis of arteriovenous malformation; however, selective spinal arteriography has not been performed in the dog because of technical difficulties. Further examinations and clinical treatments were not performed at the owner’s request.

Forty-four days after the first referral, the dog was readmitted for progression of the pelvic limb paresis. Computed tomography with contrast medium was performed, and vascular anomalies were not identified. A heterogeneous mass with high attenuation was seen [Figure 2], and these CT findings were supportive of a space-occupying mass such as a lipoma.

Following CT, the dog underwent exploratory dorsal laminectomy and resection of the mass. After removal of the vertebral arches from the 13th thoracic to third lumbar vertebrae, an extradural mass (1.5 × 9.0 cm, reddish brown) intermixed with adipose tissue was found to be compressing the spinal cord [Figure 3A]. The mass was removed from the dura using a bipolar cautery. The skin was closed routinely, and recovery was uneventful. Postoperatively, intermittent catheterization was performed to decompress the bladder.

Histopathological examination of the resected tissue revealed mature adipose tissue surrounded by hematopoietic elements, which was consistent with myelolipoma. No evidence of malignancy was detected [Figure 3B].

**Figures 1A, 1B**—Magnetic resonance images (MRIs) of a 13-year-old, male Siberian husky with myelolipoma of the lumbar spine. (A) Sagittal T1-weighted (TR, 510 msec; TE, 20 msec) MRI showing an elongated epidural mass (arrowheads) situated dorsally in the spinal canal, extending from the first lumbar (L1) to the third lumbar (L3) vertebrae. The lesion compresses and displaces the cord ventrally (arrow), most severely at the level of the second lumbar (L2) and L3 vertebrae. The predominantly hyperintense (white) signal of the mass is disrupted by focal regions of intermediate (gray) signal intensity. (B) Sagittal spin-echo T2-weighted (TR, 3000 msec; TE, 120 msec) MRI also showing the epidural mass (arrowheads) and the compressed spinal cord (arrow).

**Figure 2**—Transaxial computed tomography image of the dog in Figure 1, taken at the caudal aspect of the second lumbar vertebra after administration of contrast medium. The image reveals a heterogeneous mass (arrow) with high attenuation. L=left; R=right.
Eight weeks after surgery, the dog was able to stand and walk without assistance, but urinary retention from neurological bladder dysfunction was still noticed. One year after surgery, the owner reported that the dog is able to walk and neurological status is improved; however, residual urinary retention persists, and intermittent catheterization of the bladder is performed every day by the owner.

Discussion

On MRI, the myelolipoma reported here had high-signal intensity with foci of low-signal intensity on both T1- and T2-weighted images. The high-signal intensity lesions were suspected to be adipose tissue. The low-signal intensity structures were thought to represent calcified masses, a chronic hematoma, and/or fast blood flow in an abnormality such as an arteriovenous malformation. The low-signal intensity tissues were most likely hematopoietic material. Magnetic resonance imaging findings of an extradural spinal myelolipoma have not been previously reported in the dog, but based on the changes in this case, extradural myelolipoma should be included as a possible diagnosis when a mixed fatty and soft-tissue lesion is identified on a spinal MRI.

On MRI, an extramedullary hematopoietic tumor may look identical to extradural spinal myelolipoma, because foci of extramedullary hematopoiesis contain both fat and soft-tissue elements. Lau et al. reported an extramedullary hematopoietic tumor that compressed the spinal cord in a human, and such tumors must be distinguished from extramedullary myelolipoma. Fowler et al. provided criteria for differentiating an extraadrenal myelolipoma from an extramedullary hematopoietic tumor in humans. Patients with extraadrenal myelolipomas, unlike those with extramedullary hematopoiesis tumors, typically have no history of chronic anemia, hepatosplenomegaly, or skeletal disorders. The clinical history and physical examination of the dog reported here favored an extraadrenal myelolipoma.

Myelography was not performed in this case at the owner’s request. Myelography may have helped distinguish between arteriovenous malformation and an epidural mass, because an arteriovenous malformation usually produces an intraspinal, space-occupying effect that is present in the intradural-extradural space.

Conclusion

A spinal myelolipoma was diagnosed in a 13-year-old dog. Although rare, myelolipoma should be included in the differential diagnosis when a lesion of mixed signal intensity is identified on a spinal MRI. Careful postoperative follow-up is necessary in more cases to determine the long-term outcomes of dogs with spinal myelolipoma.

References

