A retrospective study of visceral and nonvisceral hemangiosarcoma and hemangiomas in domestic animals

Patricia C. Schultheiss

Abstract. Cases of hemangiosarcoma submitted to the Colorado State University Veterinary Diagnostic Laboratory during a 6-year period were reviewed. Visceral hemangiosarcomas represent less than 2% of canine specimens submitted for histologic examination and nonvisceral hemangiosarcoma less than 1%. Most nonvisceral hemangiosarcomas of dogs occur in skin. Hemangiosarcomas are less common in cats and usually occur in skin. They are also rare in other animal species. Animals with nonvisceral hemangiosarcomas are usually mature; dogs and cats average 10 years of age. The tumors develop in many different locations, and there is no sex predilection. A wide variety of dog breeds are affected, but Italian greyhounds, greyhounds, and whippets are overrepresented. Clinical outcomes of 76 cases of nonvisceral hemangiosarcomas in dogs and cats were obtained from submitting veterinarians. Completeness of excision of a tumor is the most important factor that can be used in predicting clinical outcome for an affected dog or cat. In all cases in which the animals were clinically normal for at least 1 year after surgical removal of a nonvisceral hemangiosarcoma, the margins were reported to be free of neoplastic cells. Degree of differentiation, mitotic rate, size of tumor, and presence or absence of epidermal ulceration, mast cells, or solar elastosis did not correlate with clinical outcome.

Introduction

Hemangiosarcoma is a malignant neoplasm of vascular endothelial cells. The proliferating cells react with immunohistochemical (IHC) staining for Factor VIII–related antigen. Hemangiosarcoma is well known as a visceral tumor of dogs with grave prognosis. Various therapeutic regimens have been recommended for dogs with hemangiosarcoma, but their effectiveness is limited. Nonvisceral hemangiosarcoma has also been described in the skin and other areas in dogs. Although uncommon, there are several case reports of hemangiosarcoma in other species. There is limited information on the biological behavior of nonvisceral hemangiosarcomas. This retrospective study was conducted to gather information about the signalment, frequency of occurrence, and clinical outcome of nonvisceral hemangiosarcomas and to attempt to find patterns in the clinical history or histologic features that correlate with the outcome. In addition, findings for hemangiomas and visceral hemangiosarcomas are provided.

Materials and methods

All cases of hemangiosarcoma in the Colorado State University Veterinary Diagnostic Laboratory database from July 1996 through June 2002 were identified. The total number of hemangiosarcoma cases in visceral and nonvisceral locations and the species affected were determined. The diagnosis of tumors in nonvisceral locations was confirmed by review of slides stained with hematoxylin and eosin. In addition, an IHC stain for Factor VIII–related antigen was performed for sections of tumors from species other than dogs and cats, and any archived slides with IHC stain for Factor VIII–related antigen were reviewed.

Numbers of canine visceral and nonvisceral hemangiosarcoma cases were compared with total canine accessions in those 6 yr. Age, breed, and sex of the affected animal plus lesion duration and location of visceral and nonvisceral hemangiosarcomas of canine and feline cases occurring in years 1, 2, and 6 were reviewed. Findings of years 1 and 2 were compared with those of year 6 to see whether there were any changes during this time period, but because no difference was found, the pooled results are reported. Animal species, age, breed, sex, duration, and location of tumor in cases of visceral hemangiosarcomas from year 6 were reviewed. Cases of hemangioma from year 1 were reviewed similarly. The number of cases of hemangiosarcoma in the most commonly affected dog breeds was compared with the numbers of these breeds registered with the American Kennel Club (AKC).

To learn the clinical outcome of the nonvisceral hemangiosarcomas, 112 veterinarians who submitted tumors from dogs and cats in the last year were contacted by letter, and 73 replies provided follow-up information on 76 cases involving 66 dogs and 10 cats. For these 76 cases in which the clinical outcome of the tumor was known; size, location, completeness of excision, level of differentiation, mitotic rate, epidermal lesions, solar elastosis, and presence of mast cells were assessed. Mitotic rate was considered low if there were 2 or fewer mitotic figures per high-power field of view and high if there were over 2. Tumors were considered well differentiated when the cells had fairly uniform morphology and were arranged in cords and vascular channels. Tumors...
Table 1. Numbers of visceral and nonvisceral hemangiosarcomas in dogs, and their percentage of the total number of dog submission in 6 years.*

<table>
<thead>
<tr>
<th>Year</th>
<th>Skin and other nonvisceral locations</th>
<th>Visceral locations</th>
<th>Total canine submissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996–1997</td>
<td>30 (0.33)</td>
<td>44 (0.49)</td>
<td>9,039</td>
</tr>
<tr>
<td>1997–1998</td>
<td>74 (0.75)</td>
<td>137 (1.45)</td>
<td>9,478</td>
</tr>
<tr>
<td>1998–1999</td>
<td>92 (0.84)</td>
<td>209 (1.91)</td>
<td>10,919</td>
</tr>
<tr>
<td>1999–2000</td>
<td>103 (0.75)</td>
<td>269 (1.95)</td>
<td>13,769</td>
</tr>
<tr>
<td>2000–2001</td>
<td>118 (0.55)</td>
<td>308 (1.44)</td>
<td>308 (1.44)</td>
</tr>
<tr>
<td>Total</td>
<td>535</td>
<td>1287</td>
<td>81,744</td>
</tr>
</tbody>
</table>

* Values in parentheses are in percent.

were considered poorly differentiated, when the cells were pleomorphic and formed solid sheets rather than channels.

Results

Numbers of hemangiosarcomas and hemangiomas.

In 6 fiscal years from July 1996 through June 2002, a total of 1,912 cases of hemangiosarcoma were diagnosed. A total of 1,305 tumors were located in internal viscera and 607 were in skin and other nonvisceral locations. All IHC stains reacted with Factor VIII–related antigen. Affected animals included 1,822 dogs (535 skin and other nonvisceral locations, 1,287 visceral), 72 cats (59 skin, 2 bone, 11 visceral), 10 horses (6 skin, 2 eye, 2 visceral), 4 ferrets (2 skin, 2 visceral), 1 rabbit (skin), and 1 rat (visceral). During each of the 6 years, the nonvisceral hemangiosarcomas represented 1% and visceral hemangiosarcomas 2% of canine specimens submitted for histologic examination (Table 1). Benign hemangioma was diagnosed in 109 cases submitted in the first year. These developed in skin of 105 dogs, 3 cats, and 1 horse. In the last year, there were 456 cases of hemangioma in 434 dogs (415 in skin and 19 visceral), 21 cats (skin), and 1 ferret (skin).

Age, sex, breed, duration, and location of lesions of dogs with nonvisceral hemangiosarcoma (N = 222).

Dogs with nonvisceral hemangiosarcoma in years 1, 2, and 6 had an average age of 9.7 ± 2.9 years, ranging from 3 to 17 years. The sexes were 97 males, 84 females, and 41 unrecorded. Forty-eight different breeds with a wide variety of size and haircoat type were represented. Golden retriever (13), German shepherd (11), Italian greyhound (11), Beagle (10), Basset hound (9), Labrador retriever (8), greyhound (7), whippet (7), and pitbull (7) were the most common. Breed was not recorded for 27 dogs. Duration was recorded for 44 dogs with skin hemangiosarcomas and ranged from 3 weeks to 6 months. The most commonly reported duration was 1 month or less. A few cases were recurrent after hemangiosarcoma removal 8–12 months earlier (Table 2).

Locations of the skin hemangiosarcomas of 185 dogs from years 1, 2, and 6 included 46 on the ventrum, 37 on limbs, 31 on the dorsum, 18 on the head, 11 on shoulder, 11 on the neck, and 31 unrecorded. No breeds were associated with any particular skin location, including Italian greyhounds, which had tumors in various locations. Tumors in other locations of 37 dogs included skeletal muscle of limbs (11), bone (10), nictitans (6), cornea (3), conjunctiva (2), oral mucosa (2), and tongue (3).

Age, sex, breed, duration, and location of lesions of dogs with visceral hemangiosarcoma (N = 308).

Dogs with visceral hemangiosarcoma in year 6 had an average age of 10.7 ± 2.4 years, ranging from 5 to 17 years. The sexes were 150 males, 123 females, and 35

Table 2. The most common breeds, ages, and sexes of dogs with visceral and nonvisceral hemangiosarcoma.*

<table>
<thead>
<tr>
<th>Breed, sex</th>
<th>Nonvisceral hemangiosarcoma (N = 222)</th>
<th>Visceral hemangiosarcoma (N = 308)</th>
<th>Hemangioma (N = 105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basset hound</td>
<td>9 (4.0)</td>
<td>3 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Beagle</td>
<td>10 (4.5)</td>
<td>3 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Boxer</td>
<td>6 (2.2)</td>
<td>8 (3)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>German shepherd</td>
<td>11 (5.0)</td>
<td>30 (10)</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Golden retriever</td>
<td>13 (5.8)</td>
<td>56 (18)</td>
<td>18 (18)</td>
</tr>
<tr>
<td>Greyhound</td>
<td>7 (3.1)</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Italian greyhound</td>
<td>11 (5)</td>
<td>0</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Labrador retriever</td>
<td>8 (3.6)</td>
<td>45 (15)</td>
<td>15 (15)</td>
</tr>
<tr>
<td>Pitbull</td>
<td>7 (3.1)</td>
<td>1 (&lt;1)</td>
<td>0</td>
</tr>
<tr>
<td>Whippet</td>
<td>7 (3.1)</td>
<td>0</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Age average</td>
<td>9.9 ± 2.9</td>
<td>10.7 ± 2.4</td>
<td>8.8 ± 3.0</td>
</tr>
<tr>
<td>Age range</td>
<td>3–17</td>
<td>5–17</td>
<td>3–14</td>
</tr>
<tr>
<td>Female</td>
<td>84</td>
<td>123</td>
<td>50</td>
</tr>
<tr>
<td>Male</td>
<td>97</td>
<td>150</td>
<td>48</td>
</tr>
</tbody>
</table>

* Values in parentheses are in percent.
unrecorded. Fifty-five breeds were affected, and the most common were Golden retriever (56), Labrador retriever (45), German shepherd (30), Australian shepherd (10), and Boxer (8) (Table 2). Duration was rarely reported. Most submissions included a splenic tumor.

**Age, sex, breed, duration, and location of lesions of dogs with hemangioma (N = 105).** Dogs with hemangioma in year 1 had an average age of 8.8 ± 3.0 years, with a range of 3–14 years. Sexes were 50 males, 48 females, and 7 unrecorded. The 105 dogs included 98 with skin masses and 7 with splenic masses. Of the 38 identified breeds of dogs with skin masses, the most common were Golden retriever (18) and Labrador retriever (15) (Table 2). Duration was recorded for 34 cases of skin hemangiomas and ranged from 2 weeks to 2 years and most were 1 to 6 months. Locations of hemangiomas in skin include 25 on limbs, 23 on the dorsum, 15 on the neck, 8 on the head, 5 on shoulder, 2 on the ventrum, and 20 unrecorded.

**Vascular tumors in cats and horses.** In the 6-year period, a total of 72 cats had hemangiosarcomas in skin (59), bone (2), and viscera (11). In year 6, 20 cats had hemangiosarcoma in skin and 5 in viscera. Ages of cats with skin tumors ranged from 3 to 17 years with an average of 10 ± 2.92 years. Sexes were 11 male/neutered, 7 female/spayed, and 2 unrecorded. Breeds included 13 domestic shorthair, 5 domestic longhair, 1 Himalayan, 1 Maine Coon cat. Skin locations were paw (5), face (5), flank (3), neck (2), ventrum (2) dorsum (1), and unrecorded (2). Hemangiomas occurred in 24 cats in years 1, 2, and 6; 23 in skin and 1 in liver.

Of the 11 horses with vascular tumors identified in the 6-year period, 1 had hemangioma in the skin of an ear pinna, 6 had hemangiosarcoma in skin (1 on the poll, 1 on eyelid, and 4 unrecorded locations), 2 had hemangiosarcoma in cornea, and 2 had visceral hemangiosarcoma.

**Clinical outcomes.** Clinical outcomes of 76 hemangiosarcoma cases (66 dogs and 10 cats) were known. These cases included 65 in skin, 7 in eye, 3 in bone, and 1 in muscle. Thirty-four animals died or were euthanized because of the hemangiosarcoma; 42 were successfully treated by surgical removal of the tumor and were free of tumor for at least 12 months after the surgery. Tissue sections from 42 animals that were successfully treated all had surgical margins that were free of neoplastic cells. Of the 34 animals that died, 28 had incomplete surgical resection, and 6 had clean surgical margins. Of the latter 6, 2 dogs had recurrent hemangiosarcomas in skin, 2 dogs had tumors in tongue and had poor quality of life after the surgery, 1 dog was euthanized for other reasons, and 1 cat already had developed metastases to a lymph node.

Tumor size could be determined for 64 cases for which outcome was known. Twenty-nine were 1.0 cm or less (small), 20 were >1 cm and <3 cm (medium), 15 were 3 cm or greater (large). Of the 25 animals that died, 8 had a small tumor, 5 medium, and 12 large. Of the 39 that were treated successfully, 21 had a small tumor, 15 medium, and 3 large. The small tumors that caused death were either recurrent (2) or incompletely resected because of difficulty of performing surgery at their location (6).

The mitotic rate and degree of differentiation were evaluated for all 76 cases for which the clinical outcome was known. The mitotic rate was judged to be low in 48 cases and high in 28 cases. Of the 34 tumors that caused death, 23 had a low mitotic rate and 11 had a high rate. Of the 42 tumors that were successfully treated, 25 had a low mitotic rate and 17 had a high rate. In these 76 cases, 44 were judged well differentiated and 32 poorly differentiated. Of the 34 tumors that caused death, 19 were well differentiated and 15 poorly differentiated. Of the 42 tumors that were successfully treated, 25 were well differentiated and 17 poorly differentiated. Sixty of the 76 tumors with known outcome were located in skin; 18 in dermis, 22 in dermis and subcutis, and 20 in subcutis. Of the 21 that caused death, 2 were in dermis, 9 in dermis and subcutis, and 10 in subcutis. Of the 39 cases that were successfully treated, 16 were in dermis, 13 in dermis and subcutis, and 10 in subcutis.

Accumulations of mast cells in the stroma were noted in 16 of 76 tumors. Nine of these tumors caused death, and 7 were removed successfully. The presence of mast cells was not correlated with the level of differentiation, mitotic rate, or any other factor evaluated.

In skin tumors, epidermal ulceration was uncommon. It was present in 7 dogs and 1 cat that were successfully treated and in 4 dogs that died. Ulceration was not correlated with the degree of differentiation or any other factor evaluated.

Solar elastosis of dermis was found in 6 dogs, which had tumors on the ventral abdomen; 2 Great Danes, a Basset hound, a Beagle, a whippet, and a mixed breed. Four were successfully treated by complete resection of the tumor, and 2 died after incomplete resection.

Of the 76 animals for which tumor outcome was known, 5 dogs with skin hemangiosarcomas were later found to have visceral tumors in spleen plus other organs. Veterinarians had observed anemia in 4 of these dogs. These 5 dogs died.

The clinical history of the 118 cases of nonvisceral hemangiosarcomas from year 6 indicated that 7 dogs had a history of multiple recurring skin hemangiosarcomas. Known outcomes for theses dogs include 2 deaths and 3 successful treatments. A pair of sibling Italian greyhounds had multiple cutaneous tumors suc-
cessfully removed from multiple locations during a 3-year period, starting when they were 6-year of age.

Eight Italian greyhounds with skin hemangiosarcoma were identified in year 6, representing 7% of the cases. Four dogs are known to have survived, including the pair of siblings with multiple cutaneous tumors. One had internal tumors as well as a skin tumor and died. The outcomes for the other 3 are unknown.

Clinical outcome was known for 7 of the 8 hemangiosarcomas from year 6 that involved the eyes of the dogs. Three tumors developed in the cornea; 1 dog had no further problems after enucleation, 1 was euthanized because of rapid local recurrence, and 1 was euthanized when multiple hemangiosarcomas developed in the tongue a year after enucleation had been performed. Three developed in the nictitans and caused no further problems after complete removal. One developed in limbal sclera, recurred exactly 1 year later, and then the dog was euthanized. No follow-up was available for the tumor that developed in the conjunctiva.

Six hemangiosarcomas occurred in bone of dogs in year 6; 4 in the hind leg, 1 in the cranium, and 1 in an unspecified site. The 3 animals for which outcome is known died or were euthanized within 3 weeks of diagnosis. Two dogs developed hemangiosarcoma in skeletal muscle of the thigh, and the dog for which outcome is known was euthanized. Four cases involved tongue, and the dogs were euthanized or died within a week of diagnosis, including a dog, which had a corneal hemangiosarcoma removed a year previously.

When outcomes for cats were assessed separately from dogs, the features of tumors that led to death and tumors that were successfully treated were similar to those of tumors in dogs. Five cats with completely resected skin tumors were successfully treated, and 5 with deeply infiltrating unresectable tumors died.

In the last year, 5 cases of hemangiosarcoma occurred in other species, including spleen of a hooded rat, liver and intestine of a ferret, eyelid of a horse, omentum of a horse, and heart of a Holstein cow. The visceral tumors were fatal. The horse was euthanized because the entire tumor could not be excised.

Discussion

In dogs, nonvisceral hemangiosarcomas occur less commonly than visceral hemangiosarcomas but still are found frequently and affect a wide variety of breeds. The percentage of canine tumors that are hemangiosarcoma appears to be stable within the 6-year period evaluated. In dog skin, hemangioma is more common than hemangiosarcoma. Cats develop hemangiosarcomas less frequently than dogs, and their tumors are usually nonvisceral. Hemangiosarcomas are rare in other animal species.

Dogs with hemangiomas are younger than those with hemangiosarcoma. Dogs with nonvisceral hemangiosarcoma are on average a year younger than those with visceral tumors. Any type of hemangiosarcoma is rare in young dogs. There are slightly more numbers of males with hemangiosarcomas and slightly more numbers of females with hemangiomas. Reported duration of skin masses is shorter for hemangiosarcoma than for hemangioma. Skin hemangiosarcomas and hemangiomas both occur in a variety of locations, but hemangiomas are uncommon on the ventrum. A thick hair coat does not appear to prevent development of hemangiosarcoma.

The popular dog breeds of Labrador retriever and Golden retriever account for a high proportion of visceral hemangiosarcomas and skin hemangiomas and a slightly lower proportion of nonvisceral hemangiosarcoma. These breeds are the first and second most common AKC registrations. Golden retrievers appear to be slightly overrepresented because AKC registrations show 3 times as many Labrador retrievers as Golden retrievers. Italian greyhounds, greyhounds, and whippets appear to be disproportionately represented among dogs with hemangiosarcoma in skin because these breeds are not among the most numerous AKC registrations.

Factor VIII–related antigen IHC stain enables accurate identification of endothelial cells in several animal species. This stain can be used to distinguish a poorly differentiated hemangiosarcoma from other poorly differentiated tumors. A definitive diagnosis of hemangiosarcoma is clinically useful because these tumors have a good prognosis after complete excision whereas other poorly differentiated sarcomas have a less favorable prognosis.

Completeness of excision is the most important factor in predicting outcome of nonvisceral hemangiosarcoma. Many tumors in skin and eye could be completely removed, and patients remained clinically normal for at least 1 year. In contrast, tumors in bone and muscle could not be completely excised and caused the death of the animal. Smaller skin tumors had a better outcome than large ones, and this was correlated with complete excision. Small tumors that lead to death had incomplete surgical excision. Skin tumors that were confined to the dermis were more likely to be successfully treated; this is correlated with complete excision. A previous study grouped subcutaneous masses with those that had spread to underlying muscle and concluded that subcutaneous tumors had a poor prognosis. In contrast, among the tumors reviewed in this study, subcutaneous tumors were evaluated separately from muscle tumors and found to have a good
prognosis if completely removed. Accumulation of mast cells in the stroma does not appear to have significance but can be a complicating factor in cytologic diagnosis of these tumors because an aspirate that obtains blood and mast cells might be misdiagnosed as a mast cell tumor. Mitotic rate, level of differentiation, epidermal ulceration, and presence of solar elastosis in the dermis and history of recurrence are not correlated with clinical outcome.

Sources and manufacturers

a. Cell Marque, Austin, TX.

References