

## Hemangiosarcoma in 11 Young Horses

Imogen Johns, Jennifer O. Stephen, Fabio Del Piero, Dean W. Richardson, and Pamela A. Wilkins

Hemangiosarcoma is a rare neoplasm of horses and hemangiosarcoma in young horses might behave differently than in mature horses. The purpose of this study was to identify the characteristics of hemangiosarcoma occurring in horses  $\leq 3$  years of age. Medical records from 1982 to 2004 were searched for horses  $\leq 3$  years of age with a histopathologic diagnosis of hemangiosarcoma. Eleven records were identified. Thoroughbred and Thoroughbred crosses predominated. Age ranged from 9 days to 3 years. All horses presented with cutaneous or leg swellings or joint effusion. Physical examination findings included tachycardia, fever, and depression. Laboratory abnormalities included anemia (5/11), hyperfibrinogenemia (4/11), hypofibrinogenemia (3/11), thrombocytopenia (2/11), and neutrophilic leukocytosis (1/11). Ultrasonographic and radiographic evaluation was not diagnostic in any case. Antemortem histopathologic diagnosis was obtained in 10 cases. Six of 11 horses were euthanized. Surgical resection was performed in 5 horses, 2 of which were later euthanized. Diagnosis was confirmed histologically at postmortem examination in all euthanized horses. Two cases resolved spontaneously. Early histopathologic diagnosis may allow cure if the mass is localized and amenable to surgical resection. In cases where the horse is medically stable, and masses are not interfering with quality of life, a period of observation may be warranted.

**Key words:** Congenital; Hemangioma; Tumor; Vascular neoplasia.

**H**emangiosarcoma, also known as angiosarcoma or malignant hemangioendothelioma, is an uncommon vascular neoplasm of horses. Hemangiosarcoma affects middle-aged horses as disseminated hemangiosarcoma with multiple organ involvement.<sup>1,2</sup> Respiratory and musculoskeletal systems are most often affected. Presenting complaints vary according to the body system or systems involved, and include cutaneous masses, leg swelling and lameness, epistaxis, depression, and poor performance. It was our impression that young horses presenting with hemangiosarcoma represented a subpopulation of horses with this disease in that disseminated disease was less common and limb and bone involvement was more common. We undertook a retrospective study of young horses with hemangiosarcoma to more clearly describe the clinical presentation of these patients.

### Materials and Methods

The medical records system of the George D. Widener Hospital for Large Animals, University of Pennsylvania, was searched between the years 1982 and 2004 for horses with a final histopathologic diagnosis of hemangiosarcoma. Records of horses  $<3$  years of age at the time of presentation, or with compelling evidence that the lesion had been present before their 4-year-old year, were retrieved and evaluated. Signalment, duration of clinical signs before presentation, physical examination findings, hematologic and serum biochemical findings, ultrasonographic or radiographic findings, method of diagnosis, treatment, and outcome were recorded.

---

*From the University of Pennsylvania, George D. Widener Hospital, New Bolton Center, Kennett Square, PA (Johns, Del Piero, Richardson, Wilkins); and The Equine Hospital, Royal Veterinary College, Hertfordshire, UK (Stephen). Portions of the information in this manuscript were presented in abstract form at the ACVIM Annual Forum 2004.*

*Reprint requests: Pamela A Wilkins, DVM, MS, PhD, DACVIM, DACVECC, New Bolton Center, 382 West Street Road, Kennett Square, PA 19348; e-mail: pwilkins@vet.upenn.edu.*

*Submitted July 26, 2004; Revised November 1, 2004; Accepted March 1, 2005.*

*Copyright © 2005 by the American College of Veterinary Internal Medicine*

0891-6640/05/1904-0012/\$3.00/0

### Results

Approximately 56,000 equine patients presented to New Bolton Center between 1986 and 2004. Data were not available for equine patient total admissions for the years 1982–1985. Twenty-six horses were identified with a final histopathologic diagnosis of hemangiosarcoma in 1982–2004. Fifteen horses were 4 or more years of age at presentation (mean 11.2 years; range 6–27 years). Thirteen of these 15 were eventually euthanized, with the vast majority (12/13) having a final diagnosis of disseminated hemangiosarcoma at postmortem examination. Two older horses were lost to follow-up. Eleven horses were 3 years of age or less at the time of diagnosis. Age at initial examination ranged from 9 days to 4 years. One 4-year-old horse was included in the study because the mass had historically been present since birth. Clinical signs had been present for several hours to 4 years. Breeds represented included Thoroughbreds (7), Thoroughbred crosses (2), Standardbred (1), and Rocky Mountain Horse (1).<sup>3</sup> All horses were examined for cutaneous masses or swelling, diffuse limb swelling, or joint effusion. Masses were evident on the thorax (2/11; horses 1 and 5), mandible or maxilla (3/11; horses 2, 7, and 9), oral cavity, prepuce, or other regions of skin (1/11; horse 7), and limbs (1/11; horse 3) (Fig 1). Diffuse leg swelling was the primary complaint in 3 of 11 horses (horses 4, 10, and 11). Two horses had both discrete masses and more diffuse swellings. Multiple masses were identified in 6 horses, typically in anatomically widespread areas. In 7 horses the mass(es) was subcutaneous and covered by normally pigmented haired skin. Two horses (horses 1 and 2) had undergone surgical resection before examination and had ulcerated lesions. In 1 foal (horse 7), the skin over the cutaneous masses was hairless and a preputial mass was eroded and hemorrhagic. One 4-year-old horse (horse 9) had an ulcerated mass of the mandible.

The duration of clinical signs prior to examination was variable, from hours up to 4 years. A history of trauma and subsequent diagnosis of hematoma was evident in a 2 year-old filly that presented with a thoracic mass (horse 1). Clinical signs rapidly progressed in 3 horses. Two horses had raced within 3 weeks of examination (horses 4 and 11), and had subsequently developed lameness, limb swelling, and



**Fig 1.** Distal limb masses horse 3.

cutaneous masses. Horse 4 had multiple masses affecting several body systems, identified initially by ultrasonography and confirmed as hemangiosarcoma at postmortem examination. Another filly (horse 6) developed cutaneous masses due to hemangiosarcoma within 2 days of admission to the hospital for a suspected body-wall hernia and intraperitoneal hemorrhage. In other cases, masses were more slowly progressive (over months) or had been nonresponsive to surgical resection. In 1 horse, a mass on the mandible had been present for 4 years, with only very gradual growth during this period (horse 9).

All horses were in good body condition based on physical examination or postmortem report findings. Physical examination findings were available for 10 horses. Tachycardia (5/10) and fever (2/10) were identified. Routine hematologic and serum biochemical analyses were performed in all horses. Mild anemia (PCV 25–31%; reference range 32–52%) occurred in 5 horses, hyperfibrinogenemia (398–722 mg/dL; reference range 150–375 mg/dL) in 4 horses, and hypofibrinogenemia (109–122 mg/dL) in 3 horses. Thrombocytopenia (75,000 and 96,910/ $\mu$ L; reference range > 100,000/ $\mu$ L) was found in 2 horses and neutrophilic leukocytosis was found in 1 horse (total white cell count 16,200/ $\mu$ L; reference range 5,500–12,500/ $\mu$ L; neutrophils 10,000/ $\mu$ L, reference range 2,700–6,700/ $\mu$ L).

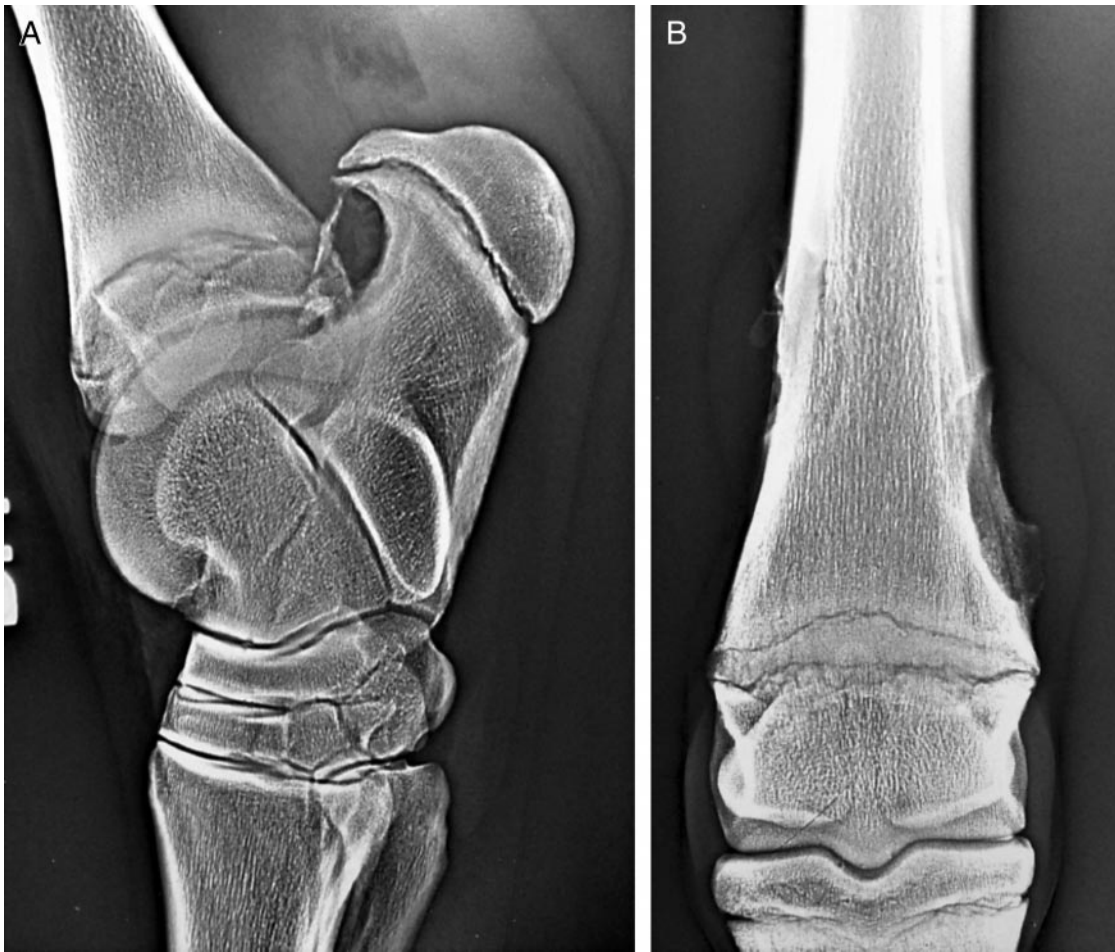
Ultrasonographic evaluation of affected areas was performed in 7 cases. Masses typically appeared as anechoic fluid spaces with hypoechoic to echogenic soft tissue between spaces. Evidence of involvement of surrounding tissue was found in 6 cases. Disseminated hemangiosarcoma was

strongly suspected in 1 horse (horse 4) after multiple masses of vascular appearance were identified throughout many organs. Ultrasonographic evaluation of the abdominal and thoracic cavity, to search for additional masses or metastasis, was performed in horse 10. This filly was suspected of having thoracic and abdominal metastases based on ultrasonography, although no clinical evidence was found of the masses, and the filly survived to long-term follow-up.

Results of radiographic examination were abnormal in 2 of 6 horses examined by radiographic techniques. Xeroradiography of the tarsus and metatarsophalangeal joint in horse 3 revealed smooth-bordered radiotranslucent defects consistent with pressure atrophy or necrosis of bones associated with the soft-tissue masses, considered most consistent with an expansile soft-tissue mass rather than an invasive tumor. (Figs 1–3). Radiographs of the skull obtained postmortem in horse 7 revealed smooth radiolucent areas within the bony structures surrounding the soft-tissue opacities in the maxilla and mandible, suggestive again of pressure atrophy of the adjacent bone. Those radiographs have been previously published.<sup>3</sup>

Fine-needle aspirate or paracentesis was performed in 4 horses. Results were most consistent with peripheral blood, although neoplasia was strongly suspected in 1 horse. Biopsy (needle<sup>a</sup> or excisional) was performed in 10 of 11 horses (15 biopsies total). The histopathologic diagnosis of hemangiosarcoma was made based on these results in all 10 horses; diagnosis in 1 horse required 3 biopsy attempts. Immunohistochemical staining for factor VIII-related antigen was performed on 7 biopsy samples, confirming endothelial origin of tissue in all cases. Histopathologic specimens, when available, were evaluated by an independent pathologist, and confirmed as hemangiosarcoma (horses 1–6, and 10).

Treatment by surgical excision was attempted in 5 cases. One foal (horse 2) had multiple surgeries to remove a mandibular mass over a period of 6 months, in conjunction with cryotherapy and topical 5-fluorouracil,<sup>b</sup> with eventual resolution. One horse (horse 3) had multiple masses removed from both hind limbs, but was euthanized 6 months later because of tumor recurrence. One horse with an initial diagnosis of organizing hematoma secondary to an observed trauma had 2 surgeries performed over a 10-week period before the diagnosis of hemangiosarcoma was made and the horse euthanized (horse 4). An additional 2 horses had masses resected at surgery (horses 8 and 9). Horse 9 has had no recurrence at the time of writing (5 months after surgery). The 2nd horse had a vascular mass arthroscopically removed from the tarsocrural joint (horse 8), and is reported to be clinically healthy 8 months after surgery. Supportive medical therapy was provided for a filly with an abdominal wall hernia, intraperitoneal hemorrhage, and multiple cutaneous masses before the diagnosis of hemangiosarcoma was made via biopsy of a cutaneous mass, and euthanasia was performed (horse 6). Treatment was not attempted in 4 horses, 2 of which were euthanized after diagnosis (horses 4 and 5). Leg swelling and cutaneous masses resolved without treatment in 2 horses, with no further abnormalities identified (horses 10 and 11). One horse returned to racing and the other became a productive broodmare.



**Fig 2.** (A) Lateral xeroradiograph of right hock of horse 3. (B) Dorsopalmar xeroradiograph of right front fetlock of horse 3.

Overall, 6 of 11 horses were euthanized as a direct result of their neoplasms. Two horses (horses 4 and 6) were euthanized secondary to acute deterioration in condition. Two horses (horses 1 and 3) were euthanized either secondary to failure to fully resect the mass(es) or recurrence of the tumor. Two horses (horses 5 and 7) were euthanized because of the owner's reluctance to pursue treatment after diagnosis.

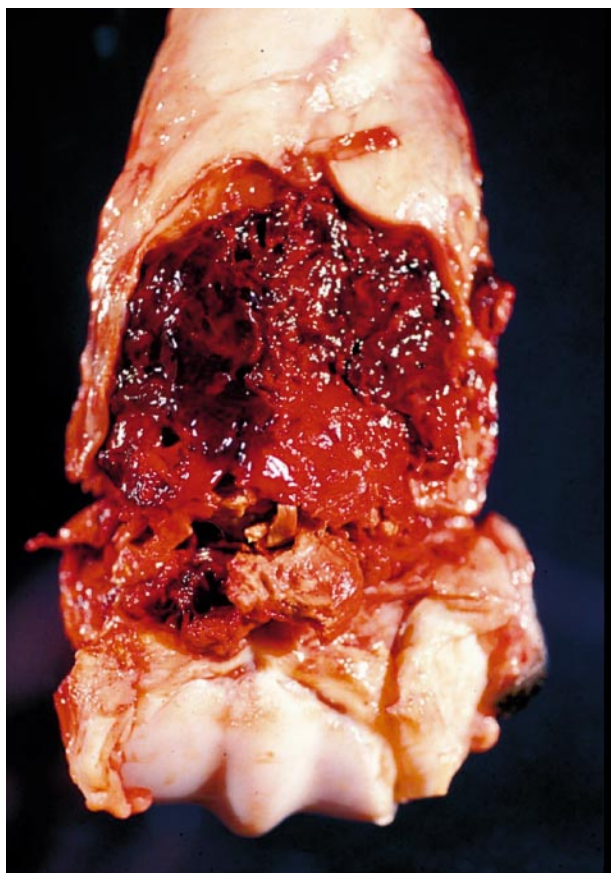
Masses identified either via physical examination or ultrasonographic evaluation were confirmed at postmortem examination. In 2 horses (horses 5 and 6), additional neoplastic foci were identified at sites distant to the masses identified antemortem. Horse 4, diagnosed antemortem with multiple masses in the heart, diaphragm, lungs, and numerous skeletal muscles, had an additional mass in the stomach at postmortem examination. Hemangiosarcoma was histopathologically confirmed from postmortem samples in all horses (Fig 4).

### Discussion

Hemangiosarcoma affecting young horses has been reported to be uncommon,<sup>1</sup> and represents a diagnostic challenge in many cases. During the period 1982–2004, 26 cases of hemangiosarcoma were diagnosed at the New Bolton Center in horses of all ages. Eleven of these cases were in

horses aged  $\leq 3$  years. A review of the literature revealed 5 additional cases of hemangiosarcoma in horses aged  $\leq 3$  years.<sup>1,2,4-7</sup> Malignant vascular neoplasms are infrequently reported in infants and children, with the largest retrospective studies reporting only 6 and 14 cases, respectively, presenting to large referral cancer centers over 20- to 25-year time periods.<sup>8,9</sup> The majority of vascular tumors in young humans are benign hemangiomas, although unlike horses, they typically spontaneously regress.<sup>10</sup> Cases in young cats, dogs,<sup>11</sup> and a calf<sup>12</sup> also have been reported. Because of the apparent difference in prognosis between hemangiomas and hemangiosarcomas,<sup>1,13</sup> differentiation antemortem between these 2 neoplasms is essential. The purpose of this retrospective study was to identify clinical features of equine juvenile hemangiosarcomas, to characterize procedures that may be helpful in its diagnosis, and to identify any differences in clinical presentation and prognosis that may exist between adults and juveniles with hemangiosarcoma.

In the series in the present report, 3 horses (horses 2, 7, and 9) apparently had masses present since birth. Johnstone<sup>7</sup> reported a case of hemangiosarcoma of the coronary band and pastern that had been present at birth, and a foal with congenital hemangiosarcoma of the oral cavity, skin, and periarticular region has been reported.<sup>3</sup> Congenital hemangiosarcoma also has been reported in humans<sup>14</sup> and a



**Fig 3.** Palmar view of gross fetlock specimen from horse 3, corresponding to radiograph in Figure 2B.

calf.<sup>12</sup> Hemangiomas<sup>15,16</sup> and hamartomas<sup>17</sup> also are reported as congenital lesions in horses.

Although the majority of affected horses were female, and Thoroughbreds appear to be overrepresented, it is not possible from this small sample size to assign breed or sex predilection. Southwood et al<sup>1</sup> reported no breed or sex predilection in a review of 35 cases of disseminated hemangiosarcoma. In dogs, German Shepherd Dogs and other large breeds are overrepresented, whereas in cats, hemangiosarcoma is more common in the Domestic Short Hair.<sup>11</sup> There is debate over whether sex predilection exists for hemangiosarcoma in dogs and cats.<sup>11</sup>

All horses in this series presented with cutaneous masses, leg swelling, or joint effusion. Hemangiosarcoma affecting the musculoskeletal system has been reported, although its identification here as the primary body system affected contrasts with cases of disseminated hemangiosarcoma in which signs referable to the respiratory tract (dyspnea or epistaxis) were the most common presenting complaint, followed by subcutaneous or muscular swelling.<sup>1</sup>

Hemangiosarcoma is usually characterized as an aggressive neoplasia.<sup>1</sup> The behavior of the mass in horse 9 was somewhat unusual in its slow growth. However, several cases had apparent rapid onset and rapid growth, making characterization of the juvenile form of hemangiosarcoma as either slowly progressive or aggressive difficult. It is interesting to note that, although extremely rare, in human

medicine progression of benign hemangioma to hemangiosarcoma has been reported. Most commonly this is associated with previous radiation therapy for benign hemangioma,<sup>18,19</sup> but it also has been reported to occur spontaneously.<sup>20</sup> In addition, an association between sun exposure and transformation of benign hemangiomas to hemangiosarcomas has been made in dogs.<sup>21</sup> Typically, this is seen only on the nonhaired abdominal skin of non- or lightly pigmented dogs. The horses presented in this case series had darkly pigmented skin. It is possible that the tumor initially may have been characterized as a hemangioma, and then transformed to a hemangiosarcoma, although this is merely speculative.

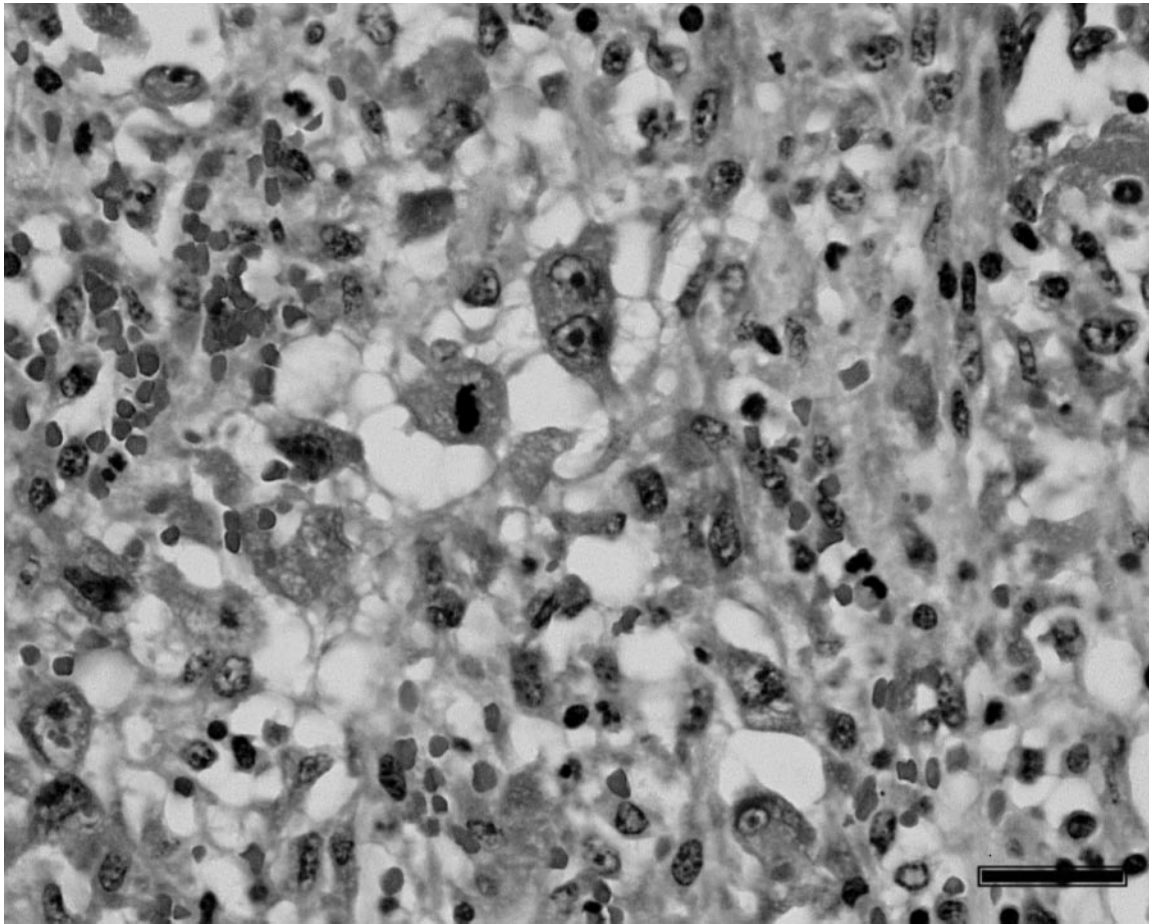
All horses were considered to be in good body condition. Abnormalities on physical examination were confined to the masses or swellings in most horses. Horse 4 was depressed, reluctant to move, tachycardic, and febrile on admission, and horse 6 was depressed and tachycardic. The limited physical examination abnormalities compared to those reported in horses with disseminated hemangiosarcoma<sup>1</sup> likely reflects the primary involvement of the musculoskeletal system as compared to diffuse organ involvement. The lack of physical examination findings such as weight loss and depression, which would more typically be associated with a neoplastic process, makes differentiation of musculoskeletal hemangiosarcoma from other more common causes of limb swelling and cutaneous masses, such as hematoma, abscess, lymphangitis, or cellulitis, potentially difficult.

Anemia, neutrophilic leukocytosis, and thrombocytopenia were reported as the most common hematologic abnormality in horses with disseminated hemangiosarcoma,<sup>1</sup> and in dogs.<sup>11</sup> Hypofibrinogenemia, present in 3 horses (horses 4, 10, and 11) is uncommonly reported in horses, with potential causes including decreased production by the liver, or increased utilization, as in disseminated intravascular coagulation (DIC)<sup>22</sup> or blood loss.<sup>23</sup> Hemostatic abnormalities have been reported in other species associated with hemangiosarcoma but were not specifically evaluated in the horses in this report.<sup>24,25</sup>

Ancillary diagnostic testing was performed in all horses. Ultrasonographic evaluation of masses and swellings was considered useful to characterize the nature and extent of swelling, but was not specific for a diagnosis of hemangiosarcoma. Ultrasonography also was useful in identifying masses not evident on physical examination. Differential diagnoses considered after ultrasonographic evaluation of masses included hematoma, septic thrombophlebitis, or unspecified neoplasia.

Radiographic evaluation of affected areas was performed to assess possible bony involvement and was useful in discriminating between bony invasion by the tumor and bone atrophy secondary to compression by the tumors. If surgical resection is considered, the degree and type of bony involvement provides useful information for management and may affect prognosis. Osseous hemangiosarcoma has been reported in dogs<sup>11</sup> and horses.<sup>26</sup>

A definitive diagnosis of hemangiosarcoma requires histopathologic confirmation. There is no generally accepted classification of tumors and malformations of vascular tissue. Hemangiosarcomas are malignant neoplasms of vas-



**Fig 4.** Horse 3. Histopathologic appearance of mass from postmortem examination specimen. The neoplasm is comprised by spindle, round, and bizarre endothelial cells with abnormal nucleus to cytoplasm ratio, anisocytosis, anisokaryosis, nucleolar abnormalities, polykaryocytes, and frequent mitotic figures. The neoplastic cells form cavities sometimes containing erythrocytes. Bar = 80  $\mu$ m.

cular origin.<sup>1</sup> Clinically, hemangiosarcomas can be seen as focal masses, masses with local infiltration, internal masses restricted to 1 organ, and disseminated neoplasia affecting multiple organs.<sup>1</sup> A wide age range has been reported in affected horses (6 months to 27 years), although most reports involve middle-aged to older horses.<sup>1</sup> Hemangiosarcomas usually progress rapidly, frequently metastasize, and carry a poor prognosis.<sup>1,9–11</sup>

The high percentage of cases diagnosed antemortem in the case series of this report is in contrast to only 4 of 35 cases of disseminated hemangiosarcoma diagnosed antemortem in the series reported by Southwood et al.<sup>1</sup> The presence of readily recognizable and accessible masses or swellings for biopsy in all horses in this series may have contributed to this high percentage. Other body systems such as the respiratory tract are less accessible for sampling, although pleuroscopic diagnosis of pulmonary hemangiosarcoma has been reported.<sup>27</sup> The potential need for multiple biopsy specimens to confirm the diagnosis should be emphasized, as the tumors are not typically homogenous in nature, and many areas may resemble hematomas.<sup>11</sup>

The use of immunohistochemical (IHC) techniques for evaluation of biopsy specimens is reported in humans,<sup>28</sup> dogs,<sup>11,29</sup> cats,<sup>11</sup> goats,<sup>30</sup> and horses,<sup>31</sup> and can be useful in confirming endothelial origin of tumors. Factor VIII-related

antigen is expressed on endothelial cells of both vascular and lymphatic origin, although it has significantly higher expression for vascular endothelium, and thus is used as a marker for vascular endothelium. Factor VIII-related antigen cannot be used to distinguish normal endothelium from neoplastic endothelium, and its expression can be limited in poorly differentiated tumors, potentially limiting its usefulness.<sup>31</sup> Seven biopsy samples in this series were examined by using IHC, and all were positive for factor VIII-related antigen.

Treatment for hemangiosarcoma in all species is generally considered unrewarding.<sup>1,8,9,11</sup> Despite aggressive surgical, drug, or radiation therapy, median survival times are short for almost all forms, dermal hemangiosarcoma possibly excepted, of primary hemangiosarcoma in dogs and cats.<sup>11,32,33</sup> Reported treatments include surgical removal, radiation, and chemotherapy (eg, doxorubicin, cyclophosphamide, or vincristine). Biologic therapy with immunomodulators (mixed bacterial vaccine and liposome-encapsulated muramyl tripeptide) have been reported to be useful in prolonging survival times in dogs and cats, especially in combination with chemotherapy, but are not currently used because of lack of availability and high cost.<sup>11,32</sup> Treatment is considered palliative rather than curative. Treatment was attempted in 5 horses in this series (horses 1, 2, 3, 8, and

9). Surgical resection of masses was performed in these cases, and was considered successful in horse 2, although multiple surgeries and extensive resection was required. The successful use of 5-fluoracil topically following surgical resection and cryosurgery in 1 horse is interesting, because this treatment has not been successfully used in the treatment of hemangiosarcoma to the authors' knowledge. Masses at surgery were typically described as locally invasive, hemorrhagic soft tissue masses. At the time of writing, 2 horses (horses 8 and 9) have survived to short-term follow-up (months). The remaining 2 horses (horses 1 and 3) were euthanized because of tumor recurrence at the original site. Postmortem examination confirmed hemangiosarcoma in all cases. Two cases were considered disseminated, based on multiple organ involvement, and local invasion of tissues was evident in all cases. Treatment was not pursued in 2 horses that were not euthanized and have survived to long-term follow-up (years) (horses 10 and 11). In both of these horses, the masses and leg swelling resolved. Given the overall poor prognosis for hemangiosarcoma in any species, it is difficult to explain the apparent resolution in these 2 horses. Histopathologic specimens from horse 10 were examined by multiple pathologists and confirmed to be hemangiosarcoma. The diagnosis in horse 11 was considered less definitive. Successful treatment of equine cutaneous hemangiosarcoma<sup>2</sup> has been reported, although spontaneous resolution has not. Hemangiomas have been reported to spontaneously resolve in older children, although this has not been reported in horses. A search of the literature identified 1 case of spontaneously resolving angiosarcoma in a human patient.<sup>20</sup>

The overall prognosis for horses with juvenile hemangiosarcoma appears to be variable, based on this case series. Six of the 11 horses were euthanized, with 2 surviving horses having only short-term follow-up to date and 2 surviving long-term with apparent tumor resolution without treatment. Euthanasia is frequently determined by economic and practical factors in the horse; only 2 horses were euthanized because of rapidly deteriorating clinical condition. Surgical excision appears unlikely to be curative based on recurrence of tumors and local invasiveness. Cutaneous hemangiosarcoma has been reported to have a better prognosis in dogs if the tumor is confined to the dermal layer.<sup>34</sup> Thus, if diagnosis is made early before the tumor has spread locally or metastasized, surgical resection may be curative. However, the multifocal nature of many of the masses in this series and the rapid and aggressive nature for the majority of the masses makes it unlikely that the prognosis for young horses with hemangiosarcoma will significantly improve even with early diagnosis. It is unknown if local therapy has potential benefit because it was attempted in only 1 horse in this series.

Although vascular neoplasia is a rare occurrence in young horses, it should be considered in the evaluation of cutaneous or muscular masses, especially those that fail to resolve despite conventional therapy. An antemortem diagnosis is possible, although multiple biopsy samples may be required. Ancillary diagnostic tests such as ultrasound, radiographs, and hematology are typically not helpful in confirming a diagnosis.

In summary, based on the results of this retrospective

study, hemangiosarcoma in juveniles may behave differently compared to mature animals. Young horses affected by hemangiosarcoma were all in good body condition and good general health at the time of presentation in our series. A significant proportion of the cases were likely congenital and present from birth. Cutaneous and limb masses were more common, although disseminated neoplasia affecting internal organs also occurred. There were no cases of hemangiosarcoma primarily affecting the respiratory tract, vertebral bodies, or eyes in this series, organs not infrequently reported affected in older patients.<sup>1,34-38</sup> In addition, an antemortem diagnosis was more commonly obtained in this group of horses, possibly because of the predominance of easily accessible masses for biopsy. Also in contrast with findings in older horses, the prognosis is variable in juvenile horses with hemangiosarcoma and seems dependent on extent and location.

---

### Footnotes

<sup>a</sup> Tru Cut biopsy needle, Baxter-Travenol, St Louis, MO

<sup>b</sup> Efudex, ICN Pharmaceuticals Inc, Costa Mesa, CA

---

### Acknowledgment

We would like to acknowledge Fairfield Bain for his assistance with case evaluation.

### References

1. Southwood LL, Schott HC, Henry CJ, et al. Disseminated hemangiosarcoma in the horse: 35 cases. *J Vet Intern Med* 2000;14:105-109.
2. Collins MB, Hodgson DR, Hutchins DR, McConaghy FF. Hemangiosarcoma in the horse: Three cases. *Aust Vet J* 1994;71:296-298.
3. Dunkel BM, Del Piero F, Kraus BM, et al. Congenital cutaneous, oral and periarticular hemangiosarcoma in a 9 day-old Rocky Mountain Horse. *J Vet Intern Med* 2004;18:252-255.
4. Freestone JF, Williams MM, Norwood G. Thoracic haemangiosarcoma in a 3-year-old horse. *Aust Vet J* 1990;67:269-270.
5. Van Pelt RW, Langham RF, Gill HE. Multiple hemangiosarcomas in the tarsal synovial sheath of a horse. *J Am Vet Med Assoc* 1972;161:49-52.
6. Valentine BA, Ross CE, Bump JL, Eng VM. Intramuscular hemangiosarcoma with pulmonary metastasis in a horse. *J Am Vet Med Assoc* 1986;188:628-629.
7. Johnstone AC. Congenital vascular tumours in the skin of horses. *J Comp Pathol* 1987;97:365-368.
8. Ferrari A, Casanova M, Bisogno G, et al. Malignant vascular tumors in children and adolescents: A report from the Italian and German Soft Tissue Sarcoma Cooperative Group. *Med Pediatr Oncol* 2002;39:109-114.
9. Lezama-del Valle P, Gerald WL, Tsai J, et al. Malignant vascular tumors in young patients. *Cancer* 1998;83:1634-1639.
10. Mulliken JB, Enjolras O. Congenital hemangiomas and infantile hemangioma: Missing links. *J Am Acad Dermatol*; 2004;50:875-882.
11. Smith AN. Hemangiosarcoma in dogs and cats. *Vet Clin Small Anim* 2003;33:533-552.
12. Badylak SF. Congenital multifocal hemangiosarcoma in a still-born calf. *Vet Pathol* 1983;20:245-247.
13. Hargis AM, McElwain TF. Vascular neoplasia in the skin of horses. *J Am Vet Med Assoc* 1984;184:1121-1124.

14. Suzuki Y, Yoshida YK, Shirane R, et al. Congenital primary cerebral angiosarcoma. Case report. *J Neurosurg* 2000;92:466–468.
15. Sartin EA, Hodge TG. Congenital dermal hemangioendothelioma in two foals. *Vet Pathol* 1982;19:569–571.
16. Platt H. Vascular malformations and angiomatous lesions in horses: A review of 10 cases. *Equine Vet J* 1987;19:500–504.
17. Rhyan JC, D'andrea GH, Smith LS. Congenital ovarian vascular hamartoma in a horse. *Vet Pathol* 1981;18:131.
18. Caldwell JB, Ryan MT, Benson PM, James WD. Cutaneous angiosarcoma arising in the radiation site of a congenital hemangioma. *J Am Acad Dermatol* 1995;33:865–870.
19. Cabo H, Cohen ES, Casas GJ, et al. Cutaneous angiosarcoma arising on the radiation site of a congenital facial hemangioma. *Int J Dermatol* 1998;37:638–639.
20. Ceroni L, Peris K, Legge A, Chimenti S. Angiosarcoma of the face and scalp. A case report with complete spontaneous regression. *J Dermatol Surg Oncol* 1991;17:539–542.
21. Hargis AM, Ihrke PJ, Spangler WL, Stannard AA. A retrospective clinicopathologic study of 212 dogs with cutaneous hemangiomas and hemangiosarcomas. *Vet Pathol* 1992;29:316–328.
22. Morris DD. Alterations in the clotting profile. In: Smith BP, ed. *Large Animal Internal Medicine*, 3rd ed. St Louis, MO: Mosby Inc; 2002:434–439.
23. Murray DJ, Pennell BJ, Weinstein SL, et al. Packed red cells in acute blood loss: Dilutional coagulopathy as a cause of surgical bleeding. *Anesth Analg* 1995;80:336–342.
24. Hammer AS, Couto CG, Swadson C, Getzy D. Hemostatic abnormalities in dogs with hemangiosarcoma. *J Vet Intern Med* 1991;1:11–14.
25. Hargis AM, Feldman BF. Evaluation of hemostatic defects secondary to vascular tumors in dogs: 11 cases (1983–1988). *J Am Vet Med Assoc* 1991;198:891–894.
26. Newton-Clarke MJ, Guffoy MRG, Dykes NL, Divers TJ. Ataxia due to vertebral haemangiosarcoma in a horse. *Vet Rec* 1994;135:182–184.
27. Rossier Y, Sweeney CR, Heyer G, Hamir A. Pleuroscopic diagnosis of disseminated hemangiosarcoma in a horse. *J Am Vet Med Assoc* 1990;196:1639–1640.
28. Ohsawa M, Naka N, Tomita Y, et al. Use of immunohistochemical procedures in diagnosing angiosarcoma. Evaluation of 98 cases. *Cancer* 1995;75:2867–2874.
29. Ferrer L, Fondevila D, Rabanal RM, Vilafranca M. Immunohistochemical detection of CD31 antigen in normal and neoplastic canine endothelial cells. *J Comp Pathol* 1995;112:319–326.
30. Bidfell RJ, Valetine BA, Whitney KM. Cutaneous vasoproliferative lesions in goats. *Vet Pathol* 2002;39:273–277.
31. Yoshinari K, Oikawa M, Yoshihara T, Kaneko M. Clinical and immunohistochemical observation of hemangiosarcoma in a racing Thoroughbred. *Equine Pract* 1996;18:24–29.
32. Clifford CA, Mackin AJ, Henry CJ. Treatment of canine hemangiosarcoma: 2000 and beyond. *J Vet Intern Med* 2000;14:479–485.
33. Ward H, Fox LE, Calderwood-Mays MB, et al. Cutaneous hemangiosarcoma in 25 dogs: A retrospective study. *J Vet Intern Med* 1994;8:345–348.
34. Hacker DV, Moore PF, Buyukmihci NC. Ocular angiosarcoma in four horses. *J Am Vet Med Assoc* 1986;189:200–203.
35. Kennedy FA, Brown CM. Vertebral angiosarcoma in a horse. *J Vet Diagn Invest* 1993;5:125–127.
36. Berry S. Spinal cord compression secondary to hemangiosarcoma in a Saddlebred stallion. *Can Vet J* 2000;40:886–887.
37. Newton-Clarke MJ, Guffoy MR, Dykes NL, et al. Ataxia due to a vertebral haemangiosarcoma in a horse. *Vet Rec* 1994;135:182–184.
38. Fatone S, Edens L, McElhaney B. Challenging cases in internal medicine: What's your diagnosis? *Vet Med* 1993;88:1039–1044.