

## SEVERE LAMENESS AND MUSCULAR SWELLING DUE TO INTRAMUSCULAR HEMANGIOSARCOMA IN A HORSE

*Ernstig manken en spierzwelling veroorzaakt door een intramusculair hemangiosaroom bij een paard*

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### ABSTRACT

**This report describes a case of a severely lame horse referred for an obvious muscular swelling at the level of the right crus. The horse was in poor condition. An initial diagnosis of trauma with intramuscular hemorrhage was made. Nineteen days following the first examination, the horse was euthanized because of disseminated hemangiosarcoma. The clinical findings, the therapeutic possibilities and the observations at necropsy are discussed.**

### SAMENVATTING

Dit artikel beschrijft een geval van een erg mank paard met duidelijke zwelling ter hoogte van de rechterschenkel. De algemene conditie van het dier was slecht. Initieel werd gedacht aan een erge intramusculaire bloeding na trauma. Negentien dagen na het eerste consult werd het paard opnieuw aangeboden. De diagnose werd herzien; euthanasie werd uitgevoerd omdat men een uitgezaaid hemangiosaroom vermoedde. Deze casuïstiek bespreekt de resultaten van het klinisch onderzoek, de behandeling en de bevindingen bij lijkschouwing.

### INTRODUCTION

Hemangiosarcoma, also called angiosarcoma or malignant hemangioendothelioma, is a malignant tumor originating from the vascular endothelium. It has been reported in horses, but is considered to be an uncommon neoplasm in this species (Collins *et al.*, 1994). Of the 27,604 equine cases presented at the Animal Health Diagnostic Laboratory, Michigan State University, from 1981 through November of 1990, only 16 horses were determined to have vascular tumors. Five of these neoplasms were hemangiomas and 11 were designated as hemangiosarcomas or angiosarcomas (Kennedy and Brown, 1993). Hemangiosarcoma is most commonly found in mature (particularly middle-aged) horses with no apparent sex predilection. Thoroughbreds seem to be overrepresented, but a true

breed predilection could not be established (Southwood *et al.*, 2000).

As hemangiosarcoma originates from endothelial cells, it can arise at many different body sites. Primary intramuscular hemangiosarcoma in the horse has been described (Valentine *et al.*, 1986; Sweeney and Gillette, 1989). Furthermore, the skin (Vos *et al.*, 1986; Jean *et al.*, 1994), the vertebrae (Kennedy and Brown, 1993; Newton-Clarke *et al.*, 1994), the thoracic wall (Freestone *et al.*, 1990; Collins *et al.*, 1994), the pericardium (Birks and Hultgren, 1988), the spleen (Geelen and Sloet van Oldruitenborgh-Oosterbaan, 1996), the ovary (Gruys *et al.*, 1976), the pelvis (Kiupel *et al.*, 2000) and the tarsal synovial sheath (Van Pelt *et al.*, 1972) have been reported as primary tumor sites. Cutaneous vascular neoplasms are nearly always benign hemangiomas. Neoplastic vascular lesions on other locations are mostly hemangiosarco-

mas that disseminate frequently and rapidly because the tumor cells easily gain access to the blood circulation. Several cases of disseminated hemangiosarcoma involving a variety of equine organ systems have been described (Waugh *et al.*, 1977; Frye *et al.*, 1983; Johnson *et al.*, 1988; Rossier *et al.*, 1990; Southwood *et al.*, 2000).

## CASE DESCRIPTION

An eight-year-old warmblood gelding was referred with a history of increasing lameness of unknown origin with muscle atrophy of the right hind limb already present for 10 days. On admission, the horse was lame at walk on the affected limb. The general condition of the horse was poor; rectal temperature was normal (37.8°C). The caudal aspect of the crus was severely swollen but not painful on palpation. There was a marked atrophy of the proximal musculature of the right hind limb and the right femoropatellar joint was distended. Radiography of the stifle revealed severe osteochondrosis dissecans (OCD) of the lateral trochlear ridge of the femur; tibia and hock were normal. This finding was concluded to be of no clinical importance since routine intra-articular femoropatellar analgesia was negative. Ultrasonography of the swelling at the caudal aspect of the crus revealed multiple anechoic areas in the right *m. flexor digitalis lateralis*. Serohemorrhagic fluid was aspirated by standard needle puncture. The puncture induced a relatively severe hemorrhage. Secondary sepsis of the intramuscular hematoma was ruled out, as the white blood cell count (3000 / mm<sup>3</sup>) of the aspirate was not indicative for infection. A preliminary diagnosis of intramuscular hemorrhage due to severe posttraumatic myositis of the right *m. flexor digitalis lateralis* was made.

The horse was treated with dexamethasone (0.01 mg/kg s.i.d. IM) and ketoprofen (2.2 mg/kg s.i.d. IV). As the *m. flexor digitalis lateralis* is one of the three muscle heads of the deep digital flexor tendon, corrective shoeing with heel elevation was used to reduce tension on the tendon's muscle bellies. The lameness partially improved and on request of the owner the horse was discharged from the hospital after one week of treatment. The owner was asked to continue the anti-inflammatory therapy and to confine the horse to a box.

One week later the horse was presented to the hospital in emergency. The horse had been turned into the field with other horses, where the owner had seen it fall. On admission, the horse had epistaxis and icteric

mucosal membranes. The swelling at the level of the crus had increased markedly. The horse was non-weight bearing lame on the right hind limb and seriously atactic. The horse was referred to the department of equine internal medicine where an ultrasonographic examination of thorax and abdomen was performed. Multiple small hyperechoic foci could be visualized in the lungs. Together with the increased swelling at the level of the crus and the lethargic condition of the horse, a tumor with secondary pulmonary metastases was suspected. An abdominal scan revealed marked liver hyperplasia in association with subcapsular hemorrhage. Because of the rapid clinical deterioration, the horse was euthanized a few hours after arrival at the clinic.

Necropsy revealed multinodular small tumoral masses in the lungs (Fig. 1). Several spots of suspicious tissue were observed in the surroundings of the subcapsular hematoma in the liver and in association with the site of hemorrhage in the *m. flexor digitalis lateralis*. Histological slide specimens were taken from the lungs, diaphragm, liver and right *m. flexor digitalis lateralis*. These were fixed in a solution of 10 % neutral buffered formalin and paraffin slides were produced by conventional methods and stained with hematoxylin and eosin. The histopathological findings were consistent with the diagnosis of disseminated hemangiosarcoma. For the immunocytochemical staining procedure, a prediluted monoclonal anti-human CD31 (Dako, Glostrup, Denmark) was used to label endothelial cells. CD31 is a transmembrane protein that plays a role in adhesive interactions between cells and is expressed on all continuous endothelia. However, immunocytochemistry could not confirm the vascular origin of the tumor.



**Fig. 1. Gross pathology of the lungs. Multinodular, relatively firm tumoral lesions (mainly dark reddish-brown in color) were observed under the pleura.**

## DISCUSSION

At first presentation to the hospital, all examinations were focused on the complaint of lameness. A traumatic origin for lameness was suspected and therefore neither a hematologic examination nor a specific internal examination were performed initially. White blood cell analysis of the aspirated serohemorrhagic fluid from the swelling was not indicative of local infection. However, the pronounced post-puncture hemorrhage was consistent with the findings of Southwood *et al.* (2000), who mentioned that biopsy of hemangiosarcoma can be complicated by extensive hemorrhaging. Histologic examination of the aspirate was initially not performed, though it could have led to the diagnosis of hemangiosarcoma. Cytologic examination of fine needle aspirates of hemangiosarcomas has been reported to be of diagnostic value when samples are obtained directly from the tumoral mass. Cytologic examination of exudates and body fluids is more likely to support hemorrhage rather than neoplasia (Southwood *et al.*, 2000). This may indicate that hemangiosarcomas, despite their invasive nature, do not "exfoliate" easily (Geelen and Sloet van Oldruitenborgh-Oosterbaan, 1996). Nevertheless, in cases of intramuscular hemorrhage where a fracture or persistent hemorrhage from a vessel can be excluded, lack of resolution of local or systemic signs should prompt histologic examination of affected muscle biopsies as hematoma formation and lameness are the second most common presenting complaint for disseminated equine hemangiosarcoma (Southwood *et al.*, 2000).

As the horse was presented a second time to the clinic, nineteen days following onset of symptoms of lameness, antemortem diagnosis of disseminated equine hemangiosarcoma was made and the horse was euthanized. The diagnosis was based on history, physical examination findings and ultrasonographic findings of thorax and abdomen. The diagnosis was made only in the very end stage of disease when the horse was already lethargic. This corresponds with the findings of Southwood *et al.* (2000), who notes that antemortem diagnosis is difficult, having been made in only 4 out of 35 horses presented with disseminated hemangiosarcoma. Clinical deterioration was always rapid and the median time from onset of clinical signs to euthanasia was 17 days.

In horses, only cutaneous hemangiomas and hemangiosarcomas are amenable to surgical excision (Vos *et al.*, 1986; Jean *et al.*, 1994). In the latter, pulmonary metastasis should always be suspected (Jean

*et al.*, 1994). Van Pelt *et al.* (1972) also described the successful surgical excision of hemangiosarcomatous masses out of the tarsal sheath of a horse. Nevertheless, the therapy in horses mostly consists of supportive care including (non)steroidal anti-inflammatory drugs and antibiotics (Southwood *et al.*, 2000). In the present case, there was only a very initial positive response to anti-inflammatory therapy. In dogs, hemostatic abnormalities seen with hemangiosarcomas may be responsive to glucocorticoid administration (Hargis and Feldman, 1991), but this has not been reported in horses.

It is generally accepted that in animals with multiple tumors, it may be difficult to determine the primary tumor site (Brown, 1985; Johnson *et al.*, 1988; Southwood *et al.*, 2000). In the study of Southwood *et al.* (2000), a primary tumor site was found in 22 out of 35 horses with hemangiosarcoma, being identified as the largest tumor mass with local extension to other tissues. In the present case, the largest tumoral mass was found in the *m. flexor digitalis lateralis*. It is the opinion of the authors that the primary tumor site in this case was the musculature of the right crus, as the evolution of the disease seems to indicate.

At necropsy no indications were found for the atactic behavior of the horse. Vertebral metastases could have been present, but as the vertebrae and the paravertebral musculature are not routinely examined during an equine necropsy, lesions in these areas may have been overlooked (Kennedy and Brown, 1993; Newton-Clarke *et al.*, 1994). Although reported by several authors (Waugh *et al.*, 1977; Sutton and McLennan, 1982; Collins *et al.*, 1994; Southwood *et al.*, 2000), metastases were not found in the brain of the present case. The uncoordinated behavior could also have been traumatically induced by the fall at home, or it may have resulted directly from extreme and generalized weakness without any co-existing neurological lesion.

Immunocytochemical staining of endothelium by use of the CD31 marker has been reported to be successful in dogs (Ferrer *et al.*, 1995). However, to the knowledge of the authors, the use of CD31 as a marker for equine endothelium has not yet been reported. Before labeling the hemangiosarcoma specimens with anti-CD31 antibody, the authors first evaluated the labeling efficacy using normal endothelium of equine skin. All these control sections showed successful immunolabeling, though the immunoreactivity was not as strong as reported for canine samples (Ferrer *et al.*, 1995). The immunocytochemistry for the endothelial marker CD31 was

negative in the pathological slide specimens of the present case. It is the hypothesis of the authors that as a result of the malignancy, the poorly differentiated endothelial cells were able to express CD31 only to a very limited extent. Performing immunocytochemistry of a poorly differentiated hemangiosarcoma may require the use of other markers, including Factor VIII related antigen and *Ulex europaeus* I agglutinin (Katayama *et al.*, 1996). Nevertheless, the interpretation of the pathologist should not rely on a single test but must be made within the context of the patient's clinical history and the entirety of diagnostic tests.

## CONCLUSION

When dealing with severe muscular swelling of uncertain origin in a horse that is in poor condition, hemangiosarcoma should be included on the list of differential diagnoses. Despite the limitations of needle aspirates and the likelihood of further hemorrhage during biopsy, persistence in obtaining a diagnostic tissue sample is worthwhile in horses suspected of having disseminated hemangiosarcoma. Indeed, antemortem diagnosis is important, even though the progression of the disease is usually rapid and therapy is generally unrewarding. On the basis of correct information provided by the veterinary surgeon, the horse owner will usually conclude that euthanasia is the right solution, as it avoids unnecessary suffering in the horse and unnecessary expenses for treatment.

## ACKNOWLEDGEMENT

The authors wish to thank Dr. G. Van Loon for the ultrasonographic examination and Prof. Dr. H. Thooenen for performing the necropsy.

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