CASE REPORT

# Recurrent Ocular Hemangiosarcoma in a Horse

***Janine Baker***, *BTech, LVT*
*Rhinebeck Equine, Rhinebeck, New York*

## Abstract

This case study details a rare diagnosis of recurrent ocular hemangiosarcoma in a horse. It highlights the importance of the veterinary team working in tandem and illustrates the role of the veterinary nurse in assisting with a timely diagnosis and prompt treatment.

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### Take-Home Points

- Hemangiosarcoma (HSA) is a well-documented disease in dogs but is less common in other animals, including cats, cows, and horses.
- HSA is a malignant neoplasia that originates in the endothelial cells of blood vessels and, therefore, can travel throughout the body via the vascular system.
- HSA can affect any body system and appear as cutaneous, locally invasive, or disseminated.
- The life expectancy of horses diagnosed with ocular HSA is 18 months.
- The veterinary nurse plays a vital role in the case of equine HSA, from assisting with diagnostics and providing appropriate sedation and analgesia for standing surgery to ensuring laboratory samples are prepared and submitted properly.

Hemangiosarcoma (HSA) is a well-documented disease in dogs but is less common in other animals, including cats, cows, and horses. HSA is a vascular tumor originating from the endothelial cells that line the inside of blood vessels. Due to the nature of the disease and the fact that it can travel anywhere within the body through the vascular system, it can be present in many different forms, such as cutaneous, locally invasive, or disseminated, and affect virtually any body system. Clinical signs of HSA vary greatly based on location and body system affected; therefore, the disease is often mistaken for other diseases in the initial stages of the workup, delaying diagnosis and treatment and affecting prognosis.[1]

Equine ocular HSA is a rarely documented, yet highly aggressive, vascular tumor that can affect the limbal conjunctiva and nictitating membranes.[2] Tumors can be removed through a variety of methods, including keratectomy, third eyelid removal, enucleation, or exenteration, and while they are locally invasive, lymphatic metastasis can also occur.[3] Even with aggressive treatment, prognosis is guarded.[4] Life expectancy for patients with ocular HSA is 18 months.[2,3]

**FIGURE 1.** Original mass on right nictitating membrane.

This case demonstrates a patient with a recurrent ocular HSA tumor whose diagnosis, workup, and treatment plan required efficient collaboration between the visiting ophthalmologist, internist, and internal medicine veterinary nurse. Special attributes of this case include the use of digital cytology to quickly rule out several differential diagnoses and the production of an active immunotherapy treatment in the form of an autologous cancer vaccine.

## SIGNALMENT AND HISTORY

An 18-year-old black castrated male Shire horse was presented to the equine hospital for an ophthalmic examination with the visiting ophthalmologist. The presenting complaint was an acute growth in the right ventral conjunctival fornix. The owners had noticed the growth 2 weeks before the ophthalmology visit, and the patient was not currently receiving any medications.

The patient had presented to the hospital 14 months earlier for a complaint of a growth in the same location (**FIGURE 1**). At that time, it was suspected the growth was squamous cell carcinoma, and the right nictitating membrane was removed.

Histopathology diagnosed HSA with clean margins, and the pathologists did not expect the disease to return. Based on the findings, no follow-up medications or examinations were recommended or performed.

## PRESENTATION AND PHYSICAL EXAMINATION

On presentation, the patient's mucous membranes were pink and moist with a capillary refill time of approximately 3 seconds, his heart rate was 44 beats per minute (bpm; reference range, 28 to 44 bpm) with a regular rhythm, his respiratory rate was 16 breaths/min (reference range, 6 to 16 breaths/min) with clear lung sounds, borborygmi were present in all abdominal quadrants, digital pulses were normal in all 4 limbs, and he had a temperature of 37.7 °C (99.8 °F) (reference range, 37.2 °C to 38.6 °C [99 °F to 101.5 °F]).

Examination of the structures of the left eye revealed no abnormalities. Examination of the right eye revealed mild lower blepharedema, but no discharge or discomfort was appreciated. When the globe was gently retropulsed, the subconjunctival mass located in the ventral conjunctival fornix could be evaluated. The mass measured approximately 3 cm in diameter and was red, soft, and bulbous with no associated conjunctival ulceration noted (**FIGURE 2**). The remainder of the right eye exam did not reveal any abnormalities, aside from mild nuclear sclerosis, which is a normal age-related change.[4,5]

## DIAGNOSTIC WORKUP

After reviewing the patient's history and previous histopathology report, there was concern that the HSA had returned. Differential diagnoses for the mass included other neoplasia, such as squamous cell carcinoma; nonspecific inflammation; and infection.

**FIGURE 2.** Acute growth in the right ventral conjunctival fornix (where the previous mass had been removed).

Options for initial diagnostic procedures included cytologic evaluation of a sample collected via fine-needle aspiration or histopathologic evaluation of a sample collected via incisional or excisional biopsy. Additional diagnostics vary based on the results of cytology or histopathology. A diagnosis of neoplasia would incite a metastasis check by the internist (thoracic radiography and abdominal ultrasonography) and enucleation or exenteration. A diagnosis of nonspecific inflammation would be treated by excision of the mass and steroid therapy, while evidence of an infection would be followed by an aerobic culture and susceptibility and appropriate antimicrobial therapy.

Due to the timing of the ophthalmologist's visit and the desire to have timely results, cytology was elected. A fine-needle aspirate of the mass was obtained without chemical restraint. Cytology slides were prepared by the internal medicine veterinary nurse using a compression smear technique and stained routinely using a

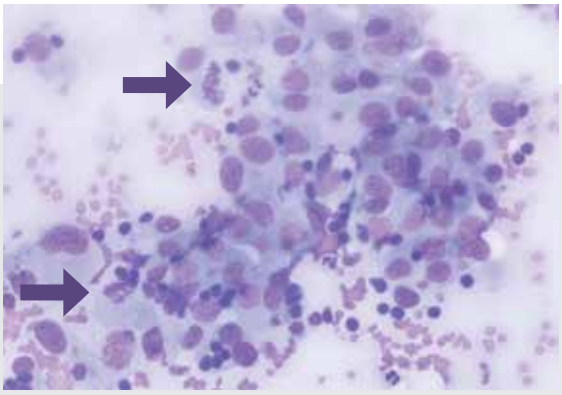

**FIGURE 3.** Mitotic figures **(arrows)**. Diff-Quik stain, 80× magnification.

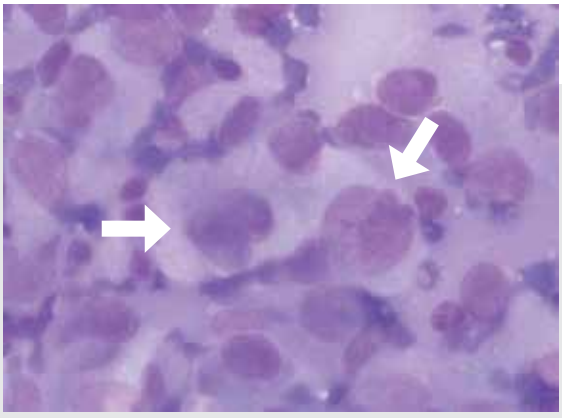

**FIGURE 4.** Binucleate cell **(left arrow)**; marked anisokaryosis **(right arrow)**. Diff-Quik stain, 100× magnification.

commercial Romanowsky stain. The slides were submitted to a board-certified clinical pathologist via digital cytology, with results returned in 90 minutes. While not conclusive, the cells were suggestive of a sarcoma-type tumor (**FIGURES 3 AND 4**). No infectious agents were identified.

The following morning, the internal medicine veterinary nurse obtained digital thoracic radiographs (**FIGURE 5**), and the internist performed full abdominal ultrasonography, neither of which showed evidence of metastasis. A CBC, full serum biochemical profile, and fibrinogen test were performed in-house. Abnormal results included mild hyperfibrinogenemia, lymphopenia, hypernatremia, hyperchloremia, and hyperalbuminemia (**TABLE 1**). These changes were attributed to mild dehydration and stress of hospitalization rather than any disease process. Normal results of note were the hematocrit, red blood cell count, and platelet count. These normal results suggested that the disease process had not become widely disseminated.[3]

Based on the results of the cytology, which indicated a high probability of a recurrence of HSA and no evidence of metastasis, a modified exenteration was performed. Besides excision of the tumor, no other practical treatments for this type of disease exist for the patient. A novel treatment using an autologous cancer vaccine was discussed and agreed to by the client. The vaccine is produced using the patient's own tumor cells. Antigens are extracted from the cells and produced into an injectable vaccine. The vaccine helps the body to recognize the antigens and mount an immune response against the tumor. The risk of the vaccine to the patient is relatively low when compared to the risk of the disease. Potential adverse effects of administration of the immunotherapy included injection-site pain and swelling, inappetence, and lethargy.[6]

The patient was sedated and prepped, and a standing modified exenteration was performed. The globe was sent to Torigen Pharmaceuticals, where a sample of the mass was removed for production of the autologous cancer vaccine, with the remainder of the sample forwarded to the Comparative Ocular Pathology

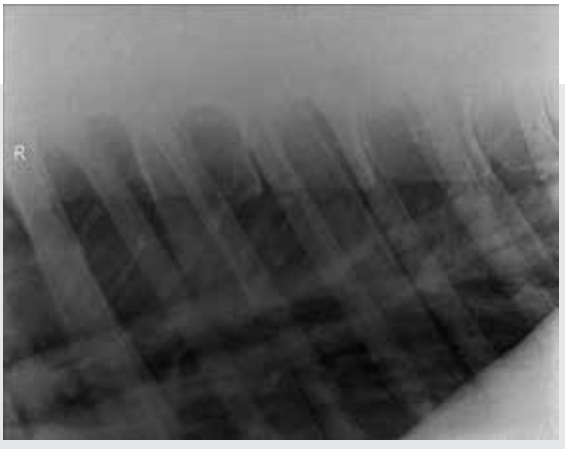

**FIGURE 5.** Digital thoracic radiography revealed no evidence of metastasis.

## GLOSSARY

**Anisokaryosis** Variation in nuclear size of the cell. Increased anisokaryosis is a marker of neoplasia.

**Autologous** Originating or derived from sources within the same individual

**Blepharedema** Eyelid edema

**Binucleate** A cell that contains 2 nuclei; can be a sign of abnormal cell division.

**Borborygmi** Rumbling noises caused by the propulsion of gas and ingesta through the intestines

**Digital pulse** A pulse felt in the lower legs

**Disseminated** Having spread throughout an organ or the body

**Endothelium** Composed of simple squamous epithelium. It lines the heart, blood vessels, and serous cavities of the body.

**Exenteration** When referring to the eye, a procedure to remove the globe and surrounding tissues. More extensive than an enucleation.

**Metastasis** Process by which a malignant cancer spreads from the primary or original site to a distant location in the body

**Mitotic** Refers to a cell actively undergoing mitosis (cell division). An increased mitotic rate is a marker of neoplasia.

**Neoplasia** Abnormal growth of tissue that may be benign or malignant

**Nictitating membrane** A thin, translucent third eyelid that is present in some animals and moves across the eye from the medial canthus laterally to protect and moisten the eye

**TABLE 1 Hematology and Chemistry Test Results***

| TEST | RESULT | REFERENCE RANGE |
|---|---|---|
| Fibrinogen | 470 mg/dL | 150–400 mg/dL |
| RBC | 7.98 M/µL | 6.4–10.4 M/µL |
| WBC | 6.43 K/µL | 4.9–11.1 K/µL |
| Hematocrit | 33.1% | 30%–47% |
| Hemoglobin | 12 g/dL | 10.7–16.5 g/dL |
| MCV | 41.5 fL | 41.1–52.4 fL |
| MCH | 16.2 pg | 14.1–18.6 pg |
| MCHC | 39 g/dL | 32.8–38.6 g/dL |
| RDW | 30.4% | 24.6–33.3% |
| Neutrophils | 5.01 K/µL | 2.5–6.9 K/µL |
| Lymphocytes | 1.15 K/µL | 1.5–5.1 K/µL |
| Monocytes | 0.23 K/µL | 0.2–0.6 K/µL |
| Eosinophils | 0.01 K/µL | 0–0.8 K/µL |
| Basophils | 0.03 K/µL | 0–0.1 K/µL |
| Platelets | 112 K/µL | 100–250 K/µL |
| Glucose | 142 mg/dL | 64–150 mg/dL |
| Creatinine | 1.5 mg/dL | 0.8–2.2 mg/dL |
| BUN | 12 mg/dL | 10–25 mg/dL |
| BUN:Creatinine ratio | 8 | |
| Calcium | 11.9 mg/dL | 10.4–12.9 mg/dL |
| Sodium | 152 mmol/L | 133–150 mmol/L |
| Potassium | 4.3 mmol/L | 3.0–5.3 mmol/L |
| Sodium:Potassium ratio | 35 | |
| Chloride | 110 mmol/L | 97–109 mmol/L |
| Total protein | 7.7 g/dL | 5.6–7.9 g/dL |
| Albumin | 3.4 g/dL | 1.9–3.2 g/dL |
| Globulin | 4.3 g/dL | 2.4–4.7 g/dL |
| Albumin:Globulin ratio | 0.8 | |
| AST | 317 U/L | 10–600 U/L |
| ALP | 153 U/L | 10–326 U/L |

*ALP = alkaline phosphatase; AST = alanine aminotransferase; BUN = blood urea nitrogen; MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; MCV = mean corpuscular volume; RBC = red blood cell; RDW = red cell distribution width; WBC = white blood cell.*
**Results from IDEXX testing. Abnormal results are shown in red.*

Laboratory of Wisconsin (COPLOW). Histopathology confirmed conjunctival HSA with episcleral and orbital extension. Clean margins were confirmed.

The patient was discharged the following day with oral antimicrobials (sulfamethoxazole and trimethoprim [30 mg/kg q12h]) and anti-inflammatories (flunixin meglumine [1.1 mg/kg q12h]). Sutures were removed and immunotherapy treatment was initiated 2 weeks after the procedure, with 1 subcutaneous injection administered weekly for a total of 6 weeks. The patient tolerated the injections without any adverse effects, healed normally from the exenteration procedure, and is reported to be doing well. No follow-up care was recommended.

## NURSING CARE

The internal medicine veterinary nurse's role in this case was instrumental to a timely diagnosis and execution of the treatment plan. The veterinary nurse assisted the ophthalmologist with the initial exam, after which the ophthalmologist and internist consulted on the case. A timely workup was imperative, as the ophthalmologist was only at the referral hospital 2 days a month, and it was in the patient's best interest to quickly determine the origin of the growth and proceed with the proper treatment.

Once the fine-needle aspirate was obtained, the cytology slides were prepared and stained appropriately in a way that allowed the pathologist to evaluate them digitally, determine they were of diagnostic quality, and confidently make recommendations. The veterinary nurse obtained diagnostic-quality digital thoracic radiographs, which allowed the internist to evaluate for metastasis. While the patient was being prepared for standing exenteration, the veterinary nurse was responsible for executing the intravenous sedation protocol using detomidine and acepromazine, implementing the intravenous pain management protocol using flunixin meglumine, administering palpebral and supraorbital local nerve blocks with lidocaine, administering topical anesthesia with proparacaine, and aseptically preparing the surgical field.

Once the globe was removed, the veterinary nurse ensured it was not fixed in formalin, as is the usual protocol for histopathology. To ensure there were viable cells for vaccine production, the globe was placed in a clean container with no additives and shipped to the lab overnight on ice. The veterinary nurse coordinated shipping the sample to Torigen Pharmaceuticals, while ensuring it would be forwarded to COPLOW for final histopathology once a sample was removed for production of the vaccine. The veterinary nurse also prepared oral antimicrobials and anti-inflammatories to be sent home with the patient. Finally, the veterinary nurse ensured all charges were captured appropriately and in real time to ensure prompt payment to the hospital.

## DISCUSSION

This case demonstrates the value of 2 specialties working in tandem. While this patient presented to the visiting ophthalmologist, a consultation with the internist occurred immediately after the initial examination. The use of digital cytology technology was instrumental in quickly ruling out nonspecific inflammation or infection, allowed the internal medicine team to plan for digital radiography and ultrasonography, then quickly move forward with the surgical procedure and processing of the sample for adjunct immunotherapy. Digital cytology is achieved by using a special microscope scanner to scan slides that are prepared in-house. The high-resolution images are converted into a digital format and sent via the cloud to a board-certified pathologist, who can review the microscopic images and return a report within hours. The use of this technology decreases the turnaround time of a traditional cytology that would be sent to a referral laboratory.

Equine ocular HSA is not a common disease, and the recurring nature of this disease in this patient is subsequently rarer. It was noted in the patient's first histopathology report that HSA of the ocular surface

Ultraviolet radiation is thought to play a role in the development of HSA,[1] and ultraviolet-blocking fly masks are recommended as the only preventive measure against the development of this neoplasia.

rarely recurs when surgical margins are clean and seldom metastasizes. Ultraviolet radiation is thought to play a role in the development of HSA,[1] and ultraviolet-blocking fly masks are recommended as the only preventive measure against the development of this neoplasia. Interestingly, the sample from this patient did not demonstrate solar elastosis, likely due to the location in the ventral fornix and the fact that it receives little direct sunlight.

While the life expectancy for patients with ocular HSA is 18 months, this patient has developed this disease twice and has well exceeded those expectations. He remains in good health 24 months after his second diagnosis. TVN

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**Janine Baker**
Janine earned a bachelor of technology degree in equine science from SUNY Morrisville and an associate of applied science degree in veterinary technology from Penn Foster College. Janine has worked at Rhinebeck Equine since 2015 as the internal medicine technician. She has developed a passion for the specialty and contemplates pursuing a VTS in large animal internal medicine. Janine lives in New York's Hudson Valley region, where she enjoys hiking with her German shorthaired pointer, Briggs.