

# Equine Sarcoid

## A Case Report

Taylor A. May  
Mississippi State University  
College of Veterinary Medicine  
Class of 2018

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Advisor: Robin Fontenot, DVM, MS, DACVS-LA  
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## **Introduction**

Equine sarcoid is the most commonly seen neoplasm in the horse, representing up to 67% of all equine skin tumors.<sup>7,14</sup> It is a benign, locally invasive, fibroblastic lesion of the skin which affects horses, ponies, donkeys, mules, and zebras.<sup>14</sup> It most typically occurs on the face specifically the periocular regions, ear pinnae, and lips, as well as the neck, extremities, and ventrum.<sup>14</sup> There are six classifications of sarcoid based on gross appearance and clinical behavior. Occult tumors, the most benign form, are flat, hairless, circular lesions while verrucous appear wart-like. Nodular masses arise beneath the skin and are noted to be firm. Fibroblastic tumors may be ulcerated and lobulated. Mixed forms are a combination of verrucous, nodular, and fibroblastic tumors. The malevolent form is the most severe as it exhibits extensive local invasion and may infiltrate local lymphatics.<sup>7,14</sup> Studies suggest that Quarter Horses, Appaloosas, and Arabians are at increased risk of developing sarcoid tumors versus Standardbreds which are at a decreased risk.<sup>14</sup> There is no sex predilection, and it more commonly occurs in three to six year olds.<sup>14</sup> It is associated with the presence of bovine papilloma virus types 1 and 2. Definitive diagnosis is made via histopathology. A plethora of treatment options are available with variable efficacy to include benign neglect, immunotherapy, surgical excision, cryotherapy, hyperthermia, brachytherapy, and intratumoral chemotherapy.<sup>14</sup> Sarcoid tumors are highly reactive to trauma and manipulation, making both definitive diagnosis and treatment a challenge for owners and veterinarians.

## **History**

Buttercup, an eight-year-old Palomino Quarter Horse mare, presented to MSU-CVM Equine Department on February 14, 2017, for a large, multi-lobulated mass on the left ear. The owner acquired the mare three years prior as a pet, and she has since been housed on pasture

with two other horses and three donkeys. Vaccination status was unknown, and she had not been dewormed in years. The owner mentioned an approximate 200-pound weight loss in the past year. At the time of purchase, Buttercup had a small, flat plaque on the left ear which was removed to the level of the skin by the referring veterinarian. One year later, the mass had returned much larger and pedunculated. The rDVM banded it and had the owner apply Xxterra ointment once it had sloughed.

### **Presentation**

Upon presentation, Buttercup was bright, alert, and responsive, although nervous. She was underweight at 960 pounds with a body condition score of 3/9. Buttercup was tachycardic at 56 beats per minute and tachypneic at 28 breaths per minute. Rectal temperature was 99.0 degrees Fahrenheit. Her coat was roughened, and she had vertical wall cracks on the right front and right hind hooves. Thoracic auscultation revealed no abnormal cardiac or lung sounds. Gastrointestinal motility was normal in all four quadrants. The left ear had a large, ulcerated, multi-lobulated mass with individual lobules measuring up to eight centimeters. The normal architecture of the ear was unappreciable, but the mass appeared to have replaced most of the margin of the pinna. The base of the ear was still visible, but small soft tissue swellings were noted subcutaneously. Upon lifting the mass away from the face, other masses were noted to include: multiple smaller nodules attached to the ear base and inner aspect of the pinna, one small mass cranial to the ear base and one small mass caudal to the ear base, as well as tracking onto the face rostrally towards the eye. The mass made contact with the left eye, and a basic ophthalmic examination revealed corneal scarring. Debris and maggots were identified within the interlobular spaces of the mass, and a significant odor was noted.

### **Differential Diagnoses**

Sarcoid was our primary differential given Buttercup's extensive history of lesions in this location. We suspect this tumor began as the occult form and, after surgical excision, it recurred in the fibroblastic form on a stalk. Following removal of the pedunculated mass, it again recurred but as a mixed sarcoid progressing towards malevolence. Of course, without further diagnostics, we could not definitively rule out squamous cell carcinoma, fibrosarcoma, or melanoma. Other differentials included pythiosis, habronemiasis, exuberant granulation tissue, and granuloma<sup>14</sup>

### **Pathophysiology**

Bovine papillomavirus (BPV) types 1 and, less commonly, 2 are causally associated with equine sarcoid and represent the only cross-species papilloma virus.<sup>7</sup> Several studies from 1993-2007 found BPV DNA in up to 100% of definitively diagnosed equine sarcoid tumors.<sup>5</sup> BPV types 1 and 2 are coined fibropapillomaviruses which infect the epithelium and dermis, resulting in fibropapillomas of the skin.<sup>7,14</sup> BPV is a double stranded DNA virus capable of latent infection.<sup>7</sup> The virus contains two capsid proteins which have been identified in pathogenicity, and it encodes three known oncoproteins: E5, E6, and E7.<sup>7,17</sup> Proteins E6 and E7 are known to inactivate tumor suppressor genes such as p53. The role of E5 is still being studied, but it is proposed that E5 is involved in cell transformation, tumorigenesis, and immune modulation, specifically the downregulation of major histocompatibility complex I.<sup>17</sup>

Horses with open skin wounds are believed to be more predisposed to developing sarcoid. It is thought that inflammatory cytokines in traumatized tissues stimulate viral gene expression and the subsequent development of fibropapillomas.<sup>7</sup> Face flies, *Musca autumnalis*, are the suspected vector for both autologous and heterologous transmission. A 2010 study by Haralambus suggests that BPV load within a sarcoid tumor correlates to disease severity. Those

with a higher virus load tend to cause more severe disease independent of sarcoid tumor classification.

### **Diagnostic Approach/Considerations**

A presumptive diagnosis of sarcoid may be made based on clinical appearance and history, but a definitive diagnosis can only be made via histopathologic evaluation of the dermoepidermal junction. Sarcoid tumors are characterized by epidermal hyperplasia with long, prominent rete ridges and perpendicular neoplastic fibroblasts.<sup>11</sup> It must be noted that surgical excision or trauma of any kind may exacerbate the tumor and cause proliferation.<sup>14</sup> Due to the large size and location of this tumor, both of which were negatively impacting Buttercup's quality of life, we decided to proceed with surgical biopsy for histopathology with intentions to surgically debulk the tumor simultaneously.

### **Treatment & Management**

Due to the variability of sarcoid tumors, each case should be addressed on an individual basis by a veterinarian to determine an appropriate course of treatment. There are several treatment methods available, but no single modality is considered universally effective.<sup>14,16</sup>

#### *Benign Neglect*

Occult, verrucous, and even nodular tumors located in inconsequential areas of the body may be best treated with benign neglect due to the tendency of sarcoid tumors to recur and proliferate with trauma of any kind.<sup>14</sup> They should be monitored for growth in order to treat while small.

#### *Immunotherapy: Topicals*

Topical immunomodulators have some reported anecdotal efficacy, but no controlled studies have been performed. Care should be taken when applied on periocular tumors as these

topicals are extremely immunostimulant and may result in a severe keratitis.<sup>7</sup> Xxterra is an antiproliferative and apoptotic cream containing bloodroot extract and zinc chloride which stimulates the local immune response against neoplastic cells. It is generally recommended for small fibroblastic sarcoids which can be expected to begin sloughing in seven to ten days after the initial treatment.<sup>7</sup> AW4-LUDES cream contains a combination of cytotoxic chemicals, 5-fluorouracil, and plant oils to stimulate a potent local immune response toward tumor cells without damaging normal cells. Due to the highly caustic nature of the drug, AW4-LUDES cream should only be applied by a licensed veterinarian. Aldara cream contains 5% imiquimod which has potent antiviral and antitumor properties.<sup>9</sup> Its use in previously untreated horses resulted in 60% complete regression of tumors. Acyclovir, an antiherpesvirus agent, has had some anecdotal success in the regression of superficial sarcoid tumors.<sup>10</sup> Of course, any topical will require several applications over a period of months to achieve any successful tumor regression, and recurrence may reach 40% with any of the topicals.<sup>3,14</sup>

#### *Immunotherapy: Injectables*

Injections of mycobacterium cell wall or whole cell Bacille Calmette-Guérin (BCG) stimulate cell-mediated immunity and increase the body's recognition of tumor specific antigen. This typically requires multiple treatments at two to four week intervals and is most successful in small fibroblastic tumors. Swelling, ulceration, and necrosis of the tumor can be expected two to fourteen days post-injection.<sup>7</sup> Generally speaking, fibroblastic and nodular sarcoids respond well to immunotherapy, but the more superficial types tend to respond poorly to BCG injections.<sup>6</sup> Some studies report up to 40% recurrence. Severe anaphylaxis is a potential complication and may be fatal.<sup>2,6</sup>

#### *Surgical Excision*

Surgical excision may be achieved via conventional methods or via carbon dioxide laser. It is important to note that true margins are not achievable since BPV is also found in normal skin of affected horses.<sup>14</sup> So, recurrence rates as high as 30-50% within six months are often seen after conventional surgical excision.<sup>14</sup>

### *Cryotherapy*

Cryosurgery is the use of pressurized liquid nitrogen in two to three freeze/thaw cycles to achieve tissue temperatures of -20 to -30 degrees Celsius which destroys unwanted tissue. This technique does not require sterility and can be performed without general anesthesia as an outpatient procedure. Repeated treatments improve initial efficacy up to 85% and reduce the risk of recurrence.<sup>1</sup> Recurrence is more common in periorbital tumors.<sup>6</sup> Significant skin contracture and depigmentation may occur.<sup>14</sup>

### *Radiofrequency Hyperthermia*

There are only a few reports of radiofrequency hyperthermia as an effective treatment of sarcoid, but their results are promising. The technique involves directly heating the unwanted tissue to 50 degrees Celsius for 30 minutes. Heat applied in such a manner can penetrate to a depth of ten centimeters, with greatest temperatures at three to five centimeters.<sup>16</sup> Some tumors may require up to eight treatments. Theory holds that neoplastic tissues are more disorganized and less able to dissipate heat than normal tissue. It is expected that neoplastic cells will undergo apoptosis as a direct result of overheating without damaging normal cells.<sup>14</sup> It has also been proposed that hyperthermic treatment causes the production and release of heat shock proteins which enhance the local immune system's response to abnormal cell development.<sup>16</sup> Furthermore, heat causes vasodilation and increases local blood flow which may improve the

uptake of adjunctive chemotherapeutic agents.<sup>16</sup> Recurrence rates are unknown at this time, but long-term prognosis is expected to be good based on short-term results.

*Brachytherapy:*

Brachytherapy is the utilization of interstitial gamma radiation such as iridium-192. Due to the licensure regulations and isolation challenges, this treatment modality is typically restricted to referral practices and costs trend high. Brachytherapy has generally been recommended for periocular sarcoids and five-year recurrence rates are 26%.<sup>7</sup>

*Chemotherapy: Injectable and Implantable*

Chemotherapeutics such as cisplatin or carboplatin, platinum-containing compounds, bind to DNA and inhibit further synthesis. They do not cause tissue necrosis, effects are dose and time-dependent, and cytotoxicity is not dependent on the growth rate of the tumor.<sup>15</sup> Current treatment techniques include intratumoral injection of carboplatin in an oily suspension or implantation of carboplatin beads. The suspension should be injected three to five times at two week intervals.<sup>15</sup> The beads may be implanted twice at one month intervals. Both techniques require great care to avoid human exposure. The Centers for Disease Control and Prevention encourage the use of chemotherapy gloves, non-permeable gowns, respiratory protection, and shoe covers. Chemotherapeutic agents must be stored appropriately, and a closed system drug transfer device should be used for administration. All hazardous waste must be discarded appropriately. It is recommended to use these methods in combination with surgical excision.<sup>14</sup> The drug may be administered post-operatively after wound healing or peri-operatively.<sup>15</sup> For small, previously untreated sarcoid tumors, control rates at four years post-treatment reach up to 96% when treated with intratumoral cisplatin.<sup>15</sup>

*Electrochemotherapy:*



Electrochemotherapy (ECT) is a method of treatment which uses electrical pulses to stimulate cell permeability and increase chemotherapeutic, cisplatin or carboplatin, delivery. Electrical impulses are delivered via electrode and a conductive paste. A retrospective analysis by Tamlazi, et al. in 2011, found a four year nonrecurrence rate of 98% in horses treated with cisplatin electrochemotherapy, either alone or in conjunction with surgical excision. ECT may require general anesthesia, and the number of treatments varies based on tumor size, location, and depth of local infiltration.

### **Expected Outcome/Prognosis**

Tumor recurrence rates vary greatly and are multifactorial. The type of sarcoid tumor, degree of local infiltration, treatment modality, and age of the horse should all be considered in determining prognosis. Of the studies available, conventional surgical excision alone and topical immunomodulators alone carry the greatest risk of recurrence, up to 60%.<sup>3,14</sup>

Electrochemotherapy with cisplatin combined with surgical excision boasts the greatest nonrecurrence rate, up to 98% in four years post-treatment.<sup>16</sup> Regardless of treatment modality, prognosis is improved for sarcoids treated in the early stages of disease and for horses treated under four years of age.<sup>18</sup>

### **Case Outcome**

At the time of presentation, the owner agreed to conventional surgical excision and cisplatin injections with hyperthermia. However, the tissue proved highly vascularized, and clear margins were unachievable. Therefore, the attempt to debulk the mass was abandoned for re-evaluation. Same day complete blood count and chemistry panel revealed a decreased PCV 20% (26-42%), moderate anemia RBC 4.85 M/ul (6-12), mild leukocytosis WBC 12.1 K/ul (5-11.9) characterized by mild neutrophilia 6655/ul (2500-6000) and eosinophilia 968/ul (0-1000), mild

hyperproteinemia TP 9.0 g/dL (6.1-8.4) characterized by severe hypoalbuminemia 1.5 g/dL (2.8-3.9) and severe hyperglobulinemia 7.5 g/dL (2.5-4), and severe hypocholesterolemia 32 (78-120). A more aggressive approach under general anesthesia would be necessary to completely remove the abnormal tissue, and non-recurrence could not be guaranteed. Therefore, the owner authorized euthanasia. Necropsy report confirmed sarcoid on the left ear pinna and in the groin. Further findings included otitis media within the left ear, stomach bot larvae, evidence of cyathostomes, eosinophilic infiltration of the large colon, and pinworms.

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