Mule Skinnin'101

Equine Sarcoid

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Introduction

Accounting for over half of all equine skin tumors, equine sarcoid is the most common tumor of equids. Sarcoids are benign, fibroblastic, and locally invasive tumors that may appear in all equine species including horses, mules, donkeys, and zebras. Equids of all ages may be affected, however, initial presentation of younger horses between two and nine years of age is most common (Knottenbelt 2019). Presumptive diagnosis of sarcoid is typically based on clinical appearance and characteristics of the lesion. Six types of sarcoid have been described and include occult, verrucous, nodular, fibroblastic, mixed, and malevolent (Taylor, Haldorson 2013).

Lesion appearance can vary greatly by type. Occult sarcoids are typically flat, alopecic, circular lesions with mild scaling. Verrucous sarcoids have a wart-like appearance, are often raised, and may affect a small or large area. Nodular sarcoids commonly form in the subcutaneous space, vary in size, and form firm, well defined lesions. Fibroblastic sarcoids often appear as ulcerated, hemorrhagic, wet, irregular masses. Malevolent sarcoids are the rarest form of sarcoid and form large, aggressive, invasive tumors that infiltrate the subcutaneous tissue. Often lesions of this type appear nodular and fibroblastic in nature. A sarcoid tumor is labeled "mixed" if it contains two or more of the previously mentioned sarcoid types. Sarcoids can develop anywhere on the body, either as a single tumor or as multiple tumors of different types. Sarcoids develop most commonly within the periocular region, ear pinnae, lips, neck, extremities and ventrum (Taylor, Haldorson 2013).

Although considered a benign tumor, sarcoids may become locally aggressive with inappropriate treatment or trauma. Tumor formation is not only a cosmetic issue but may affect the function of the animal, become infected, or become ulcerated and lead to further

complications. Due to the invasion into local tissue and aggressive nature of the tumors, treatment and resolution is often difficult to achieve.

History and Presentation

Ruby is a 16-year-old, female (molly) mule who was presented to MSU-CVM Equine Services on October 9, 2019 for evaluation of sarcoid tumors which she had possessed for approximately ten years. Previously, sarcoid tumors were located across her forehead and were treated with surgical removal and injections of chemotherapy. This year, the sarcoids have spread to her right neck, left shoulder, and right ear.

Upon initial presentation, Ruby was bright, alert, and responsive. She weighed 1055 pounds with a body condition score of 8/9, with 5/9 being ideal. Her heart rate was slightly elevated at 52 beats per minute, which was likely due to the stress of traveling and being in a new environment. Her respiratory rate was 28 breaths per minute, and her temperature was 99.6 F. Her mucous membranes were pink and moist with a capillary refill time of less than 2 seconds. Cardiac and thoracic auscultation were within normal limits and normal gastrointestinal borborygmi could be heard within all four quadrants. She had a sarcoid tumor on her left shoulder that was 10x7 cm in diameter, one on her right neck that was 6x7 cm, and one circling her right pina that was 13 cm beginning at the base of her ear. The tumors were irregularly shaped and there were also several smaller nodules of varying size on her forehead. The remainder of her physical exam was within normal limits and otherwise she was apparently healthy.

Due to the large size and extent of Ruby's sarcoids along with follow up appointments necessary for chemotherapy, it was recommended that she return to MSU CVM for a newly

developed treatment. On February 17, 2020 Ruby presented for an evaluation prior to her procedure. The three areas with tumor (left shoulder, right shoulder, and right pinna) were clipped to fully visualize their extent. Measurements of the masses revealed unchanged size since the previous examination. At this time, surgical excision in combination with photodynamic therapy was deemed the best option to control Ruby's sarcoids.

Diagnostic Approach

Ruby returned to MSU CVM on February 25, 2020 for surgery the following day. Upon presentation, a fecal sample was obtained to ensure Ruby was not infected with salmonella and serial samples were collected throughout her stay. A complete blood count and serum chemistry were then conducted. Ruby's complete blood count revealed no abnormalities. Serum chemistry revealed mildly elevated glucose of 133 (60-122), ALP of 162 (61-153), and CK of 353 (57-283). Ruby's chemistry revealed a mildly decreased BUN of 8 (10-24), Creatinine of 1.04 (1.2-1.9) and OSMO of 263 (270-300). Each of these values were considered of minimal significance and Ruby was deemed an acceptable surgical candidate.

Because Ruby's condition was presumptively diagnosed as sarcoid, biopsy prior to surgical excision was not conducted. It has been shown that biopsy-induced trauma or irritation may cause further spread or worsening of the lesions (Knottenbelt 2003). The location of Ruby's masses, along the right neck, left shoulder, and right pinna were consistent with common predilection sites for sarcoid. Ruby's lesions were raised, firm, irregular, and non-ulcerated with the pinna of the right ear being the most affected. They were well defined and felt firmly attached to the underlying tissue making them most consistent with the nodular form of this

condition. Due to the classical location and appearance, it was decided to surgically debulk the lesions and submit a sample for biopsy at that time.

Pathophysiology

Although there are many factors which predispose an equine to sarcoid development, bovine papillomavirus (BPV) types 1 and 2 are universally recognized as the causative agent. Papillomaviridae is a large family of double stranded DNA viruses which commonly result in papilloma, wart, or condyloma formation in humans and animals alike. Most papillomaviruses are species specific. Bovine papillomavirus and its association with equine sarcoid is the only known cross-species papillomavirus infection. DNA of bovine papillomavirus has been found in almost 100% of examined sarcoid tumors. This evidence along with oncogenes and capsid gene transcripts indicate that bovine papillomavirus has direct involvement in pathogenesis of the disease (Taylor, Haldorson 2013). It is now known that sequence variation occurs within papillomavirus types that may influence cellular location and oncoprotein function. Because of this, pathogenesis and transformation of the virus within the host is variable between species and may explain the differences observed in equine sarcoid compared to papillomatosis noted in cattle (Chambers 2003). Integration of viral DNA into the host's genome results in changes within epithelial cells and fibroblasts, resulting in lesional development (Chambers 2003).

Though bovine papillomavirus is necessary for disease development, there is a variety of factors which predispose an animal to sarcoidosis. Quarter Horse, Arabian, and Appaloosa breeds are at increased risk (Angelos et al. 1988). Relation to affected horses and the presence of the ELA W13 allele also act as predisposing factors (Taylor, Haldorson 2013). Areas of trauma and open wounds are most likely to become affected by sarcoid. The route of transmission is not

fully known, however, direct contact with cattle, indirect contact between cattle and horses (insect vectors), and direct or indirect exposure via caretakers and fomites may result in transmission (Bogaert et al. 2008). Insect vectors such as flies may aid in transmission as BPV–1 DNA has been detected in flies trapped in the proximity of sarcoid-bearing equids (Finlay et al. 2009). Transmission is most likely from equine to equine because equine sarcoids arise from their own variants of BPV DNA.

Prevention, Treatment, and Management

Currently, there is no uniformly accepted treatment for equine sarcoid. Typically, treatment is geared toward physical removal of the tumor, reduction and/or destruction of the tumor, or immunomodulation to facilitate the body's destruction of the tumor. Traditional surgical excision as well as laser excision is commonly utilized for large, easily accessible lesions impeding movement or patient comfort. Chemotherapy, radiotherapy, cryotherapy, hyperthermia, immunotherapy, and vaccination have each been utilized on tumors of varying size and location with variable success. Most recently, photodynamic therapy has been utilized in treatment of equine sarcoid. For the purpose of this report, we will focus briefly on this modality.

Photodynamic therapy is a relatively new treatment modality which utilizes the interaction of a photosensitizer, light, and oxygen to destroy neoplastic cells. The photoactive drug is injected into the neoplastic tissue and is then activated by a diode laser set to a specific wavelength, placed over the affected area in 15 second increments. The photochemical reaction produced by this process results in direct destruction of neoplastic cells and impairs neoplastic vasculature. It is utilized most commonly on superficial tumors and regions of tissue where neoplasia has been surgically removed. It is most effective on nonpigmented integument and in

areas where the neoplastic tissue is no more than 2 cm thick. General anesthesia is necessary for laser treatment and should always include analgesia. Administration of oxygen to the patient is important as oxygen is known to correlate with clinical efficacy. Most of the research conducted with photodynamic therapy in veterinary medicine is with squamous cell carcinoma in feline patients but shows promising results. Treatment proves to be challenging in equine patients due to thickness of the skin and heavy pigment (Buchholz, Walt 2013). At this point, Ruby is one of the few patients to be treated with photodynamic therapy for equine sarcoid therefore long-term effectiveness is unknown at this time.

Treatment efficacy is difficult to assess because most studies conducted on equine sarcoid are based on referral populations and are not controlled. Cases presenting to referral services are likely more severe and unrepresentative of those successfully treated by private practitioners in the field (Chambers 2006).

Case Outcome

On February 26, 2020 Ruby underwent surgical removal of her sarcoid tumors. Preoperatively, an intravenous catheter was placed in the left jugular vein. Prior to surgery a variety of medications were administered. Gentamicin was given at 6.6 mg/kg intravenously, Procaine Penicillin at 22 000 IU/kg intramuscularly, Flunixin Meglumine at 1.1 mg/kg intravenously and a 5-way (including tetanus toxoid) vaccine was administered intramuscularly. She was sedated with xylazine and butorphanol and general anesthesia was induced with ketamine and diazepam. She was maintained on sevoflurane inhalant anesthesia for the duration of the procedure. Ruby was placed in left lateral recumbency and the right ear and right neck was clipped and aseptically prepared with 4% chlorhexidine soap followed by 70% isopropyl alcohol. A sterile preparation of the two proposed surgical fields were then performed once entering

the surgical suite.

The surgical sites were draped in routine fashion using sterile towels and secured with backhaus towel clamps. An incision was made through the skin in an ellipse around the affected tissue in the right ear and neck, attempting to spare as much normal tissue as possible. All abnormal tissue was then resected. The sarcoid located on the ear did not appear to extend past the facial plane directly below the subcutaneous tissue, however the sarcoid on the neck appeared to extend into the muscle directly beneath it. Five milliliters of a photodynamic dye (indocyanine green) were injected around the periphery of the surgical site on the neck. Within the middle portion of the lesion, photodynamic dye was spread in a paintbrush pattern covering the entire surface of the wound. A diode laser was then used to activate the dye, resulting in a cytotoxic response. The same procedure was performed on the surgical site of the right ear, however, due to the larger surface area 7 milliliters of photodynamic dye was used. Due to the hemostatic nature of this procedure the wound was only temporarily bandaged and was left to heal by second intension. Ruby recovered from surgery uneventfully. Just two days later, on February 28, 2020, Ruby was discharged with Uniprim (trimethoprim and sulfadiazine) antibiotic powder to prevent infection, Banamine (flunixin meglumine) for pain control, and Aldera (imiquimod) cream for topical application on the remaining lesions. To improve the rate of healing, it was recommended that Ruby remain on stall rest until her recheck examination.

Ruby returned on March 11, 2020 for her first post-surgical recheck. The previous sarcoid tumor noted on her left shoulder was still present but appeared less raised. Three other small, approximately 1 cm x 1 cm, focal raised areas were noted: two on the left neck and one on the dorsal right neck. The surgical sites on her right ear and right neck appeared to have healthy granulation tissue formation and the skin edges were pink. Nodules previously noted on her

forehead were still present but appeared to be less raised as well. Ruby did not appear to be painful and swelling was minimal around the surgical sites. The surgical sites were the same size as they were when previously discharged, or slightly smaller.

On August 27, 2020 Ruby returned to MSU CVM for a second recheck examination. At this time, the remaining wound bed over the pinna appeared raised and nodular rather than flat. Because this finding was more consistent with sarcoid than with healthy granulation tissue, samples were submitted for histopathologic evaluation. Histopathology confirmed that this tissue was sarcoid and repeat surgical debridement of the wound bed was deemed the most appropriate treatment. Ruby was placed under standing sedation and the right pinna and ear base was clipped and roughly prepared with betadine followed by alcohol. The affected areas were locally anesthetized with mepivacaine and sterile preparation of the two areas was performed. Tumorous areas were incised with 5 mm margins and were dissected by a combination of sharp excision and cautery for hemostasis. Photodynamic dye was injected around the periphery and throughout the surgical bed once again and the laser was applied to activate the dye. Following this procedure, instructions were given to follow up with imiquimod topically at home three days a week. A follow up exam was suggested in four weeks.

Ruby's last recheck examination was on October 5, 2020. At that time, it was noted she had a bed of granulation tissue at the base of her right ear extending dorsally and covering half of her outer pinna. Two nodules remained, one at the dorsal base of the right ear and another at the caudal base of the right ear. The tumors had not resolved but appeared less raised than the previous visit in August. The remaining lesions were healing up nicely and were decreasing in size. Ruby's owner was advised to continue using imiquimod topically in effort to resolve the

tumors more completely. It was recommended Ruby come back in four weeks for recheck, however, no further follow up appointments have been made at this time.

Although not completely resolved, her sarcoidosis remains in check is more controlled. While it appeared to work very well on the right neck lesion, success was only partial on the pinna and ear base. This procedure may not be considered a cure or appropriate treatment for all patients, however, for patients like Ruby it may be a viable treatment option.

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