Squamous cell carcinoma of the vulva and perineum in a Katahdin ewe

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Summary

An 8 year-old, 12 weeks pregnant, white Katahdin ewe was presented for a malodor associated with a vulvar lesion. Physical examination was unremarkable with the exception of an ulcerated, necrotic lesion involving the entire vulva and a small part of the surrounding perineum. Squamous cell carcinoma was suspected. Eight weeks after initial presentation the ewe was again presented for dystocia due to malposition of the first lamb. One deceased and two live lambs were delivered with vaginal assistance. In the four days following the dystocia the dam was lethargic, anorexic, and did not properly care for her lambs. With the visible progression of the lesion and suspected poor prognosis for future reproduction the owner decided to humanely euthanize the ewe. Necropsy confirmed squamous cell carcinoma on histopathology. Bacterial pneumonia was considered to be the cause of the ewe's clinical signs at the time of euthanasia based on lung pathology and culture. No squamous cell carcinoma metastases were found.

Keywords: Squamous cell carcinoma, vulva, perineum, ewe

Background

In sheep, squamous cell carcinoma is an uncommon lesion typically found on the ears and muzzle, but is well documented on the vuvla, perineum, and tail. To date, squamous cell carcinoma has only been described in wooled-breeds. Predisposing factors include tail docking, Mules operation, solar exposure, branding, and papilloma virus infection. Rate of metastasis of squamous cell carcinoma appears to be relatively low. Very limited information about the reproductive prognosis for vulvar squamous cell carcinoma diagnosed during pregnancy is published. To the authors' knowledge, this is the first report of squamous cell carcinoma in a haired sheep and the first report regarding pregnancy maintenance after presentation. Although this ewe did not have the predisposing management factors described in the literature, she was pink-skinned and kept in a poorly-shaded pasture.

Case presentation

An 8 year-old white Katahdin ewe was presented to the Production Management Medicine Service at the Virginia-Maryland College of Veterinary Medicine in February for a malodor associated with a vulvar lesion. The owner had noticed a mass on her vulva prior to presentation but could not recall when the mass first appeared. Six weeks prior to presentation the ewe had been confirmed 40 to 45 days pregnant via abdominal ultrasound and a mass was not noticed at that time. The number of fetuses was not counted. Upon presentation, the physical findings were within normal limits and the ewe was approximately 85 days pregnant. The ewe's FAMACHA score was 2/5 (1= bright pink/ideal; 5 = very pale.) An ulcerated, necrotic lesion was found involving the entire vulva and a small part of the surrounding perineum with thickening of the affected integument (Figure 1.) The lesion had a purulent discharge and an associated malodor. The lesion was cleaned with chlorhexidine solution.

Differential diagnosis

The most likely diagnoses for this vulvar/perineal lesion was squamous cell carcinoma with differential diagnoses including hyperkeratosis, papilloma, other integumentary neoplasia, or infected laceration/trauma.

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Treatment

Biopsy was recommended to confirm a diagnosis. The ewe was intended as a production animal and it was expected that she would be rejected from an abattoir with such a lesion. Therefore, the owner declined the biopsy with the intention of humanely euthanizing the ewe after her lambs were weaned.

At discharge (approximately 85 days pregnant), the owner was instructed to clean the lesion at least weekly with chlorhexidine gluconate and monitor the ewe for change in attitude, change in appetite, and abortion. Additionally, the owner moved the ewe from the poorly shaded pasture into the barn where she could be monitored more closely. Two weeks after presentation (approximately 99 days pregnant), maggots were found throughout the lesion. The recommendation to apply permethrin (Catron ® IV, Bayer, Shawnee Mission, KS) topically and was performed daily by the owner for two weeks and then every three days until parturition. Due to the progression of the lesion over those two weeks and the value of the pregnancy, the owner requested a second pregnancy ultrasound evaluation. The ewe was reconfirmed pregnant via abdominal ultrasound the following week (three weeks after initial presentation; approximately 106 days pregnant).

Outcome

Nearly eight weeks after initial presentation (approximately 141 days gestation), the ewe presented for dystocia. The first lamb was in posterior presentation, dorsal-sacral position, with left hip and right hock flexion. That lamb was dead upon assisted vaginal delivery. The second and third lambs were in a normal presentation, position, and posture and were delivered vaginally with minimal assistance. The second and third lambs were both alive upon delivery. The live lambs were fed 60 mL of the dam's colostrums by orogastric intubation. The dam was not treated at that time but it was noted that she was not attentive to the lambs. The day after parturition the owner reported the ewe was anorexic and lethargic. The owner administered electrolytes (163.4g, Hydra-Lyte, AgriLabs, St. Joseph, MO) and nutritional drench (150g, AAS Drench Mix with Extra Calcium, Advanced Agri Solutions LLC, Lancaster County, PA) via an orogastric tube. Four-days after parturition the ewe remained lethargic and anorexic. She had not been producing enough milk for two lambs so the lambs were bottle fed milk replacer. The vulvar lesion had progressed to involve more of the perineum and the ventral aspect of the anus (Figure 2.) Due to grave prognosis for future reproduction and a poor prognosis for being able to raise the lambs on her own, euthanasia was elected (15mL IV, Fatal-Plus, Vortech Pharmaceuticals LTD, Dearborn, MI) and a necropsy was performed.

At necropsy the vulvar and perineal lesion measured roughly 12 cm X 7 cm and was confirmed to be a squamous cell carcinoma by histopathology (Figure 3.) The endometrium was grossly ulcerated and on histopathologic examination was found to be covered with a layer of neutrophils; no squamous cell carcinoma was seen in the uterus (Figure 4.) Local lymph nodes did not contain histopathologic evidence of metastasis. Lung pathology included cranioventral consolidation with 40% of the left lung and 20% of the right lung being affected (Figure 5.) Aerobic culture of the lung lesions resulted in isolation of *Bibersteinia trehalosi*, *Pasteurella multocida*, and *Trueperella pyogenes*. All three bacteria are considered pathologic in sheep and were considered to be the cause of the ewe's clinical signs at the time of euthanasia. No squamous cell carcinoma metastases were found and pneumonia was confirmed by histopathology.

Although the ewe was euthanized for a poor productive prognosis, it is unknown if treating the pneumonia would have allowed her to raise the lambs on her own. At two months of age both lambs were thriving.

Discussion

Squamous cell carcinoma in sheep is considered an uncommon occurrence, with reported prevalence of 0.5-3%. In certain instances, outbreaks have been reported in which the prevalence increased up to 18%.[1] In outbreak situations, it has been hypothesized that photosensitizing agents or carcinogens have contributed to the increased prevalence; however, no evidence has been found to support those theories.[2,3]

The majority of squamous cell carcinoma cases are in Merino or Merino-cross ewes.[2-4] One author reported squamous cell carcinoma in two Merino wethers.[4] Other breeds in which squamous cell tumors have been reported include Awassi,[5] Berrichon du Cher,[1] and Khorasan-Kordi.[6] All of these breeds are wooled breeds. In this report squamous cell carcinoma was found in a Katahdin ewe, a haired breed. Increased risk of squamous cell carcinoma occurs with increased age, although it has been confirmed in sheep as young as three years of age.[3]

Solar radiation is known to contribute to the development of epithelial neoplasia in many species. It has been linked to the development of basal cell and squamous cell carcinomas in humans, squamous cell carcinoma in goats, and epitheliomata of cats with white pinnae. Pigmented eyelids in cattle result in decreased squamous cell carcinoma incidence. It is very plausible that sunlight contributes to the development of squamous cell carcinoma in sheep, as the most commonly affected areas are those exposed to sunlight.[1,2] Sheep undergoing Mules' operation appear to be at a greater risk of developing vulvar or perineal squamous cell carcinoma.[2,3] The Mules' operation is the surgical removal of wooled skin around the perineum in order to stretch the woolless region to reduce myiasis and fecal matting. Shorter tail docking also results in increased sunlight exposure to the perineal area and therefore may affect the incidence of squamous cell carcinoma in that area.[2,3] In the current case, the ewe developed a perineal squamous cell carcinoma without having either the Mules' operation or her tail docked. Papilloma viruses are well-documented to contribute to squamous cell neoplasias in humans and horses. A possible link has been found between *Ovis aries* papillomavirus 3 and squamous cell carcinoma in sheep.[7] In cattle, branding has been associated with papilloma and squamous cell carcinoma formation at the site of branding. Heat branding may contribute to squamous cell carcinoma at that site in sheep.[5]

Lesions are most common on the ears and muzzle[2,4]; although perineal, vulvar and tail lesions are also well documented.[2-4] Individual case reports have demonstrated lesions on the eyelids[1] and on wooled-areas (thoracic[2] and lumbar.[6]) In one study, metastasis was found in 12% of cases. Metastatic sites included submandibular lymph nodes, parotid lymph nodes, prescapular lymph nodes, the parotid salivary gland,[4] and lungs.[2]

Several treatment options are available for squamous cell carcinomas in humans and sheep are considered an excellent model for human squamous cell carcinoma. Chemotherapy studies in sheep have demonstrated reduction in tumor size and growth.[8] Sheep are a minor food production species and withdrawal times for chemotherapeutic agents have not been established. Therefore, if treated, the sheep would have to be permanently removed from the food supply. The ability to accomplish permanent removal of a food animal from the food chain is controversial.

Learning points:

- In sheep, squamous cell carcinoma is typically found on the ears and muzzle, but is well documented on the vuvla, perineum, and tail.
- Rate of metastasis of squamous cell carcinoma appears to be relatively low.
- Very limited information about the reproductive prognosis for vulvar squamous cell carcinoma diagnosed during pregnancy is published.

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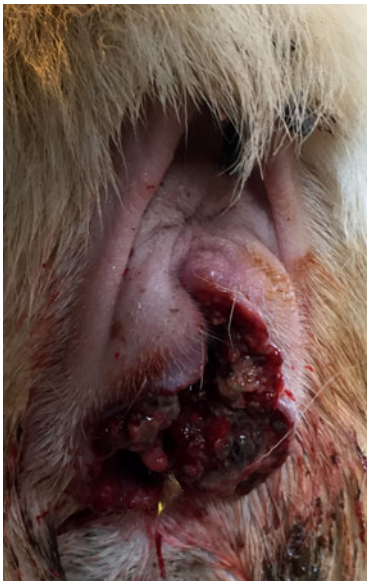

Figure 1. On initial presentation, an ulcerated, necrotic lesion involved the entire vulva and a small part of the perineum.

Figure 2. At the time of euthanasia, the vulvar lesion had progressed to involve more of the perineum and involve the ventral aspect of the anus.

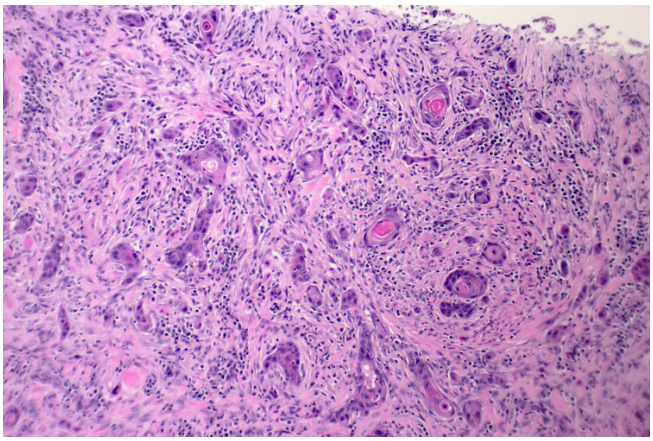

Figure 3. The vulvar lesion was confirmed to be a squamous cell carcinoma by histopathology as seen in this image.

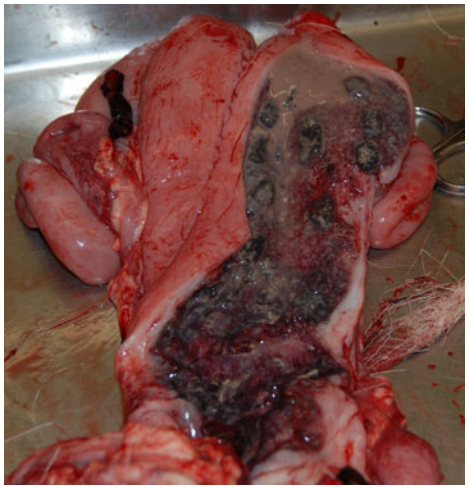

Figure 4. Image of the Katahdin ewe's uterus with an incision made on the dorsal aspect of the right uterine horn and uterine body. On necropsy, the endometrium was found to be grossly ulcerated but no gross lesions associated with squamous cell carcinoma were found. Histopathologic examination found the endometrium to be covered with a layer of neutrophils.

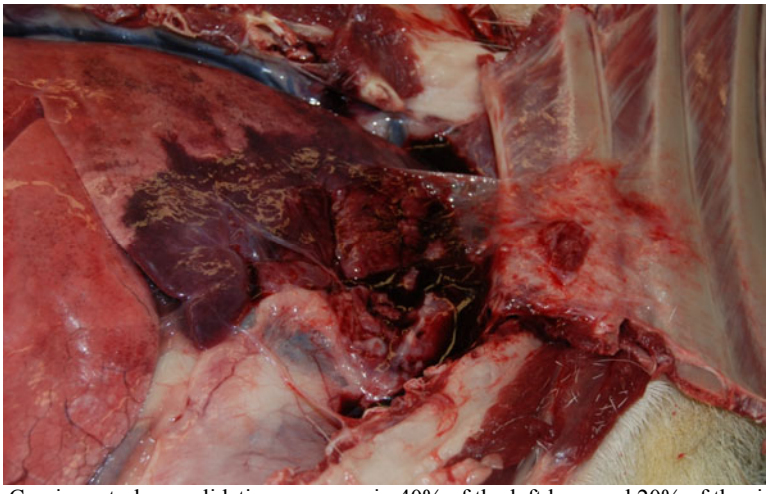

Figure 5. Cranioventral consolidation was seen in 40% of the left lung and 20% of the right lung.

(Editor's note: The photographs in this manuscript are available in color in the online edition of Clinical Theriogenology.)