

## Squamous cell carcinoma and papilloma virus in the prepuce of a Boer buck

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### Abstract

**Case description:** A 4.5-year-old Boer buck was presented for chronic posthitis and reluctance to breed.

**Clinical findings:** Gross examination of the buck's prepuce revealed numerous small ulcerated masses. Histopathology and immunohistochemistry of the biopsied preputial tissue identified squamous cell carcinoma with cytoplasmic immunoreactivity for papillomavirus antigens present in the neoplastic epithelial cells.

**Clinical relevance:** Squamous cell carcinoma (SCC) occurs sporadically worldwide in a variety of anatomical sites in small ruminants. Papillomavirus has been occasionally reported in goats and other wild caprine species as a suggested cause of neoplasia. This report describes a unique case of posthitis associated with SCC and papillomavirus in a breeding buck.

**Keywords:** Genital neoplasia, goat, squamous cell carcinoma, papilloma virus

### Background

Squamous cell carcinoma is a primary malignant neoplasm of the squamous epithelium that has been reported in a variety of domestic animals. The reported predilection sites of SCC in small ruminants are ears, eye and eyelids, base of the horns, on the shoulder, back, and flank regions, lateral to the umbilicus, udder, hind limbs, anus, perineum, vulva, and on the inner aspect of the tail.<sup>1</sup> Squamous cell carcinoma is not uncommon in small ruminants and occurs sporadically worldwide.<sup>2</sup>

The suggested predisposing factors for SCC include ultraviolet exposure of non-pigmented epithelium, genetic predisposition, and viral involvement. Papillomaviruses (PV) are DNA viruses that typically cause hyperproliferative lesions of the mucosal and cutaneous epithelia.<sup>3</sup> In addition to the typical papilloma lesions, PV infection is also associated with tumor development in several species.<sup>2-6</sup> To the best of our knowledge, preputial SCC in a goat with strong, diffuse, cytoplasmic immunoreactivity for papillomaviral antigen has not been described.

### Case presentation

A Boer buck, 4.5-years-old, weighing 86 kg with a body condition score of 3 (range 1 minimal and 5 maximum), was presented to the University of Illinois Veterinary Teaching Hospital with a four month history of swelling and purulent discharge from the prepuce and a reluctance or inability to breed. Similar signs were first noticed by farm personnel nine months prior to admission but the clinical signs subsided with unknown topical treatments. However, the clinical signs recurred and increased in severity about four months prior to admission. The buck was treated once with ceftiofur crystalline free acid and oxytetracycline (doses unknown) and the prepuce was flushed daily with water during the month prior to presentation. The buck was able to urinate and defecate normally and demonstrated a good appetite.

Upon physical examination, there was alopecia and crusting of the skin of the flanks, scrotum, dorsal neck, and ventral abdomen, and the patient was pruritic (Fig. 1A). Based on a skin scraping, an acetate tape test, and a trichogram, the dermatologic condition was diagnosed as chorioptic mange with secondary pyoderma and *Malassezia* spp infection.

The internal lamina of the prepuce was partially prolapsed, slightly swollen, ulcerated and partially covered with gray exudate. A *Corynebacterium renale* infection was the primary differential for the ulcerated and inflamed prepuce, as it is a common finding with small ruminant posthitis cases. The right testicle was firmer than the left testicle. The scrotal circumference of 28.5 cm was smaller than the 32-40 cm normal circumference range expected for a prospective breeding buck. Ultrasound examination

of the buck's testes revealed numerous hyperechoic areas present in the parenchyma of both testes. This finding was suggestive of testicular degeneration and dystrophic testicular mineralization. A complete blood count and biochemistry panel, along with a breeding soundness examination were offered but declined by the owner. The rest of the examination was unremarkable.

### **Treatment**

To treat the chorioptic mange and dermatitis, the buck was treated with ivermectin 1% at 200 mcg/kg subcutaneously once every two weeks for a total of three treatments. The animal was also bathed with gentle shampoo and lime sulfur dip once while the buck was hospitalized. To treat the suspected *Corynebacterium renale* induced posthitis, the buck was initially treated for five days with meloxicam (0.5 mg/kg, PO, q 24 hours), florfenicol (20 mg/kg, IM, q 48 hours), daily flushing of the prepuce with 500 mls of a 1:40 dilution of chlorhexidine solution every 12 hours, and a topical ointment consisting of lanolin, scarlet oil, and oxytetracycline that was applied to the interior of the preputial cavity. The buck appeared to improve during initial treatments as indicated by decreased preputial swelling and discomfort; however, four days after stopping treatment, the preputial swelling returned.

### **Preputial and penile examination**

Since the presumed bacterial posthitis did not resolve with treatment after nine days in the hospital, further investigation was deemed necessary. The buck was sedated with an intravenous combination of ketamine (0.1 mg/kg), butorphanol (0.025 mg/kg) and xylazine (0.05 mg/kg). The buck was positioned in lateral recumbency for examination of the penis and prepuce. Gray, inspissated material was present in the preputial cavity. With difficulty, the penis was exteriorized and numerous small, raised, round, coalescing masses, many of which were ulcerated, were observed covering most of the prepuce (Fig. 1 B-D). Adhesions between the prepuce and the penis were also present. Three 4 mm punch biopsies were taken from representative affected areas of the prepuce. A biopsy sample was submitted for histopathology. A sample of the inspissated exudate and two punch biopsy specimens were submitted for bacterial culture and antibiotic sensitivity.

The buck was treated with ceftiofur hydrochloride (2 mg/kg intramuscularly) once daily for seven days to help control the secondary bacterial infection of the prepuce. Meloxicam (0.5 mg/kg orally) was continued once daily and morphine (0.2 mg/kg intramuscularly), as needed for pain relief.

### **Histopathology and microbiology**

Histopathologic evaluation revealed that the specimen comprised polymorphic, infiltrative islands of non-keratinizing, squamous, epithelial cells with dyskeratosis and central cystic degeneration supported by inflamed fibrous stroma. The epithelial cells were polygonal with indistinct cellular borders and a small to moderate amount of amphophilic, slightly vacuolated cytoplasm. Nuclei were abnormally large, round to oval, central and hypochromatic with vesicular chromatin and prominent nucleoli. There was marked anisocytosis, marked anisokaryosis, frequent apoptosis, and 30 mitotic figures per ten 400X fields. The overlying epithelium was ulcerated. The microscopic diagnosis was SCC. An immunohistochemical stain using a broad spectrum antibody cocktail against BPV-1/1H8 and CAMVIR-1 papillomaviral antigens (Biocare Medical, LLC, Concord, CA) was applied to the specimen. There was diffuse, cytoplasmic immunoreactivity for papillomaviral antigen in all the neoplastic epithelial cells (Fig. 2).

Aerobic culture of the biopsy specimen resulted in a mix culture of moderate amounts of *Proteus*, *alpha Streptococcus ovis*, *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*. Antimicrobial susceptibility results indicated that the *Staphylococcus aureus* and *Pseudomonas aeruginosa* were susceptible to several antibiotics, including ceftiofur, enrofloxacin, gentamicin, and florfenicol.

## Outcome

After the definitive diagnosis of SCC of the prepuce was made, euthanasia was recommended because the buck could not function as a breeding animal, progression of local disease with possible metastasis would occur, and treatment options were limited. The owners elected to take the buck back to the farm and the buck was discharged from the hospital with meloxicam (0.5 mg/kg PO every 24 hours). It was recommended to keep the buck isolated from the other goats and not use him for live-cover breeding. According to the owners, the buck appeared to do well after returning to the farm. He had a good appetite and gained weight. However, because he was unable to perform as a breeding buck, the owners elected to euthanize him five months after being discharged from the hospital. A necropsy was not performed.

## Discussion

The prepuce is not a predilection site for SCC in goats and this is the first report of this type of tumor involving the prepuce in goats. In addition, this is the first description of papilloma virus infection being associated with SCC in goats. Infection of humans with certain types of PV is associated with oropharyngeal, penile, and cervical SCC.<sup>4,7</sup> Infection with equine papilloma virus is associated with SCC of the penis in horses.<sup>6</sup> Papilloma virus infection is usually species-specific; however, infection of horses with bovine papilloma viruses types 1 and 2 is associated with development of sarcoids.<sup>3</sup> It is unknown if the papillomavirus in the present animal induced SCC, but it is possible that the papilloma viral infection identified in the preputial epithelium preceded the SCC and could have been responsible for the neoplastic changes in the preputial epithelium.

Options for treatment of SCC in the prepuce of domestic mammals are surgical excision, cryotherapy, hyperthermia, radiation, chemotherapy, and intralesional chemotherapy.<sup>8-11</sup> The biologic behavior of cutaneous SCC is locally invasive and not often metastatic. Based on this, the treatment of choice for tumors in amenable locations is wide surgical excision.<sup>12</sup> A combination of two or more methods of treatment is recommended for complete resolution.<sup>13</sup> Intralesional chemotherapy has been used in horses with SCC in various locations and with varying results.<sup>14,15</sup> In the present case, intralesional chemotherapy could not be pursued due to the fact that chemotherapeutic agents are illegal in food animals in the United States. Surgical excision was not possible because such a large excision would not permit normal penile function during mating. Penile amputation or a perineal urethrostomy were possible, but not acceptable for a breeding buck. Cryotherapy or hyperthermia are appropriate for small, localized lesions but were not deemed viable options because of the large area affected.

The general health of the buck appeared to be compromised based on the chronic dermatologic conditions and abnormalities of the prepuce. However, the clinical history precludes us from being completely certain of the chronological order of the lesions and any potential immunosuppression playing a role in the development of the skin condition and the preputial masses. It is also unknown what role the farm treatments may have played in the occurrence of SCC and PV infection.

In conclusion, we describe the first case of papillomavirus associated with SCC in the prepuce of a goat. While papillomavirus infection is associated with development of SCC in some species, the broader implications for PV infection and risk of SCC in goats is not clear at this time. Future reports of SCC in goats should be screened for the presence of PV to determine if there is an association between PV infection and risk for this type of tumor. Finally, this case serves as a reminder to thoroughly evaluate the prepuce in all cases of preputial abnormalities.

## Learning points

- The prepuce is not a predilection site for SCC in goats and this is the first report of this type of tumor involving the prepuce in goats.
- This is the first description of papilloma virus infection being associated with SCC in goats.
- There is strong evidence in the literature concerning other species to indicate that papillomaviruses are responsible for inducing SCC, as may be the case in this buck.

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## Conflict of interest

No financial support was received for this project and none of the authors have any conflict of interest or bias for the publication of this report

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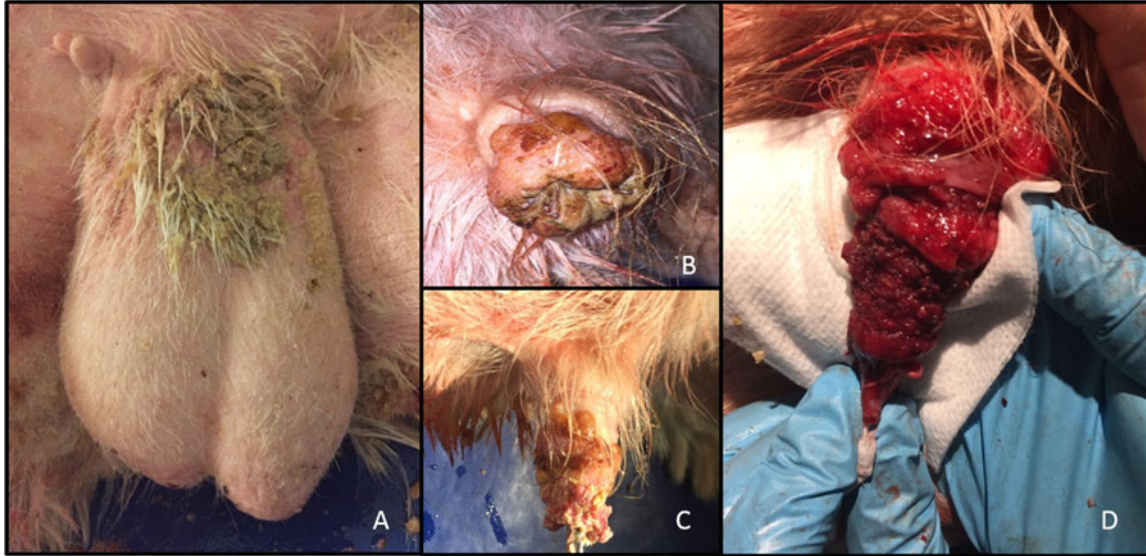


Figure 1. Photographs of a 4.5-year-old Boer buck presented with preputial squamous cell carcinoma. A.) Cranial view of the scrotum showing crusting dermatitis. B.) Cranial view of the partially prolapsed, erythematous prepuce. C.) Lateral view of the partially exteriorized prepuce with gray, inspissated material present in the preputial cavity. D.) Lateral view of the exteriorized penis with numerous squamous cell carcinoma lesions.

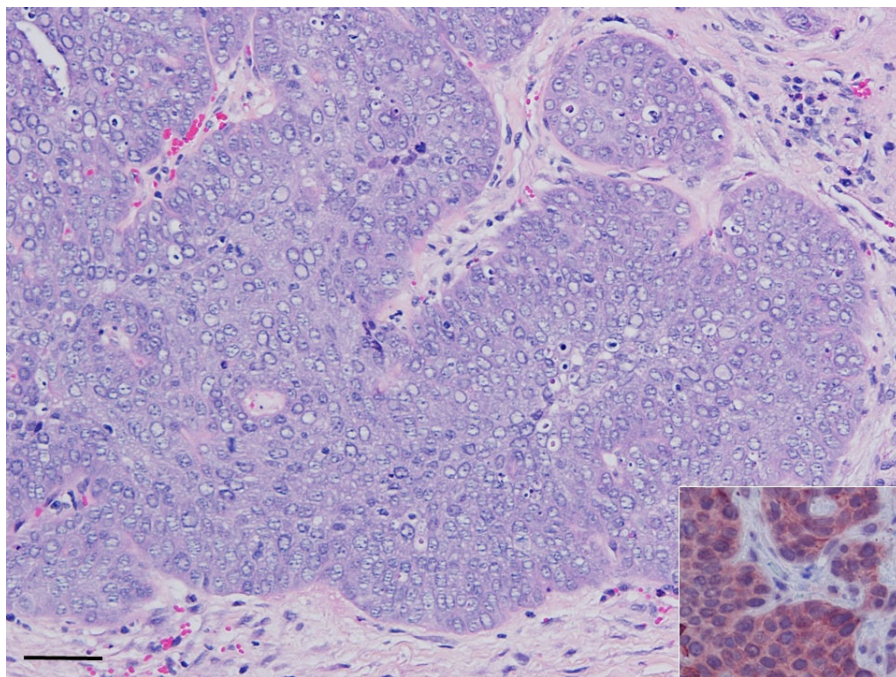


Figure 2. Histopathology of preputial masses taken from a 4.5-year-old Boer buck with squamous cell carcinoma. Nuclei are abnormally large, hypochromatic with vesicular chromatin, contain prominent nucleoli and frequent mitotic figures. H&E stain. Bar = 50µm. Insert: There is diffuse, cytoplasmic immunoreactivity in all the neoplastic epithelial cells by an immunohistochemical stain using cocktail broad spectrum antibodies against papillomaviral antigens.

(Editor's Note: Photographs in this manuscript are available in color in the online edition of *Clinical Theriogenology*.)