

Penile fibropapilloma in a Belgian Blue breeding bull

Peniel fibropapilloom bij een Belgisch wit-blauwe dekstier

¹B. Beci, ^{2,3}K. Proost, ¹J. Govaere, ¹G. Opsomer, ¹M. Meesters

¹Department of Internal Medicine, Reproduction and Population Medicine, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, B-9820 Merelbeke, Belgium

²Department of Large Animal Surgery, Anesthesia and Orthopedics, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, B-9820 Merelbeke, Belgium

³Wooly Veterinary Dentist, Nederkouter 17, B-9810 Eke (Nazareth), Belgium

Barbara.Beci@ugent.be

ABSTRACT

Penile fibropapilloma or a penile wart associated with bovine papillomavirus-1, is a neoplastic disease frequently encountered in young bulls. Penile warts can cause paraphimosis or phimosis, and can impede copulation and overall breeding performance. In this case report, the diagnostic approach and surgical treatment of large penile masses are described in a 2.5-year-old Belgian Blue breeding bull, with the inability to copulate. During clinical examination, the exteriorization of the penis proved to be impossible. A bilateral internal pudendal nerve block completely desensitized the penis, subsequently facilitating exteriorization and examination. The neoplastic masses were highly suggestive to be fibropapillomas and were surgically removed. An autogenous vaccine derived from the excised masses was produced by the laboratory Dierengezondheidszorg Vlaanderen (DGZ) and administered to the bull to reduce potential recurrence of the warts. After a month of sexual rest, the bull was able to resume breeding and produced viable offspring.

SAMENVATTING

Een peniel fibropapilloom of een peniswrat wordt veroorzaakt door het boviene papillomavirus-1 en is een neoplastische aandoening die meestal voorkomt bij jonge stieren. Peniswratten kunnen parafimose of fimose veroorzaken en kunnen de copulatie en de algemene fokprestaties beïnvloeden. In deze casus worden de diagnostische aanpak en chirurgische behandeling van peniswratten beschreven bij een 2,5 jaar oude Belgisch wit-blauwe fokstier die niet in staat was om te dekken. Tijdens het klinisch onderzoek bleek het onmogelijk om de penis uit te schachten. Een bilaterale zenuwblok van de nervus pudendus zorgde voor een volledige desensitisatie van de penis, waardoor deze uitgeschacht en onderzocht kon worden. De neoplastische weefselmassa's waren vermoedelijk fibropapillomen en werden chirurgisch verwijderd. Een autoloog vaccin werd geproduceerd door het erkend laboratorium Dierengezondheidszorg Vlaanderen (DGZ) en aan de stier toegediend om het risico op recidief te verkleinen. Na een maand seksuele rust kon de stier het dekken hervatten en produceerde hij gezonde nakomelingen.

INTRODUCTION

Abnormalities causing sub- and infertility in male animals can be classified in conditions causing a partial or complete inability to impregnate normal cycling females (impotentia generandi) and conditions causing partial or complete failure of normal copulation (impotentia coendi) (Parkinson and McGowan, 2019;

Van Camp, 1997). The inability to copulate is further divided into erection failure despite normal libido (impotentia erigendi) and the inability or unwillingness to copulate due to physical limitations (Maxwell, 2021; Parkinson and McGowan, 2019; Van Camp, 1997). These physical constraints may be attributed to non-reproductive conditions that compromise fertility, such as obesity, heat-stress and musculoskeletal

dysfunctions, as well as due to conditions of the reproductive tract, like problems of the secondary sex glands, scrotal, preputial and/or penile problems (Van Camp, 1997).

Common penile problems in bulls leading to copulatory problems are hair rings encircling the penis, inflammation of the penis and prepuce, a persistent frenulum, penile deviations and penile fibropapillomatosis (Hopkins, 2007; Van Camp, 1997).

The only common tumor of the bovine penis is the virally induced fibropapilloma (Parkinson and McGowan, 2019; Hopkins, 2007). Papillomavirus is a double-stranded DNA virus found in various species (Borzacchiello and Roperto, 2008). Fifteen genotypes of bovine papillomavirus (BPV) have been characterized so far (Franco de Carvalho et al., 2016). These genotypes are strictly species-specific; only BPV-1 and BPV-2 can infect equids (Borzacchiello and Roperto, 2008). Bovine papillomavirus induces papillomas of cutaneous and mucosal epithelia in cattle (Campo, 1997), causing a multitude of different histopathological lesions (Borzacchiello and Roperto, 2008). The most common virus types identified are BPV-1 and BPV-2, which are classified as deltapapillomaviruses (Franco de Carvalho et al., 2016). Both types are associated with the clinical appearance of papillomas and fibropapillomas (Franco de Carvalho et al., 2016; Antonsson and Hansson, 2002), which are benign tumors of the epithelium and underlying dermis (Antonsson and Hansson, 2002; Campo, 1997). They predominately consist of fibroblast proliferations with variable overlying epithelial hyperplasia and hyperkeratosis (Foster, 2017), and are not locally invasive or metastatic (Hopper and Wolfe, 2021). Tumors caused by BPV-1, BPV-2 and BPV-4 are self-limiting and will generally regress (Pusterla et al., 2020; Campo, 1997). However, occasionally, they can persist and undergo alteration into malignant squamous cell carcinomas (Pusterla et al., 2020; Campo, 1997). This occurrence particularly manifests in cattle that ingest bracken fern, subsequently rendering them immunocompromised (Pusterla et al., 2020).

In male and female cattle, genital fibropapillomas are caused by BPV-1 and -2 (Mauldin and Peters-Kennedy, 2016), although penile fibropapillomatosis is caused by BPV-1 (Yamashita-Kawanishi and Haga, 2020; Foster, 2017; Van Camp, 1997). The penile integument, and particularly the terminal 5 cm, is a common site for fibropapillomas, which may present single or multiple, sessile or pedunculated. Penile fibropapillomas can be found in both intact and castrated bulls but rarely persist beyond three years of age (Parkinson and McGowan, 2019; Van Camp, 1997). Bulls are most likely infected during homosexual mating behavior at a young age (Hopper and Wolfe, 2021), causing abrasions of the penis which serve as entry-points for the virus (Hopkins, 2007). The disease is usually self-limiting, but can go undiagnosed until copulatory problems and pain arise (Van Camp, 1997; Dawson and Bierchwal, 1983; Hall

et al., 1976). The clinical symptoms vary according to the size and morphology of the lesions. The penile tumor may bleed or ulcerate during mating, and the associated pain is sometimes sufficient to impair libido. Very large tumors may result in intermittent or complete failure of retraction of the protruded penis (paraphimosis). More rarely, very rapid growth of the fibropapilloma within the preputial cavity can cause phimosis (Hopkins, 2007; Parkinson and McGowan, 2019; Van Camp, 1997).

CASE DESCRIPTION

A 2.5-year-old Belgian Blue breeding bull was referred to the Department of Internal Medicine, Reproduction and Population Medicine at the Faculty of Veterinary Medicine of Ghent University (Belgium) because of a suspected penile neoplasm.

The bull had been purchased as a breeding bull four months earlier. His libido was reported to be excellent, although the owner did not observe the penis in full erection when the bull tried to breed cows. The local veterinarian examined the bull and found no abnormalities other than a palpable mass in the sheath, seemingly surrounding the penis. The bull was referred to the clinic for further examination and eventual treatment.

Upon arrival, the bull was weighed (926 kg), restrained and underwent a full physical examination during which no clinical abnormalities were found. By palpating the preputial sheath, a mass could be clearly identified, although this mass was not apparent on visual inspection. The penis could not be exteriorized for full examination without desensitization. A standing approach was chosen for diagnostic procedures and possible surgery. The differential diagnosis for lack of erection and a palpable mass comprised penile neoplasia, trauma, hematoma, fracture, abscessation and adhesions. Also, the presence of a foreign body, an abscess in the prepuce and sheath, paraphimosis, a persistent frenulum and short-penis syndrome were included.

The bull was restrained in a simple examination box. After clipping, scrubbing and disinfecting the skin overlying the needle insertion point, a low caudal epidural anesthesia was performed using 30 mg of xylazine hydrochloride (Xyl-M 2%, V.M.D. N.V., Arendonk, Belgium) added to 2 ml of 4% procaine hydrochloride (Procaine hydrochloride 4%, V.M.D. N.V., Arendonk, Belgium). For pain relief, 0.5 mg/kg meloxicam (Melovem 20mg/ml, S.C., Dopharma Research B.V., Raamsdonksveer, the Netherlands) was given preoperatively. To desensitize the penis, a bilateral internal pudendal nerve block as described by Edmondson (2008) was applied. The skin at the ischio-rectal fossa on either side was clipped, disinfected and desensitized with 2 mL of local anesthetic (Procaine hydrochloride 4%, V.M.D. N.V., Arendonk, Belgium). A 14-gauge 2.5-cm needle (hypodermic needle with



Figure 1. Internal pudendal nerve block (A and B) and the resulting desensitized penis (C and D).

Aluminium Hub 2.0 x 25mm, 14G, Kruuse, Langeskov, Denmark) was inserted through the desensitized skin at the ischio-rectal fossa to serve as a guiding needle. A 20-gauge 8.8-cm spinal needle (Spinocan®, 20G, 88mm, B. Braun Medical N.V., Diegem, Belgium) was then directed through the guiding needle to the pudendal nerve (Figures 1A and 1B). Due to the large size and muscular hypertrophy of the bull, 60 ml of local anesthetic (Procaine hydrochloride 4%, V.M.D. N.N., Arendonk, Belgium) per side was needed to allow desensitization of the pudendal nerve. After twenty minutes, the penis was desensitized and could be exteriorized from the sheath for further inspection (Figures 1C and 1D). The owner wished to keep this bull as a breeding animal, and consented on having the observed penile tumor surgically removed. A perfusion line was used as a tourniquet to reduce the blood flow in the penis, ensuring good visibility while excising the tumor (Figure 2).

Once the penis was exteriorized, the penile neoplasm could be inspected more closely. The glans penis was completely covered by two large (3 x 5 cm) masses with cauliflower-like appearance. These were suspected to be pedunculated fibropapillomas with a broad base. Some smaller masses, suspected sessile fibropapillomas, were also present on the glans and on the free portion of the penis, about 1-2 cm above the large pedunculated warts (Figure 2). Due to the size of the tumors, the urethral opening was not discernable,

thus, a large portion of the most cranial mass was removed to be able to access the urethra. A urinary catheter (Dog Catheter with Female Luer Mount, 2.0 mm (6F) x 50.00 cm, Portex®, Smiths Medical International Lt., Hythe, Kent, UK) was placed to make



Figure 2. Pedunculated penile warts completely covering the glans penis, as well as sessile penile warts (circle) one to two cm above. A perfusion line (*) was used to reduce the blood flow in the penis, to ensure good visibility while excising the tumors.



Figure 3. Excision of the penile warts (A and B) and the resulting complete removal of these warts (C and D).

sure the urethra would not be damaged while removing the remainder of the penile warts (Figures 3B and 3C). To remove the pedunculated and sessile warts, an electrocauterizing unit was used (Coag&Cut M120 Electrosurgery Unit, Mano Médical, Taden, France). Both the large pedunculated, as well as the smaller sessile warts were excised completely, and small bleeding blood vessels were cauterized (Figures 3A en 3B). Whilst excising and coagulating, great care was taken to ensure the integrity of the urethra at all times. Good hemostasis was achieved upon finishing as there was limited postoperative bleeding after the removal of the tourniquet.

Postoperative care

Urination was observed three hours after surgery. The penis remained desensitized for four hours, after

which the bull was able to retract his penis completely into his sheath. On the owner's request, the bull left the clinic on the same day of the surgery. Analgesia by 0.5 mg/kg meloxicam (Melovem 20mg/ml, S.C., Dopharma Research B.V., Raamdonksveer, the Netherlands) was repeated after 48 hours by the farmer. No systemic antibiotics were administered. The local veterinarian inspected the bull a week later and the bull had recovered well. The bull was given a month of sexual rest, to assure complete healing of the penile integument. Afterwards, he successfully impregnated cows and heifers, producing viable offspring.

Autogenous vaccine

To prevent wart reoccurrence, the whole tumor (120 g) was sent to a commercial laboratory (Dierengezondheidszorg Vlaanderen (DGZ), Belgium) to

produce an autogenous vaccine. The vaccine was made by homogenization of the wart (a minimum of 30 g was required) in a buffer, followed by filtration, centrifugation and inactivation of the supernatant in a formaldehyde solution. The procedure was concluded with the confirmation of the vaccine's sterility through rigorous validation. The specific methodology employed to produce this autogenous wart vaccine, adheres to a proprietary protocol exclusive to the DGZ laboratory, and therefore, cannot be divulged in this context. The bull was vaccinated subcutaneously four times, with an interval of five days. The volume of injections were: 3 ml, 5 ml, 8 ml and 10 ml. The owner did not notice any new wart reoccurrence in the following months.

DISCUSSION

Phimosis can be noted during observation mating, or by inducing an erection with an electro ejaculator. It can result from a penile wart larger than the preputial opening (Maxwell, 2021), as was the case in the present report. Desensitizing the pudendal nerves ensured successful manual exteriorization of the penis. If the prepuce would not permit penile extension, an incision of the internal lamina of the prepuce would be necessary to exteriorize the penis to enable surgical removal of the penile warts (Maxwell, 2021).

In the present case, the bull was restrained in a simple examination box with minimal sedation. In this bull, the internal pudendal nerve block provided a very efficient desensitization of the penis. This allowed for the bull to remain standing during the surgery. In the literature, restraining the bull on a tilt table or in a squeeze chute has been recommended (Hopper and Wolfe, 2021; Maxwell, 2021). This was not necessary due to the calmer nature of Belgian Blue animals in general, and in particular, the bull in the present report.

The surgical steps used in this case were in line with previous reports of penile wart removal (Monke et al., 2018; Prado et al., 2016). Performing the internal pudendal nerve block was challenging due to the hypermuscularity of the Belgian Blue breed. Because of the large intrapelvic muscle mass, the spinal needle used could not reach the internal pudendal nerve. Therefore, a larger dose of the local anesthetic was needed, to be able to desensitize the internal pudendal nerves. An alternative method to desensitize the penis would be a local block of the dorsal nerve of the penis, just proximal to the surgical site or at the location where the penis passes over the ischial arch (Maxwell, 2021; Sidelinger, 2021). Penile fibropapillomas are most often found on the craniodorsal side of the penis and on the junction of the glans penis and sheath (Hall et al., 1976). The location of the wart in this case was consistent with what has been described in the literature, although due to the large size of the

warts, the glans penis was completely covered. No fibropapillomas were present on the junction of the glans penis and the prepuce or on the mucocutaneous junction of the sheath. Penile warts are typically attached to the penile epithelium by a stalk of tissue, creating a pedunculated mass (Monke et al., 2018). Diffuse or sessile growth of penile warts is possible, which makes surgical removal more complex (Monke et al., 2018). Both pedunculated and sessile tumors were present in this case, although complete removal of all tumors was achieved. Other than surgical removal by excision, cryotherapy or the use of laser surgery, alone or in combination with immunization are possible (Hopper and Wolfe, 2021; Hopper, 2016). During surgery, special care should always be taken to avoid perforation of the urethra, leading to the development of an urethral fistula (Heppelmann et al., 2019). While penile fibropapillomas are not invasive and do not metastasize, a small proportion of tumors does exhibit aggressive recurrence after surgical removal. A possible 10% of penile fibropapillomas recur and are visible again within three to four weeks after surgery (Parkinson and McGowan 2019). Complete removal of the fibropapilloma including a margin of unaffected epithelium reduces the risk of recurrence (Hopper and Wolfe, 2021), although partial excision due to close proximity to the urethra has also been described without tumor recurrence (Heppelmann et al., 2019).

Fibropapillomas are the most common neoplasm of the vulva in cows and the penis in bulls (Yeruham et al., 1999; Naghshineh et al., 1991; Hall et al., 1976). In the present case, the mass was diagnosed as fibropapilloma based on its clinical appearance and anatomical location. To confirm the diagnosis, histopathology and polymerase chain reaction (PCR) analysis to detect BPV-1 should have been performed (Foster, 2017; Gardiner et al., 2008). However, due to the fact that fibropapillomas found on the penis are generally attributed to BPV-1 (Foster, 2017), and other neoplastic growth on the bovine penis is extremely rare (Hopper and Wolfe, 2021), the whole wart (120 g) was sent to the laboratory for autogenous vaccine preparation. No further diagnosis was done in this case.

Autogenous or commercially made vaccines containing BPV-1 or BPV-2 have been used effectively for fibropapilloma prevention and to reduce its recurrence (Pusterla et al., 2020; Khodakaram-Tafti and Kargar, 2009). However, they are not as efficient as a stand-alone treatment (Elzein et al., 1991), as their efficacy is variable and not well documented (Monke et al., 2018). Nevertheless, when clients are not prepared to pay for surgery to remove penile fibropapillomas, autogenous vaccine administration should be considered (Parkinson and McGowan 2019). There is no commercially available wart vaccine on the Belgian market, thus Belgian veterinarians have to resort to autogenous vaccines if vaccination is attempted. To make an autovaccine, a minimum of 20

grams of warts per animal is requested by the laboratory (DGZ). In this case, the whole wart was sent for vaccine preparation. Autogenous vaccines often provide favorable results because they contain the virus type associated with the disease causing the problem (Pusterla et al., 2020), and as autogenous vaccines are herd-specific, it is important to know they can only be used on the herd from which the warts were provided (DGZ, 2024). When using an autogenous vaccine, a vaccination protocol of three 1 ml to 5 ml intradermal injections given at one-week intervals is recommended (Pusterla et al., 2020). However, in the present case, the farmer followed the vaccination protocol as indicated by the laboratory (DGZ) that provided the vaccine. The DGZ laboratory's autogenous vaccine protocol differs substantially from that described by Pusterla et al. (2020), as the four injections are given subcutaneously at five-day intervals, with an increasing volume from 3 ml to 10 ml. The methodology as well as the protocol of the autogenous vaccine used in this case report is patented by the DGZ laboratory, and can thus not be revealed. In herds with a high prevalence of fibropapilloma cases, it might be an option to use an autogenous vaccine as a management tool and separate young bulls to avoid homosexual behavior (Hopper and Wolfe, 2021).

CONCLUSION

In this case report, the diagnostic approach of a bull's inability to copulate was described. Penile neoplasia should be considered when phimosis occurs in a breeding bull. When penile tumors are present, the most common cause is BPV-1, although histopathology and PCR should be performed to confirm this diagnosis. Penile fibropapillomas are self-limiting; however, surgical removal of the penile warts is frequently indicated. Desensitization of the penis is necessary for surgical wart removal, and complete desensitization can be achieved by using a bilateral internal pudendal nerve block, although the hypermuscularity of the Belgian Blue breed can complicate this type of local anesthesia. The prognosis in breeding animals is generally good, although great care should be taken to protect the urethra to avoid either strictures or fistulas. Autogenous vaccines may help reduce the risk of recurrence of fibropapillomas.

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Smaken verschillen: kat en hond

Mully Gatowny had een kat
Die beschuit met muizen vrat
Vleer- of veld maakte niks uit
Het ging alleen om de beschuit

Mully Gatowny's laatste duit
Gaffie aan beschuiten uit.
Toen zaidie dattie 't welletjes vond,
Verzoop de kat en kocht een hond

En die vrat alles wattie vond,
Tot platgetreden paardenstront
Paardenkeutels, paardenvijgen,
Hij kon er niet genoeg van krijgen.

*Fragment uit Mully Gatowny in 'Literary Larycook in Dutch and Doubledutch'
1977. John O'Mill, Andries Blitz, Amersfoort.*