



Theriogenology Question of the Month

History

A breeding soundness evaluation was performed at the Veterinary Medical Teaching Hospital of the University of California-Davis on a 3-year-old Hereford bull. Four weeks previously, the bull had been evaluated because of a suspected laceration to the penis. No treatment was implemented at that time, except reproductive rest to allow for healing. The bull had been one of several used for breeding of the herd during the previous reproductive season; thus, the fertility and reproductive history of the bull were unknown.

Results of physical examination were unremarkable. The bull was in good body condition with a score of 5 (scale of 1 to 9). Findings during palpation of the testes, epididymides, spermatic cords, and accessory sex glands were within anticipated limits. Scrotal circumference was 40 cm. Electroejaculation was performed. The bull achieved an erection, and protrusion of the penis from the prepuce and ejaculation of semen were observed. During ejaculation, it was observed that the semen exited through an opening located approximately 4 cm from the tip of the penis. Semen evaluation revealed that the spermatozoa had fair gross motility, 50% of the spermatozoa had progressive forward motility, and 96% of the spermatozoa were morphologically normal.

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Figure 1—Photograph of the right side of the penis of a 3-year-old Hereford bull obtained during a breeding soundness examination. Four weeks previously, the bull had been examined because of a suspected laceration to the penis; no treatment was initiated at that time, except reproductive rest to allow for healing.

Further evaluation of the distal portion of the penis was performed. The extent of the defect, which was only visible from the right side, was not evident initially because a left-sided hydraulic chute was used. Examination of the penis from the right side resulted in detection of a 4-cm defect of closure in the distal portion of the urethra (Figure 1). There were no signs of trauma or injury, such as blood, fibrin, inflammatory exudate, or fibrosis. The edges of the opening were smooth and shiny and appeared similar to the penile mucosa.

Question

What is the most likely diagnosis for this bull's condition? *Please turn the page.*

Answer

Hypospadias.

Outcome

Because of concerns regarding breeding soundness of the bull, the cost of surgical correction, and the fact that this is potentially a heritable condition, the owner elected to send the bull to slaughter. The penis, bladder, and accessory sex glands were collected for postmortem evaluation.

Results

Gross examination of the penis revealed that there was a 4-cm-long, linear defect on the right lateral aspect of the penis that extended from the external urethral orifice to the tip of the penis (Figure 2). The urethral mucosa was visible in the defect, and the lumen communicated with the external surface. The border between the urethral mucosa and penile epidermis was smooth and slightly mottled tan-pink. The urethral mucosa was pale tan, smooth, and shiny. The testes, bladder, and seminal vesicles were grossly unremarkable.

Histologic examination revealed that the transitional epithelium lining the urethral lumen (urothelium) was continuous with and transitioned into the keratinized stratified squamous epithelium of the external skin of the penis. This transition was evident in all sections examined along the entire length of the grossly evident defect. Within the submucosa around the urethra and occasionally disrupting the undulating urothelium, there were moderate numbers of plasma cells and lymphocytes, a few neutrophils, and reactive congested vessels. This was consistent with a moderate, multifocal, chronic urethritis. The epidermis of the penile skin adjacent to the defect and on the dorsal aspect of the penis was variably hyperplastic, with projecting anastomosing rete pegs. A few clusters of lymphocytes and plasma cells were evident multifocally within the superficial

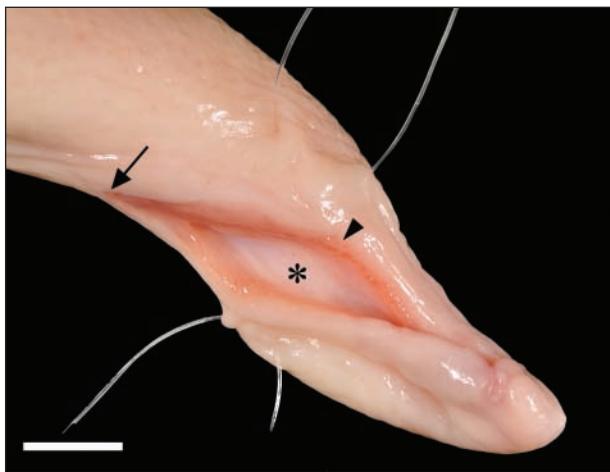


Figure 2—Photograph of the distal aspect of the penis of the bull in Figure 1. Notice the linear defect of the distal portion of the urethra and that the lumen of the urethra is exposed (asterisk). The margin between the urethra and epidermis (arrowhead) is mottled tan-pink and smooth. Also notice that the opening of the urethra through which the semen exited during electroejaculation (arrow) is located 4 cm from the tip of the penis. Bar = 1 cm.

and perivascular dermis, which was consistent with a moderate, lymphoplasmacytic balanoposthitis (Figure 3). There was no evidence of trauma or repair of the epithelium between the mucosa of the urethra and the

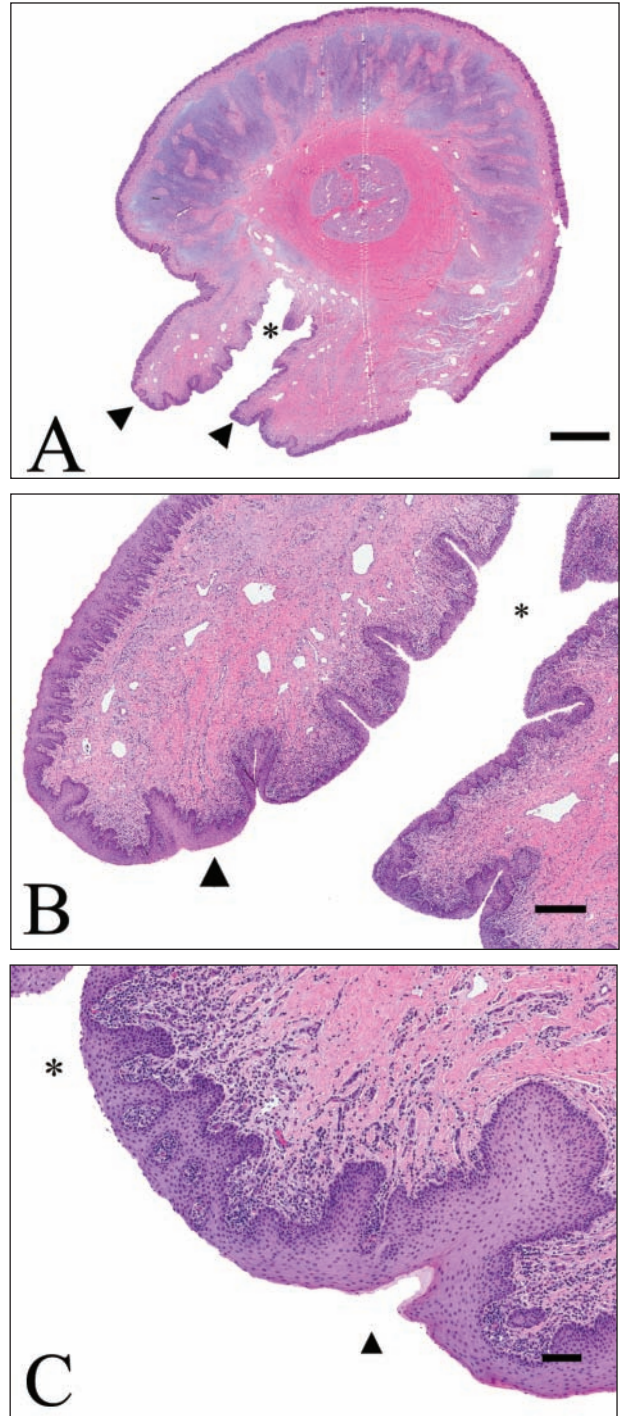


Figure 3—Photomicrographs at lower (A), higher (B), and highest (C) magnification of a tissue section obtained through the cross section of the penis of a 3-year-old Hereford bull. In panels A and B, notice that the urinary epithelium lining the urethral lumen (asterisk) is continuous with the external skin (arrowheads). In panel C, notice that the transitional epithelium lining the urethral lumen (asterisk) is continuous with a keratinized stratified squamous epithelium of the external skin (arrowhead) and that the submucosa of the urothelium is moderately infiltrated with lymphocytes and plasma cells. H&E stain; bar = 2 mm in panel A, 500 μ m in panel B, and 100 μ m in panel C.

external skin. These findings were not consistent with a laceration and instead indicated a segmental failure of closure of the ventral floor of the urethra, which was most consistent with a hypospadias.

Discussion

Hypospadias is a congenital defect in males in which the external urethral orifice is malpositioned. In normally developing male embryos, the urogenital folds fuse, which converts the urethral groove into a tube to form the penile urethra. Later, canalization of an ectodermal cord forms the opening of the penile urethra at the tip of the penis.¹ A defect in fusion of the urogenital folds, which are located at both sides of the urethral groove, results in hypospadias.² This condition has been subdivided into 4 forms (glandular, penile, scrotal, and perineal) on the basis of the anatomic location of the defect.³

Hypospadias has been described in several species, including humans, dogs, cats, cattle, goats, sheep, and stallions.³ In cattle, the prevalence of hypospadias in postmortem studies^{4,5} has been reported to be between 0.35% and 0.46%. In one of those studies,⁵ it was reported that hypospadias in cattle was most commonly perineal (83%) and much less frequently periscrotal (11%) or rarely glandular (5%). The condition in the bull described here involved the least common location (ie, glandular location).

Concurrent developmental abnormalities in animals with hypospadias have been reported and include penile aplasia, an incomplete ventral sheath, a bifid scrotum, cryptorchidism, and atresia ani.^{6,7} None of these abnormalities were found in the bull described here. Furthermore, the lack of concurrent developmental malformations may explain the late age of detection of hypospadias in this bull because clinical signs were minimal.

The events that lead to hypospadias are not completely characterized. In embryos, development of the genital tubercle is under androgen influence, and any alteration of the genes responsible for phallic development or androgen pathways may lead to hypospadias. It has been suggested that an interaction between genetic factors and the environment may also be associated with hypospadias. Endocrine-disrupting chemicals, such as estrogenic or antiandrogenic chemicals from the environment, may interfere with androgen synthesis or androgen action during development of the genital tubercle in embryos.^{6,8} Some examples of

these endocrine-disrupting chemicals are chlorinated pesticides (dithiothreitol and lindane), phenolic derivatives, phthalates, dioxine, xenoestrogens, and diethylstilbestrol.^{3,8} In humans, mutations of the genes involved in phallus development (*HOX*, *FGF*, and *Shh*), testicular determination (*WT1* and *SRY*), androgen biosynthesis (*MAMLD1*), and the androgen receptor (*AR*) have been associated with hypospadias.^{6,8} In cattle, although the genes involved have not been studied, familial clustering has been reported,⁷ which suggests a genetic basis.

The cause of hypospadias in the bull described here is not known. Exposure to endocrine-disrupting chemicals was not reported, and testing for chromosomal abnormalities and hormonal concentrations was not performed. The situation for examination of the bull described here is an example of how chute configuration and concerns for safety may limit a complete visual examination of the genitalia.

In an animal with hypospadias, surgical correction is an option but only has a fair prognosis. Because of the potential genetic basis for this condition, the use of a male with hypospadias as a breeding animal is not recommended.³ A sample of whole blood or hair from an animal with hypospadias can be submitted to a genetic laboratory for genotyping when the progenitor sire is unknown, and results can prevent use of the same progenitor sire again in the future.

References

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