Male pseudohermaphroditism of the testicular feminization type in a heifer

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Development of the reproductive system in mammals involves several discrete but interrelated processes. During embryogenesis, androgens initiate the development of the sex organs in the male. Failure of the embryonic forerunners of the sex organs to respond to androgens will lead to their aberrant development. The testicular feminization syndrome is one such condition, it has been reported in various mammals including in cattle (1,2). The condition is characterized by a female phenotype, an XY sex chromosome complement, and testes which may be in the abdominal cavity, inguinal canal, or area of the labia. Affected animals are sterile. They may have an inguinal hernia which may reveal a testis at surgery. An unusual phenotype in a case of testicular feminization is described in this report.

The animal was raised as a heifer. As a calf, she had poorly developed hindquarters with unsteady gait of the hind limbs. In addition, she had audible respiratory sounds suggestive of a restricted upper airway. The level of noise increased with exercise or excitation, or both. She became notably irritable at six months of age and gradually developed a hostile and aggressive attitude. When the heifer was 10 months old, testicular swellings appeared in the subcutis of the inguinal area and she exhibited bull-like behavior, including mounting, fence-line contact with other heifers, and vocalization. A partially developed penile structure was also observed beneath the tail, ventral to the rectum, inside a vulva-like structure. Other secondary male sexual characteristics included a short muscular neck, a bullish face, and heavy-muscling of the hindquarters. She urinated via the penis-like structure.

The animal was examined at the Veterinary Medical Teaching Hospital at Purdue University. Her behavior was uncontrollably aggressive; therefore, she was restrained in a chute. Upon examination a 12 cm penile structure was observed just ventral to the rectum. A glans penis-like structure could be extruded inside the vulva-like structure (Fig. 1). The vulva-like structure lacked the typical thick and wrinkled lips with ill-defined commisures. There was no vagina or cervix. Urine was collected via urethral catheterization. Rectal examination was performed followed by ultrasonic examination to evaluate the internal reproductive structures. Ultrasonic examination was carried out transrectally using a 5 mHz transrectal transducer. A blood sample was collected to estimate the serum testosterone concentration. The heifer was challenged with 10,000 IU of human chorionic gonadatrophin (hCG-Chorionic Gonadotropin, Butler Company, Columbus, Ohio, USA), and blood samples were collected at one hour and three hours posttreatment to estimate the changes in serum testosterone concentrations. Ten microliters of peripheral venous blood were collected from the tail vein into a vacutainer tube containing 0.2 mL of sodium heparin for lymphocyte culture and cytogenetic analysis.

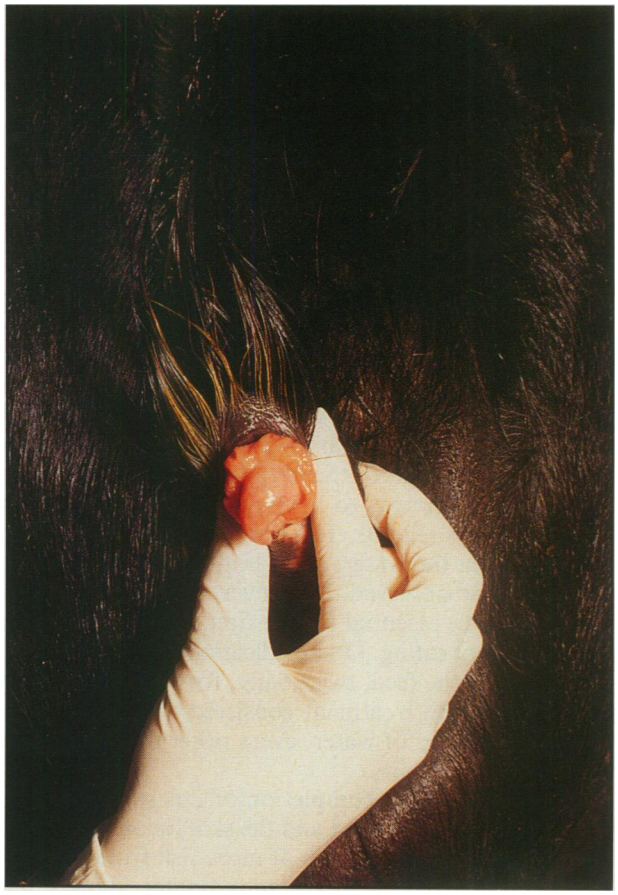

Figure 1. Glans penis-like structure exposed by digital manipulation.

After the completion of tests the animal was euthanized and the internal and external reproductive structures were recovered, examined, and photographed. Two pieces of tissue (1.5 × 1.5 cm) obtained from each gonad at random were fixed in Bouin's solution, six micron thick paraffin sections were cut serially, and five sections were stained in hematoxylin and eosin for histological examination. Samples were taken from peritoneum, spleen, and gonads. All tissues were cultured according to the method described by Basrur *et al* (3).

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Leukocyte cultures were prepared and lymphocytes were harvested using standard techniques (4). Cell suspensions were placed onto ethanol cleaned microscope slides and air-dried. To identify individual chromosomes, the Giemsa (G) banding technique was employed: The slides were immersed for 10–15 seconds in 0.30% trypsin and stained for five minutes in 4% Giemsa stain. Fifty-six metaphase spreads were analyzed. Representative metaphase spreads were photographed and karyotyped according to currently accepted guidelines (4).

Rectal examination determined the presence of a seminal vesicle and an ampulla on each side. The remnant of the müllerian duct (uterus masculinus) was felt as an enlarged and unpaired structure between the seminal vesicles. Transrectal ultrasonic examination confirmed the rectal palpation findings. Rectal palpation of the internal genitalia resulted in the expulsion of approximately 1.0 mL of purulent material from the urethra. Stained slides of the purulent material revealed the presence of 20–29 neutrophils in each 400 × magnification field. Microbiological examination of the material failed to isolate any pathogenic organisms. Results of urine analysis were within normal limits.

Chromosome analysis was carried out on the 95 metaphases from four tissues (peritoneum 22, spleen 25, and gonads 48). All complete cells from different tissues showed an XY sex chromosome complement. The cytogenetic studies identified the animal's karyotype as that of a male *Bos taurus* (60, XY). The basal concentration of testosterone was 5.3 ng/mL. An hour after treatment with hCG, the testosterone concentration had increased to 10.4 ng/mL, and three hours posttreatment, it reached 15.5 ng/mL.

The animal had normal testicles and epididymes with each ductus deferens enlarging into an ampulla on the respective side (Figure 2). Histologically, the parenchyma was composed of seminiferous tubules and Leydig's cells. The testicular tissue appeared normal and seminiferous tubules showed absence of spermatogenesis.

The fundamental defect in testicular feminization is the inability of the target organs to respond to testosterone secreted by the gonads. In such cases, during embryogenesis, testosterone-dependent tissues, such as the wolffian ducts, the urogenital sinus, and the external genitalia, do not differentiate. The undescended testes of these individuals secrete androgens, but the target tissues (accessory sex glands, skin of genital region) are nonresponsive to androgen, because either they are not capable of converting testosterone to its biologically active form, dihydrotestosterone, or they have reduced cytosol androgen receptor activity. In the absence of an androgen response, female external genitalia and a female-like phenotype develop.

In a previously described case of testicular feminization syndrome, the internal genitalia of the affected animal resembled those of a female (2). In the present case there was development of ductus deferens, seminal vesicles, and partial development of a penis-like structure in an abnormal position; hence, the present condition can be described as a case of incomplete testicular feminization syndrome. The role of the "müllerian inhibiting factor" in the testicular feminization syndrome is not known. However, it is conceivable that this factor had only partially suppressed the development of the müllerian duct system in the present case, since the internal genitalia consisted of an enlarged uterus masculinus.

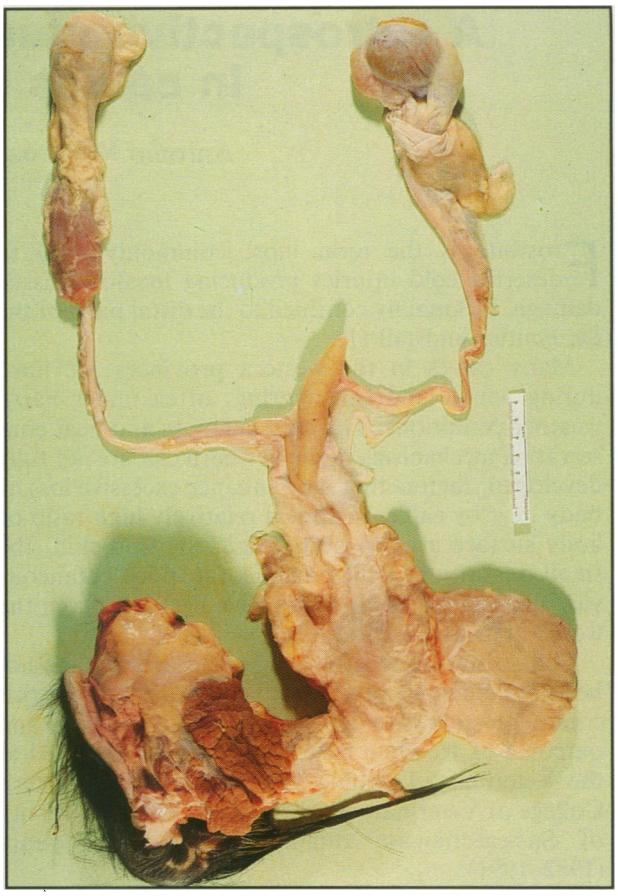

Figure 2. The internal genitalia of the affected animal.

In the present case there was preputial and scrotal development, and incomplete development of a penis-like structure in an abnormal position. In conclusion, the defect may be attributed to either lack of cytosol receptor for androgen or the lack of the enzyme which converts testosterone to its biologically active form, namely dihydrotestosterone. CVJ

References

1. Nes N. Testikulaer femininisering hos storfe. Nord Vet Med 1966; 18: 19–29.
2. Long SE, David JSE. Testicular feminisation in an Ayrshire cow. Vet Rec 1981; 109: 116–118.
3. Basrur PK, Basrur VR, Gilman JPW. A simple method for short term cultures from small biopsies. Exp Cell Res 1963; 30: 229–232.
4. Halnan CRE. Karyotype and phenotype in cattle and hybrids of the genus. In: Halnan CRE, ed. Cytogenetics of Animals. Oxford: CAB International Press, 1989: 235–255.