64,XY (SRY-negative) phenotypic mare

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A 7-year-old American Quarter Horse mare was presented for reproductive evaluation. The owner's goal was to have the mare carry her own foal to term, but the mare had never been observed to show behavioral estrus and had not received any medications. Physical examination revealed a phenotypically normal mare with a normal vulva and clitoris and a small mammary gland consistent with that of a maiden mare. Transrectal ultrasonographic examination showed very small gonads adjacent to the tip of each uterine horn. The gonadal structures were 1.5 cm in length and devoid of any visible follicles. Speculum examination revealed a normal vaginal vault and a normal external cervical os. Videoendoscopic examination revealed a normal uterine body, two uterine horns and a utero-tubular junction at the tip of each horn. Hormone analysis indicated low concentrations of anti-Müllerian hormone (AMH) (0.01 ng/ml; normal range 0.1 to 3.8 ng/ml), inhibin (0.21 ng/ml; normal range 0.1 to 0.7 ng/ml), testosterone (27.6 pg/ml; normal range 20 to 45 pg/ml) and progesterone (0.12 ng/ml). A blood sample was subsequently submitted for chromosomal analysis, which indicated that the mare had a 64, XY karyotype. Further analysis of the Y chromosome revealed that the sex-determining region of the Y chromosome (SRY) was absent. Specifically, PCR test results indicated that the mare was negative for all male-specific Y chromosome markers. Fluorescent in situ hybridization (FISH) test results confirmed that the small chromosome fragment was a portion of the heterochromatic part of the Y chromosome. The entire male specific region of Y (MSY) and the pseudoautosomal region on the Y were absent. The gonads were subsequently removed by standing laparoscopic surgery. Histologically the gonads were devoid of any normal ovarian or testicular structures. Development of a male or female reproductive tract is normally dictated by the genetic sex of the spermatozoon that fertilizes the oocyte. If the sperm carries a normal Y chromosome, the horse should have a 64, XY karyotype. The presence of an SRY region on the Y chromosome should drive differentiation of the gonads toward testicular development. Production of AMH by Sertoli cells and testosterone by Leydig cells of a normal testis would suppress development of the Müllerian duct and stimulate development of the Wolffian duct, respectively. Conversion of testosterone to dihydrotestosterone (DHT) by the enzyme 5α-reductase in peripheral tissues should lead to formation of a penis and scrotum. However, in the present case, absence of an SRY region on the Y chromosome lead to failure of gonadal development and subsequent low concentrations of the hormones AMH, testosterone and DHT led to formation of female internal and external genitalia. A chromosomal abnormality should be suspected in adult mares with bilaterally small, inactive ovaries during the physiologic breeding season that have not been treated with exogenous hormones or vaccinated against gonadotropin releasing hormone.

Keywords: Equine, genetic infertility, sex-reversal syndrome, chromosomal abnormality