History

A 6-year-old 31-kg sexually intact male German Shepherd Dog was presented to an emergency hospital because of a sudden-onset of lethargy, vomiting, and inappropriate urination. The owner recalled that 3 weeks earlier, the dog had a small amount of blood in its urine, which quickly resolved without treatment. The dog had no prior history of medical issues. The owner acquired the dog when it was approximately 8 weeks of age. The dog was administered heartworm, flea, and tick preventatives, and kept up-to-date with vaccinations against rabies, canine distemper, adenovirus, paramyxovirus, and parvovirus. The dog was reported to be bilaterally cryptorchid and had not been castrated.

Clinical and Gross Findings

On physical examination, the dog had mildly enlarged nipples, signs of pain elicited during abdominal palpation, high rectal temperature (39.6 °C), results of serum biochemical analyses within reference limits, and leukocytosis (28,000 WBCs/µL; reference range, 5,050 to 16,760 WBCs/µL), with neutrophilia (22,800 cells/µL; reference range, 2,950 to 11,640 cells/µL) and band neutrophils. The dog’s urine pH was 8.0, with a urine specific gravity of 1.033 and sediment that contained cocci, RBCs (3+ on a scale of 4), and WBCs (2+ on a scale of 4). The dog was admitted to the hospital and administered lactated Ringer solution and ampicillin-sulbactam IV. Ultrasonography revealed moderate abdominal effusion and a possible undescended right testicle that was mottled and irregular in appearance but well encapsulated. In the leftward midportion of the abdomen, a hypoechoic, encapsulated mass was caudal to the left kidney and was continuous with a fluid-filled structure that appeared to abut or originate from the cranial aspect of the prostate. The dog was taken to surgery for exploratory laparotomy (Figure 1).

Formulate differential diagnoses, then continue reading.

Figure 1—Photograph obtained during exploratory laparotomy in 6-year-old sexually intact male German Shepherd Dog with sudden-onset of lethargy, vomiting, and inappropriate urination. The penis (asterisk) lies to the left of (above) the incision.

Clinical and Gross Findings

At surgery, thin purulent effusion originated from a perforation in a large bicornuate structure, consistent with a distended uterus. This structure extended into the pelvic canal such that its caudalmost extent could not be identified. Gonads grossly appeared to be an enlarged right testicle and atrophied left testicle (Figure 2). The abnormal tissues were removed and placed in neutral-buffered 10% formalin for histologic evaluation. Cytologic examination of the fluid revealed moderate numbers of neutrophils with rare intracellular cocccoid bacteria, consistent with a septic effusion. While hospitalized, the dog received IV administration of lactated Ringer solution, antimicrobials (ampicillin-sulbactam and enrofloxacin), and hydromorphone. Following hospital discharge, the dog was treated with amoxicillin-clavulanic acid, carprofen, and gabapentin. The dog recovered from surgery uneventfully, and the clinical signs resolved.

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https://doi.org/10.2460/javma.19.07.0336
Histopathologic and Microbiological Findings

Histologic examination of sections of the removed tissue confirmed that the observed bicornuate tubular structure was a uterus, with walls of smooth muscle and a central mucosal lining of endometrium. Mucosal glands were dilated. There were extensive infiltrates of mixed inflammatory cells, including neutrophils, lymphocytes, plasma cells, and macrophages, in the tubular lumen as well as in the dilated mucosal glands and lamina propria. Regionally, the mucosa was ulcerated, and the underlying lamina propria was edematous and superficially necrotic. Transmurally, blood vessels were dilated and surrounded by perivascular cuffs of lymphocytes and plasma cells (Figure 3). Bacteria were not seen in the examined sections.

The enlarged right gonad had a broad, irregularly expanding multilobular mass within the preexisting testicular parenchyma. The mass was composed of closely packed irregular tubules lined by pseudostratified to stratified rows of hypertrophic, hyperchromatic, and elongated Sertoli-type cells. Each cell had a moderate amount of deeply amphophilic cytoplasm and an eccentric to basally oriented, round, and vesicular nucleus. Nests and clusters of tubules were supported by fibrovascular stromal septa (Figure 4). The mass was confined by the testicular tunics, and the mitotic rate was low.

Both testicles had marked atrophy of seminiferous tubules, which were lined only by Sertoli cells, and had a loose fibrous intertubular stroma containing clusters of interstitial cells. Epididymal tubules associated with both testicles were well formed and did not contain spermatocytes. Neither testicle contained any ovarian tissue, and both were closely associated with the uterus.

Results of aerobic and anaerobic microbial cultures of septic effusion specimens were negative. However, the dog had received treatment with antimicrobials during the course of stabilization and diagnostic evaluation prior to surgery.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis and case summary: bilateral cryptorchidism with seminiferous tubule atrophy, unilateral Sertoli cell tumor, and pyometra attributable to persistent Müllerian duct syndrome (PMDS) in a male German Shepherd Dog.

Comments

In the dog of the present report, the presence of a uterus was consistent with PMDS, a condition in which a male has testes and male genitalia but also
retains oviducts, a uterus, a cervix, and the cranial portion of a vagina that terminates on the prostate. The condition is exceedingly rare, being most frequently reported in humans. There are rare reports of PMDS in male cats, goats, and beavers and European bison. Persistent Müllerian duct syndrome in dogs has been described, and a familial predisposition to PMDS among Miniature Schnauzers was initially noted in 1982. During embryonic development of males, the primitive mesonephric kidney is invaded by germ cells and becomes a testis, and its associated ducts become the male sexual duct system, which is sustained by secretion of testosterone by testicular Leydig cells. In females, the mesonephric ducts regress in the absence of testosterone. Concurrently, a paramesonephric duct, also known as the Müllerian duct, forms laterally alongside the mesonephric system and persists in females as the female sexual duct system (oviducts, uterus, and cranial portion of the vagina). In male embryos, Sertoli cells produce Müllerian inhibiting substance (MIS), a glycoprotein of the transforming growth factor-β family, which causes regression of this paramesonephric ductal system. Failure of the paramesonephric duct to regress in a male is usually attributable to an abnormality in the gene encoding for either MIS or its receptor. In Miniature Schnauzers, the condition is the result of a point mutation in the gene encoding the MIS type II receptor. Human cases have been linked to various mutations both in the MIS gene and in the gene for its receptor. Genetic testing of humans for persistent Müllerian duct syndrome is available; for other animals, histologic confirmation of the nature of the gonad and associated reproductive ducts is diagnostic.

In males with PMDS, the presence of a uterus frequently interferes with normal testicular descent, resulting in cryptorchidism. In other cases, the paramesonephric structures are pulled through the inguinal canal, resulting in an inguinal hernia. An important consideration of PMDS and the associated cryptorchidism is the neoplastic transformation of the descended testis. The incidence of Sertoli cell tumors in cryptorchid dogs is approximately 13 times that of dogs with descended testicles, and 25% to 50% of those tumors are functional; seminomas are slightly less common and develop most commonly in testes that are retained in the inguinal canal. Dogs with Sertoli cell tumors often have signs of hyperestrinism, such as gynecomastia, bone marrow suppression, and truncal alopecia, and the dog of the present report did have gynecomastia. However, high serum estrogen concentration is absent in a considerable percentage of dogs with signs of hyperestrinism. In dogs with signs of hyperestrinism, it is possible that estrogen secretion is episodic or that the estrogen hormones that are secreted do not react with the standard assay. Functional Sertoli cell tumors also secrete high amounts of inhibin, which reduces testosterone secretion through negative feedback on the hypothalamic-pituitary-gonad axis. Low testosterone concentrations lead to atrophy of normal seminiferous tubules in both the affected and contralateral testicles. Aspermatogenesis is expected in cryptorchid testicles because the production of viable sperm requires that testicular temperature is 2 °C to 4 °C less than core body temperature.

Other embryonic disorders of development related to the male reproductive system include hermaphroditism, pseudohermaphroditism, and sex reversal. True hermaphrodites have both ovarian and testicular gonadal tissue, whereas pseudohermaphrodites have gonads appropriate to their chromosomal sex but external genitalia of the opposite sex. Sex reversal is an exceedingly rare condition wherein a patient's gonadal sex does not correspond to their chromosomal sex (eg, a female with an XY genotype or a male with an XX genotype). Patients with PMDS are neither true hermaphrodites nor pseudohermaphrodites because the gonad is entirely testicular and the external genitalia are consistent with the testicular gonad, and sex reversal is not consistent with PMDS because phenotypic males do not develop a female reproductive tract. Therefore, PMDS is characterized as an XY disorder of sexual development.

Although exceedingly rare, there have been other case reports of pyometra in male dogs (all with cryptorchid testicles), a male cat, and a male goat. Production of sex steroids by the Sertoli cell tumor may have predisposed the dog of the present report to the development of pyometra.

Acknowledgments

The authors thank Dr. Stacey Dworkin for her intraoperative and gross pathology photographs and Dr. Joan Smyth for the photomicrographs.

The authors declare that there were no conflicts of interest.

Presented in poster form at the 2016 American College of Veterinary Pathologists/American Society for the Veterinary Clinical Pathology annual meeting in New Orleans, December 2016.

References


