Hermaphroditism in a Miniature Schnauzer

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Abstract

A nine-year-old male Miniature Schnauzer was examined because of a one month history of progressive abdominal distention and lethargy. The patient presented with gynecomastia and neither testicle was identified within the scrotum. Abdominal radiographs and abdominal ultrasonography revealed bilateral gonadal masses and an enlarged and elongated fluid-filled uterus with echogenic contents, consistent with pyometra. Gonadohysterectomy and histopathology were consistent with true hermaphroditism, with the abdomen containing one right testicle with an associated Sertoli cell tumor and contralaterally a left ovary with a granulosa cell tumor. The dog recovered from surgery without complications. There appears to be no association between true hermaphroditism and persistent Mullerian duct syndrome, a common inherited disorder in the Miniature Schnauzer breed, where the Mullerian ducts fail to regress after testicular development. Cryptorchidism is an important clinical problem and affected animals and/or carriers of this genetic defect should not be used for breeding. Either persistent Mullerian duct syndrome or true hermaphroditism should be considered as a cause for cryptorchidism in the Miniature Schnauzer breed.

Keywords: Hermaphroditism, cryptorchidism, Miniature Schnauzer

Clinical report

A nine-year-old male Miniature Schnauzer was referred for examination following a one month history of progressive abdominal distention and concurrent lethargy. Findings observed upon physical examination included a distended abdomen with a pendulous appearance and bilateral perineal hernias. Testes were not present within the scrotum nor palpable within the area of the external inguinal rings. A large (approximately 5 cm) non-painful mass was palpated in the mid-abdomen. The prepuce and penis appeared to be normally developed. Gynecomastia was also evident. The results of a complete blood count and serum biochemistry tests showed a mildly decreased hematocrit (29%; reference range, 36-62%), along with a mild non-regenerative anemia (5.01 x 10^6/ul; reference range, 5.5-8.5 x 10^6/ul) and hyperglobulinemia (4 g/dl; reference range, 1.6-3.6 g/dl).

Imaging diagnosis and outcome

Abdominal radiographs were performed (Figure 1). There were multiple round, smoothly marginated soft tissue structures within the ventral abdomen, which caused caudal displacement of the urinary bladder, dorsal displacement of the small bowel, and dorsal displacement of the pylorus of the stomach on the lateral view. On the ventrodorsal view, an elongated soft tissue opacity extended along the left and right lateral abdominal walls. This tubular structure was approximately 6 cm in width on the ventrodorsal view. There was slightly reduced serosal detail within the ventral mid-peritoneal space. The nipples of several mammary glands were prominent. The primary differentials for the two well-defined oval masses within the ventral abdomen included cryptorchidism and testicular neoplasia. Based on these findings an ultrasound examination of the abdomen was recommended and performed.

On abdominal ultrasonography, there was echogenic swirling fluid contained within a tubular, elongated and thin-walled structure, which extended cranially to the level of the right lateral liver lobe (Figure 2). The structure was located superficial to the duodenum, caudate lobe of the liver and right kidney. There was a heterogenous hypoechoic 9 cm long by 7 cm deep mass within the left

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hemiabdomen cranial to the head of the spleen. Additionally, a hyperechoic distal shadowing 11 cm long mass was noted within the right abdomen. The urinary bladder was caudally displaced. Two medial iliac lymph nodes were enlarged and measured 1.9 cm in diameter. On the basis of the collective ultrasound findings, pyometra, hydrometra, or mucometra with concurrent ovarian or testicular neoplasia associated with hermaphroditism was suspected. The enlarged medial iliac lymph nodes were most consistent with lymphoid hyperplasia.

An exploratory celiotomy was performed. A grossly enlarged fluid filled uterus was observed upon entering the abdomen. The uterus joined what appeared to be the cervix just prior to entering the prostate gland. The uterus was ligated immediately adjacent to its entry into the prostate gland. The prostate was enlarged, but appeared smooth and symmetrical. Two masses were observed and appeared to be the right and left gonads. Each mass was also found to be attached and closely associated to the distal aspect of the fluid-filled uterine horn (Figure 3). The left gonadal mass was severely enlarged and irregular. The right gonadal mass was much smaller (approximately 4 cm). A gonadohysterectomy was performed and the abdomen was closed routinely. The uterine body was opened and several hundred milliliters of thick, dark green malodorous fluid consistent with a purulent exudate was drained from the uterus. The dog had an uneventful recovery from surgery, was subsequently discharged and was reported to be normal one month following the surgery.

Each gonadal mass was submitted for histopathological examination. The larger left gonadal mass was identified as an ovary completely effaced by a variably multicystic and solid mass obliterating the normal ovarian architecture. The mass was composed of nests, tubules and cords of triangular to papillary structures supported by fibrous stromal septae that formed and partially delineated cystic spaces. The neoplastic cells had ill-defined borders and vacuolated eosinophilic cytoplasm. The nuclei were oval and had smudged chromatin. The nucleoli were indistinct. Mitotic figures were uncommon.

The smaller right gonadal mass was identified as testicle, containing an attached epididymis. The testicle was moderately enlarged and effaced by irregularly sized tubules filled with Sertoli cells. The Sertoli cells were triangular shaped and were often palisading. They had moderate amounts of vacuolated light basophilic cytoplasm. The nuclei were ovoid and mildly pleomorphic. The tubules were subdivided by a fine fibrous to fibrovascular stroma.

The diagnosis was true hermaphroditism, with the abdomen containing one right testicle with an associated Sertoli cell tumor and contralaterally, a left ovary with a granulosa cell tumor.

Discussion

Since the reproductive tracts of males and females develop fundamentally from the same embryonic primordium, incidental fusion defects or the occasional failure of structures to unite results in the idiosyncrasy of both sexes being identified within the same individual.[1] In true hermaphroditism, there is both ovarian and testicular tissue recognized as being either united or separated.[1] On the other hand, pseudohermaphroditism is a much more common condition in which the chromosomal and gonadal sexes are identical, but the development of the internal or external genitalia is indeterminate or opposed.[2]

In normal males, the Mullerian ducts regress after testicular development, secondary to androgen-dependent masculinization.[2] Mullerian inhibiting substance (MIS), which is made by Sertoli cells, must be generated at a specific period in the development of the embryo to allow for the proper regression of the Mullerian ducts in males.[2] The Mullerian ducts will eventually develop into the fallopian tubes, uterus, cervix and the cranial portion of the vagina. Persistent Mullerian duct syndrome (PMDS) is a syndrome in which these derivatives do not regress in individuals having normal male chromosomal composition (XY karyotype) and bilateral testicles.[2] Several cases and case series involving PMDS in Miniature Schnauzers have been reported.[2-8] These animals are sometimes cryptorchid (either unilaterally or bilaterally) but have no clinical abnormalities. This is due to the fact that testosterone production or action is not modified in any way, and the animal has the visible appearance of being male.[8] A recent study has identified that genetic defects in the MIS receptor, *MISRII*, are causative in canines.[9] Mutation of the *MISRII* receptor gene results in the encoded receptor protein being shortened and impaired or dysfunctional.[2] In patients with genetic defects in the MIS receptor, the MIS bioactivity was equivalent during regression of the Mullerian ducts, when compared with age-matched controls, confirming normal functional levels of MIS.[9] Persistent Mullerian duct synrome has been identified as an inherited disorder in both the Miniature Schnauzer breed and Bassett Hound breeds in various countries.[9,10] There have been other reports in the literature describing this syndrome in other breeds as well.[11-15] Persistent Mullerian duct synrome is a representation of male pseudohermaphroditism, and is inherited as an autosomal recessive trait in the Miniature Schnauzer breed.[16]

Other abnormalities in addition to neoplasia and pyometra have also been associated with PMDS, including urinary tract infections and prostatitis.[8] The uterus of the dog described here was severely dilated with several hundred milliliters of greenish colored, malodorous fluid consistent with a purulent exudate. The severely enlarged uterus was causing displacement of the intraabdominal organs, including severe caudal deviation and compression of the urinary bladder, to the point where it was partially intrapelvic in location. In spite of this, the animal had no clinical history of urinary abnormalities or infection involving the urinary tract. Given the fact that the cervix appeared to be communicating with the prostate gland, we suspect that the most likely route of infection for the pyometra was via this communication with the prostate gland and prostatic urethra.

The Miniature Schnauzer of the present report was bilaterally cryptorchid, and therefore, sterile. The patient was never recognized as being abnormal by the owners, and no clinical abnormalities were ever displayed by the dog until, approximately 1onemonth prior to presentation when progressive abdominal distention was noticed by the owners. Subsequent examination by the referring veterinarian revealed bilateral perineal hernias, an abdominal mass and gynecomastia. One of the two masses described in this dog was a Sertoli cell tumor. Sertoli cell tumors are a common sequelae to cryptorchidism in PMDS. Additionally, pyometra has also been noted in older Miniature Schnauzers with PMDS. The historical and physical examination findings of cryptorchidism, in conjunction with gynecomastia, cultivated the belief that at least one of the intraabdominal testes had undergone neoplastic transformation (Figure 4). Outward physical signs of feminization in male dogs can be the result of exuberant estrogen being produced by the Sertoli cells and is frequently associated with testicular neoplasia, particularly Sertoli cell tumors.[8] Attractiveness to other male intact dogs in our patient could not be confirmed as the dog was never around other dogs. Preputial cytology could have been used to quickly verify the exposure to estrogen, by visualizing superficial cells.[17] With estrogen exposure, keratinization of the preputial mucosa may be present. The preputial mucosa becomes cornified and cytologically will have a similar appearance to that of vaginal cytology from an estral bitch. Preputial cytology is highly sensitive and specific for diagnosis of estrogen producing testicular tumors in canines and in particular, dogs with estrogen-induced alopecia,[17] although alopecia was not detected in the patient of this report. Repeated exposure to estrogen likely caused the cervix to dilate, leading to an ascending infection, and subsequent pyometra.

There is no apparent association between PMDS and true hermaphroditism. Persistent Mullerian duct syndrome is associated with pseudohermaphroditism and true hermaphroditism is a separate disorder. Affected animals and/or carriers of this genetic defect should not be used for breeding. This is especially important as the condition cannot be confirmed with physical examination alone. Additionally, some animals with PMDS may only be unilaterally cryptorchid, allowing them to be capable of fertile matings. A molecular diagnostic test has been reported for PMDS in the Miniature Schnauzer breed to diagnose all affected animals, as well as carriers.[10] The test involves polymerase chain reaction amplification and gel electrophoresis, which would allow a relatively quick interpretation.[10] Clearly, the test would only need to be performed in dogs that are not cryptorchid. There is optimism that this test will allow breeders to avoid breeding affected dogs, as well as carriers. The test would serve to promote the well-being of the Miniature Schnauzer breed, and should allow this syndrome to be eradicated from the breed completely.

The lack of genetic testing including chromosomal analysis, and historical pedigree analysis in our patient was unfortunate as it would have added to the academic knowledge of this case and allowed us to more accurately describe the disorder of sexual development. Important information can be attained by including genetic testing with chromosomal and endocrinologic analysis. For example, it would have been easy to test for estrogen production by the Sertoli cell tumor, as well as for the presence of progesterone, which could have further validated the suspicion of pyometra in this dog. However, the presence of a testicle with Sertoli cells indicates the probable presence of a Y chromosome and the likelihood of a normal XY karyotype. The clinical signs of feminization of this patient, in conjunction with historical cryptorchidism and abdominal distention indicated the need for diagnostic imaging to visualize potential neoplastic transformation. It should be noted that the physical examination finding of bilateral cryptorchidism in a Miniature Schnauzer may signify either PMDS or true hermaphroditism, as in the present report. In either case, an exploratory celiotomy should be performed.

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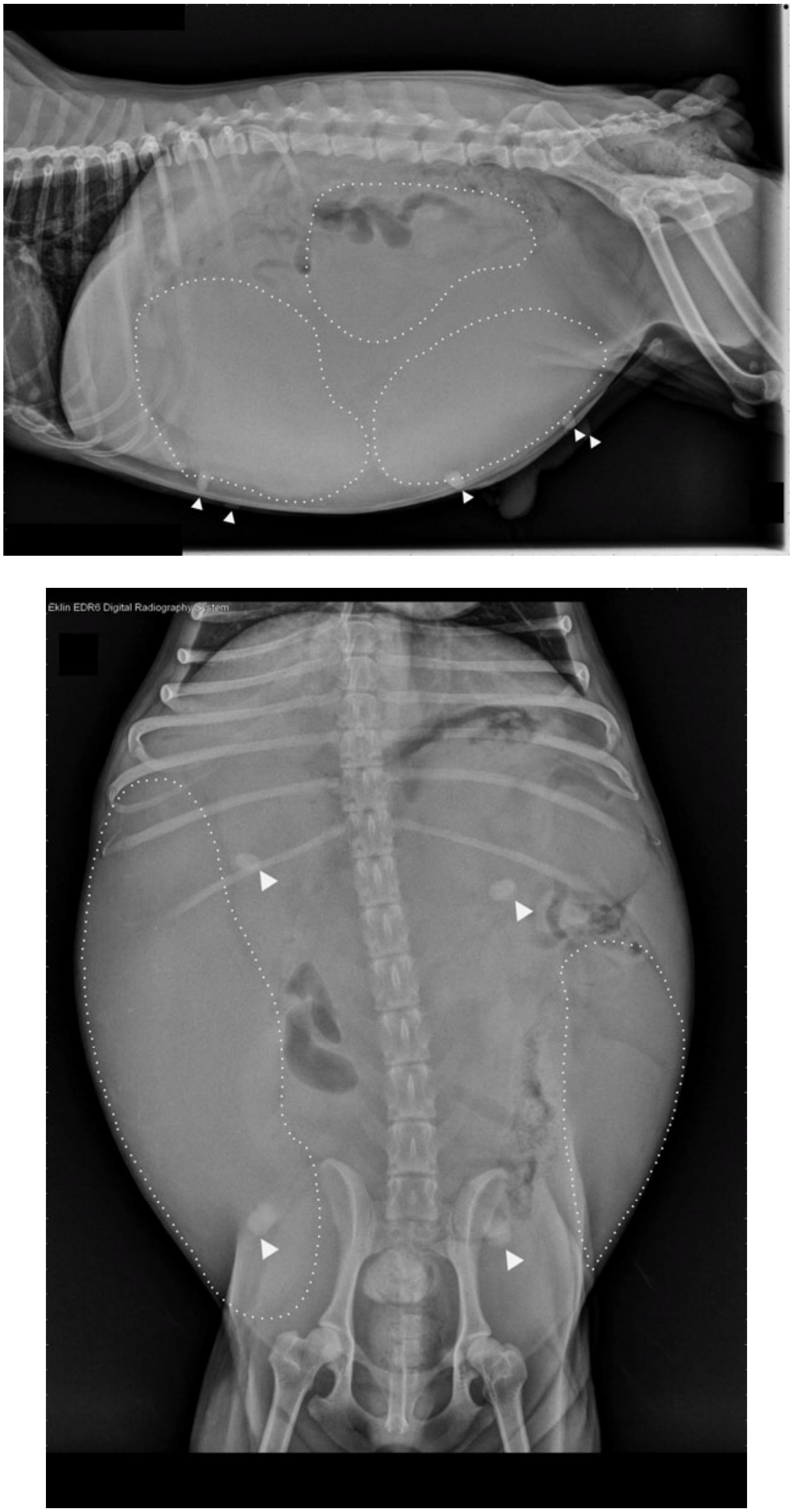

Figure 1. Right lateral (top) and ventrodorsal (bottom) radiographs. Multiple enlarged soft tissue opacities are noted in the abdomen, displacing the small intestinal tract dorsally and the stomach craniodorsally on the lateral image (outlines). Enlarged tubular soft tissue opacities are noted along the lateral abdominal walls on the ventrodorsal image (arrows). The nipples are prominent (arrowheads).

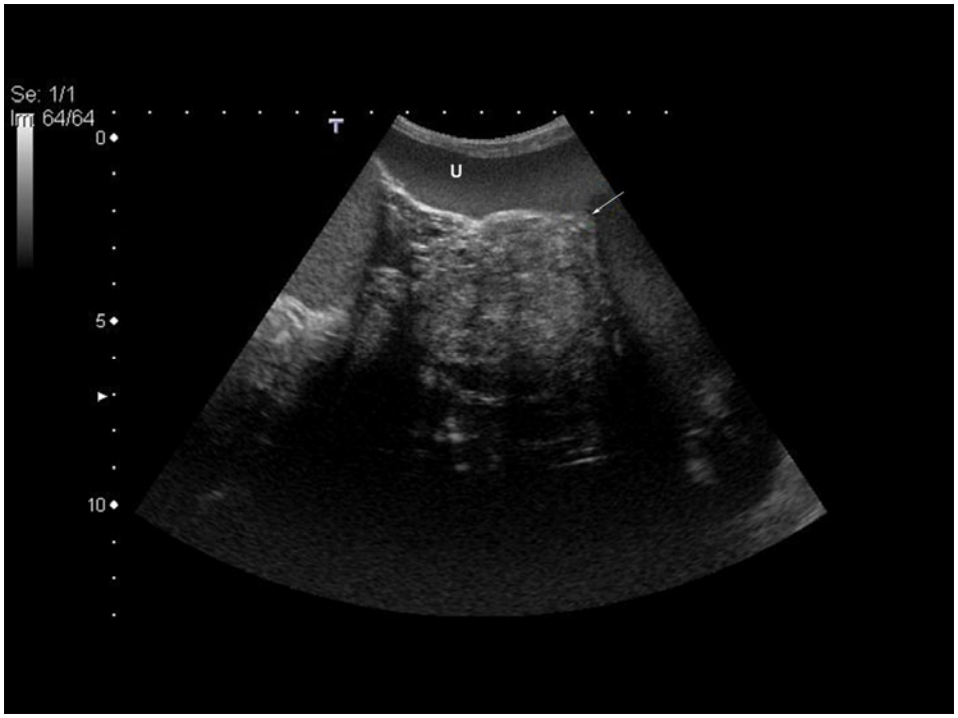

Figure 2. Longitudinal ultrasound image of the lateral aspect of the left hemiabdomen. The left uterine horn (U) is markedly enlarged and contains echogenic material within the lumen. A large, rounded, heterogenous and predominantly solid ovarian tumor is noted (arrow).

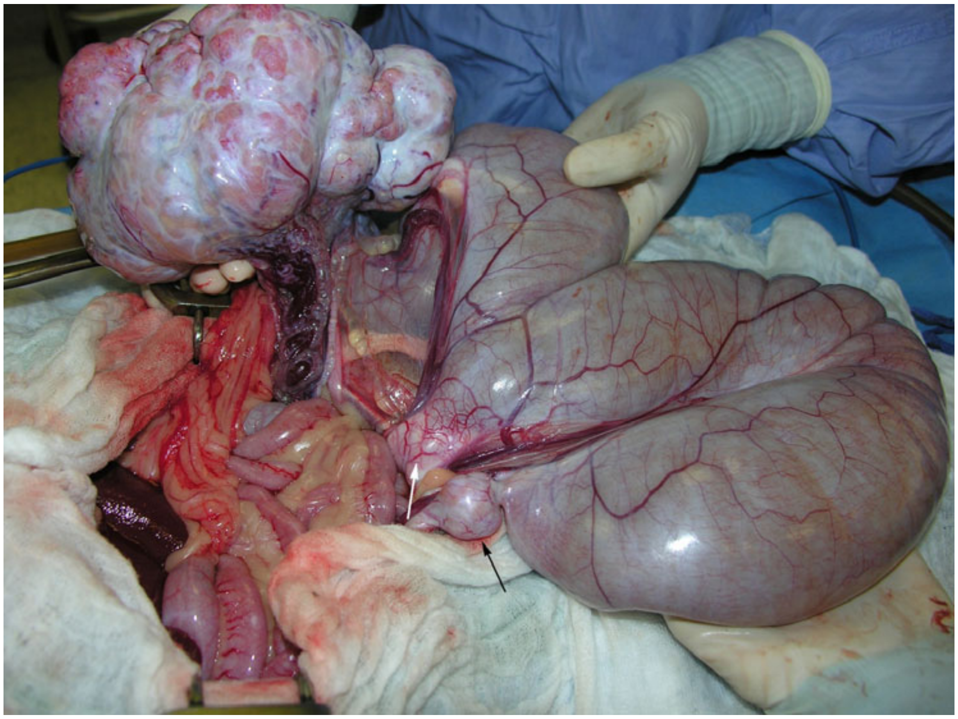

Figure 3. Exteriorization of the reproductive tract intraoperatively. Both tumors can clearly be seen, along with the pyometra, as well as their anatomical association. The cervix is also visible (white arrow). The larger ovarian mass is being held by the surgeon's hand. The smaller testicular mass is indicated by the arrow.

Figure 4. Postoperative image demonstrating the gynomastia.

(Edotor's note: The photographs in this paper are available in color in the online edition of Clinical Theriogenology.)