Developmental uterine anomalies in cats and dogs undergoing elective ovariohysterectomy

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Objective—To describe the characteristics and frequency of gross uterine anomalies in cats and dogs undergoing elective ovariohysterectomy.

Design—Prospective and retrospective case series.


Procedures—Clinics prospectively reported gross anomalies and submitted tissues from abnormal reproductive tracts identified during surgery. Records from a feral cat spay-neuter clinic were evaluated retrospectively.

Results—Suspected congenital anomalies of the uterus were identified in 0.09% (49/53,258) of female cats and 0.05% (15/32,660) of female dogs. Uterine anomalies included identified unicornuate uterus (33 cats and 11 dogs), segmental agenesis of 1 uterine horn (15 cats and 3 dogs), and uterine horn hypoplasia (1 cat and 1 dog). Ipsilateral renal agenesis was present in 29.4% (10/34) of cats and 50.0% (6/12) of dogs with uterine anomalies in which kidneys were evaluated. Mummified ectopic fetuses were identified in 4 cats with uterine anomalies. Both ovaries and both uterine tubes were present in most animals with uterine anomalies.

Conclusions and Clinical Relevance—Urogenital anomalies were twice as common in cats as in dogs. Identification of uterine developmental anomalies in dogs and cats should trigger evaluation of both kidneys and both ovaries because ipsilateral renal agenesis is common, but both ovaries are likely to be present and should be removed during ovariohysterectomy. (J Am Vet Med Assoc 2010;237:542–546)

It is not uncommon for veterinarians to observe anomalies of the uterus during elective ovariohysterectomy surgeries in cats and dogs. In animals in which 1 abnormality is found, other urogenital anomalies, particularly ipsilateral to the abnormality, may also be present.1–12 Uterine anomalies such as unicornuate uterus and segmental agenesis have been detected in many domestic species, including cats, dogs, cows, horses, deer, sheep, pigs, ferrets, and alpacas.1–8,14–22 In several retrospective studies, the prevalence of uterine anomalies in livestock13–16 and women has been evaluated.9 However, no large-scale studies have been conducted to determine the frequency of congenital uterine anomalies in cats and dogs. An association between uterine anomalies and renal agenesis has long been recognized in women,10 as well as in dogs and cats,1–8 but has not been reported for any other domestic species. One common finding in all species is the presence of both ovaries in most individuals with detected urogenital anomalies.1–8,14–16

Uterine anomalies in women are classified according to the degree of failure of usual development.23 The classification scheme for women cannot be directly applied to dogs and cats because women have a simplex uterus and dogs and cats have a bicornuate uterus, but the same principles can be applied. Uterine horns can have developmental abnormalities ranging in severity from hypoplasia to complete agenesis. The degree of development or developmental failure is determined by the histologic appearance of the tissue. In cats and dogs, anomalies are best described as hypoplastic uterine horn, segmental agenesis of a uterine horn, and unicornuate uterus. Hypoplastic uterine horn is defined as a uterine horn that is underdeveloped but still possesses fairly normal tissue layering and a lumen connecting it to the uterine body. Unicornuate uterus is defined as complete agenesis of 1 uterine horn. In that situation, the tissue in place of the uterine horn that connects the uterine body to the uterine tube lacks normal layering and a lumen and is often referred to as a rudimentary horn in human and veterinary medicine. Segmental agenesis is defined as an undeveloped portion of the uterine horn.

The purpose of the study reported here was to determine the types and frequency of uterine anomalies and the incidence of concomitant ipsilateral renal agenesis in cats and dogs undergoing elective ovariohysterectomy.

Materials and Methods

Animals and case selection—Data on dogs and cats from 26 spay-neuter clinics from across the United States and Canada were eligible for inclusion in the study. For the prospective portion of the study, each

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clinic reported the total number of ovariohysterectomy procedures performed in cats and dogs during the study period of January through December 2007. A detailed report form was completed for each reproductive tract in which developmental anomalies were identified grossly. Acquired anomalies such as ovarian cysts and pyometra were not included. Although examination of the kidneys is not routinely performed during elective ovariohysterectomy, surgeons were asked to evaluate the presence and location of both kidneys when anomalies in the uterus were identified. The kidneys were not evaluated in animals with grossly normal tracts.

For the retrospective portion of the study, records from February 2002 through December 2006 from a feral cat spay-neuter program in Florida were reviewed for recorded anomalies. Tissues were not available for these cases, but the gross descriptions were included with the prospectively collected cases.

Tissue collection and evaluation—Reproductive tracts in which anomalies were identified were submitted in neutral-buffered 10% formalin for histologic evaluation. Each tract was photographed and measured. Representative cross-sectional samples of each ovary, uterine horn, and uterine body were paraffin-embedded, sectioned, and stained with H&E. Sections of the rudimentary horns were stained with Masson trichrome stain to differentiate between connective tissue and smooth muscle. The uterine horns were evaluated for the presence and thickness of the endometrium, endometrial glands, myometrium, and perimetrium. The ovaries were evaluated for the presence and number of follicles and corpora lutea.

Gross and histologic findings were used to classify the anomalies into anatomic groups and to identify their likely embryological basis. Uterine horns and the uterine body are usually composed of 3 layers (endometrium, myometrium, and perimetrium), with endometrial glands in the endometrial layer and organized blood vessels in the myometrium and perimetrium. Uterine horns lacking a central lumen and endometrial layer and composed of disorganized connective tissue, smooth muscle, and blood vessel components were classified as unicorneatus uterus. Similar findings involving only a portion of the horn were classified as segmental agenesis. Depending on the portion of the uterine horn affected, the horn was classified as communicating or noncommunicating with the uterine body. Horns with a central lumen containing microscopic remnants of intact endometrial, myometrial, and perimetrical layers were classified as hypoplastic (Appendix).

Results

Animals—During the 1-year study period, 46,229 cats and 32,660 dogs underwent ovariohysterectomy at the spay-neuter clinics. Records from 7,029 feral cats undergoing ovariohysterectomy from February 2002 through December 2006 were retrospectively evaluated. Forty-nine of 53,258 (0.09%) cats and 15 of 32,660 (0.05%) dogs had gross uterine anomalies that were detected by the surgeon. Most cats (45/49 [92%]) and dogs (8/15 [53%]) with uterine anomalies were of mixed breed. Of the cats, there was also 1 Ragdoll and 3 unknown breeds. Age of affected cats ranged from 8 weeks to 8 years. Of the dogs, there was 1 each of Rottweiler, Australian Terrier, Beagle, Japanese Chin, Jack Russell Terrier, Chihuahua, and Pekingese. Age of affected dogs ranged from 8 weeks to 4 years.

Uterine abnormalities—The most common anomaly in cats was unicornuate uterus, which was present in 33 (0.06%) cats (Table 1). Ipsilateral renal agenesis was reported for 7 of the 25 (28%) cats with a unicornuate uterus in which the kidneys were evaluated. Other findings associated with unicornuate uterus included umbilical hernia (n = 1 cat), ipsilateral kidney positioned in the pelvic region (1), cranially displaced ovaries (2), and inability to locate the ipsilateral ovary during ovariohysterectomy (4). Fifteen cats had segmental agenesis of a uterine horn. Most abnormal tracts (n = 11) with segmental agenesis had obvious fluid distention in the proximal patent segments of the horns. Most horns (n = 13) with segmental agenesis were noncommunicating with the uterine body and missing the caudal portion of the uterine horn just proximal to the uterine bifurcation. One tract was missing the midsection, and another had segmental agenesis of both horns at both cranial and caudal locations. Ipsilateral renal agenesis was reported for 3 of the 9 cats with segmental agenesis in which the kidneys were evaluated.

Three dogs had segmental agenesis of a uterine horn. The kidneys appeared grossly normal in the 1 dog in which they were evaluated. One tract was missing the midsection of a horn. A second had segmental agenesis affecting both horns, one located cranially closest...
to the ovary and the other located caudally and non-
communicating with the uterine body. In both dogs, the
affected uterine horns were grossly distended with
fluid cranial to the undeveloped segment. The third dog
had segmental agenesis of the uterine body just cranial
to the cervix. A short segment of the uterine body was
present, allowing the horns to communicate with each
other, but the lumen ended in a blind pouch and did
not communicate with the cervix. Both uterine horns
were severely distended with fluid.

Uterine horn hypoplasia was identified in 1 cat and
1 dog. In both situations, the horn of the affected side
was markedly smaller than the contralateral horn and a
central lumen was identified. The affected dog also had
ipsilateral renal agenesis.

Eight cats and 1 dog with unicornuate uterus were
pregnant, lactating, or both or had a history of previ-
ous litters, abortions, or both. Two of these cats also
had mummified ectopic fetuses in their abdominal cav-
ity identified at surgery. One of the affected cats had 2
ectopic fetuses attached to the abnormal tissue on the
side of the anomaly and was nursing 1 kitten. The other
cat was pregnant in the left uterine horn and was miss-
ing the right uterine horn and ovary, and the mummifi-
cated fetus was floating free in the abdomen. Five cats
with segmental agenesis were pregnant, lactating, or
both or had a history of previous litters, abortions, or
both. Two of these cats also had mummified ectopic fe-
tuses in their abdomen. Both fetuses were attached to
the abnormal tissue on the side of the anomaly, and in
both situations, the ovary on the affected side was not
identified.

Surgeons were unable to identify both ovaries in 8
of the 49 (16%) cats and in 1 of the 15 (7%) dogs with
uterine anomalies. Of these animals, ovaries were iden-
tified in the submitted tissues of 1 cat. Three cats and 1
dog did not have tissues available for evaluation, and 4
had tissue in which an ovary was not identified grossly
or histologically. Confirmation that ovarian tissue was
present but not observed during surgery in these cases
would require postsurgical hormonal testing, which
was not performed in this study. The dog with the lack-
ing ovary had ipsilateral renal agenesis. None of the cats
had renal agenesis, and 7 of the lacking ovaries were
reported on the ipsilateral side.

In animals with a unicornuate uterus, the underdevel-
oped horn was often lacking or described as threadlike (Figure 1). Feline uteri were often clamped and ligated at the uterine bifurcation during ovariohysterectomy, so submitted unicornuate horns were often received by the investigators in a sepa-
rated state. Endometrial components were not identi-
fied in histologic evaluation of the abnormal horns in
unicornuate uteri. Fibrous mesenchymal tissue with some smooth muscle differentiation and blood
vessels was present, and the tissue was similar to the
broad ligament microscopically (Figure 2). Uterine
horns with segmental agenesis were commonly non-
communicating and had fluid accumulation and dis-
tention in the proximal segment and uterine tube.
The aplastic segment of these horns was microscopi-
cally similar to the abnormal horn of a unicornuate
uterus, whereas the proximal fluid-distended por-
tion of the affected horn and uterine tube had tis-
sue layering, with attenuation and compression of
endometrial glands, fibrous proliferation in the stra-
tum spongiosum of the endometrium, and accumula-
tion of hydrated mucin. The hypoplastic horn of the
single affected feline tract had typical uterine layers,
whereas the hypoplastic horn of the canine tract had
columnar epithelium lining the lumen, but lacked
endometrial stroma and glands.
Discussion

In the study reported here, uterine anomalies were more than twice as common in cats (approx 10/10,000 cats) as in dogs (approx 5/10,000 dogs). More than half of cats and dogs with uterine anomalies also had ipsilateral renal agenesis, but both ovaries were identified in most affected animals.

The association of uterine anomalies with ipsilateral renal agenesis in women has been well described.10,11 Case reports1–8 of similar findings in dogs and cats have also been published, yet large-scale abattoir studies involving cows, sheep, or pigs have revealed no correlation between uterine anomalies and renal agenesis. It appears that most livestock reproductive tracts in those studies15,16 were evaluated after removal from the carcasses, perhaps without concurrent evaluation of the urinary system. Concurrent uterine and renal anomalies can arise as a result of the interdependence between the tracts during embryological development. Both tracts are derived from a common embryonic intermediate mesoderm.24,25 The embryonic mesonephric urinary system develops first, followed by the definitive kidney and reproductive tract.24 The Müllerian duct system gives rise to the uterine tubes, uterus, and vagina. It is believed that the mesonephric ducts induce Müllerian duct formation and guide the ducts in their growth caudally.11 Damage to the mesonephric duct may affect the development of the associated Müllerian duct.11 Many of the same genes and proteins that are required for the development of the reproductive tract are also necessary for the formation of urinary tract tissues, and gene deletions lead to renal agenesis as well as reproductive tract abnormalities.12,20

Aberrations in the development of the Müllerian duct can occur with varying degrees of severity, affecting uterine horn segments (segmental agenesis) or the entire uterine horn (unicornuate uterus).3,6,19,20 Different genes appear to control the differentiation of various segments of the uterine tube, uterine horns, and uterine body.27 In the present study, the unaffected segments of uterine horn contained completely differentiated endometrium and myometrium, although the components were often physically altered by distention and accumulation of luminal debris. The Müllerian ducts form in a cranial to caudal direction; therefore, it is logical that in most situations the cranial portion developed normally, then development arrested before completion.

The cause and heritability of uterine anomalies in dogs and cats are not known.2 It remains uncertain whether genetic, endocrine, or environmental influences are involved or whether abnormalities are primary conditions, develop secondary to the absence of the mesonephros, or are induced by compromise of the blood supply. In segmental uterine horn agenesis, disruption of the blood supply to 1 portion of a uterine horn and the subsequent degeneration or agenesis of the affected segment may occur. This phenomenon appears more likely in situations in which the midsection of a horn is affected rather than the segment proximal to the uterine body. The common finding of agenesis of the segment closest to the uterine body suggests that faulty induction signals or growth factors that control differentiation may be to blame for the defects. Investigations of genetic factors in mice suggest that the mode of inheritance of Müllerian anomalies in women may be polygenic or multifactorial, but most emphasis has been focused on developmental inhibition during embryogenesis.20,21 Mice exposed to diethylstilbestrol have similar anomalies such as absent uterine glands, stratified epithelium, disorganized muscle, and a thin stromal layer.21 Given the many variables involved in the growth and differentiation of the female urogenital tract, the pathogenesis of each abnormality may be multifactorial.

Although uterine anomalies reportedly decrease litter size and increase the incidence of hydrometra, mucocoea, and pyometra in many species,2 fertility in the healthy uterine horn may be preserved as suggested by findings in several animals in our study that were pregnant at the time of surgery or had a history of previous litters. Several cats were found at the time of surgery to have mummified ectopic fetuses in their abdominal cavity that were most often associated with the abnormal uterine horn, but no clinical signs of illness had been detected. Other than in primates, the abdominal cavity is the most common location of ectopic pregnancies.31 Previously reported instances of ectopic fetuses in cats were believed to be secondary to uterine rupture or abnormal uterine anatomy such as unicornuate uterus, with most affected cats having no clinical signs.31

A common characteristic of segmental agenesis in dogs and cats in the present study was the accumulation of fluid in the lumen of the affected uterine horn proximal to the occlusion. The secretion of progesterone during diestrus increases secretory activity of the endometrial glands, allowing fluid to collect in the uterus.2 When there is an occlusion caused by segmental agenesis, fluid accumulates with each estrous cycle.1,3,12 Affected dogs and cats are unlikely to have clinical signs unless they develop pyometra.3,22 No clinical signs were reported in the present study; all animals were undergoing elective ovariohysterectomy at the time of discovery. Only 1 animal, a dog, had segmental agenesis of the uterine body. This abnormality is rare because both uterine horns join to create the uterine body, and for agenesis of the body to occur, there must be agenesis in both uterine horns.

In the present study, 2 cats with unicornuate uterus also had cranial displacement of the ipsilateral ovary. In women, the prevalence of ovarian malposition is higher in patients with uterine anomalies than in patients with unaffected uteri, particularly when the uterus is absent or only partially present.33 In dogs with a unicornuate uterus, the ovary may be located farther from the uterine body on the affected side.3 In situations of segmental or complete uterine horn agenesis, both ovaries are likely to be present, although the ipsilateral ovary may be malpositioned. The surgical incision may need to be extended cranially and the region adjacent to the kidney visualized so that both ovaries can be located and removed.

Our findings suggested that developmental uterine anomalies are uncommon in cats and dogs. However, when anomalies were present in the study animals, they were commonly associated with renal anomalies and occasionally associated with mummified ectopic fetuses.
in the abdomen. Therefore, the finding of unicorneate uterus or segmental uterine horn agensis should trigger an assessment of both kidneys because associated ipsilateral renal agensis may require specific management practices in the future and an exploration of the abdomen for ectopic fetuses. Also, surgeons should be aware that uterine anomalies are usually accompanied by 2 healthy ovaries, both of which should be located and removed during ovariohysterectomy.

References


Appendix

Classification of gross and histologic uterine horn anomalies in dogs and cats.

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Histologically normal layers</th>
<th>Central lumen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unicorneate uterus</td>
<td>No</td>
<td>Genetic difference</td>
</tr>
<tr>
<td>Uterine horn segmental agensis</td>
<td>Only in the healthy segment; usually attenuated by fluid distention</td>
<td>No</td>
</tr>
<tr>
<td>Uterine horn hypoplasia</td>
<td>All layers present, but variably underdeveloped</td>
<td>Only in the healthy segment; enlarged by fluid accumulation</td>
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