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Authors: Brookshire, Wilson C, Shivley, Jacob, Woodruff, Kimberly, and Cooley, Jim

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Uterus unicornis and pregnancy in two feline littermates

Wilson C Brookshire¹, Jacob Shivley¹,
Kimberly Woodruff¹ and Jim Cooley²

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Abstract

Case series summary A queen, tom and four 1-year-old female offspring presented for routine neuter. Two of the littermates (cats 1 and 2) were diagnosed with a uterine abnormality during surgery. The left uterine horn of both cats appeared as a thin, solid, cord-like structure, whereas the right uterine horn of both cats appeared to have intermittent bulges consistent with pregnancy. The two other littermates, queen and tom were reproductively normal. The uteruses of the affected cats were nearly identical with a gross and histopathologic diagnosis of uterus unicornis with concurrent pregnancy. Ovaries were present, bilaterally. An oviduct was present only on the single normally developed and pregnant uterine horn in both cats. At a postoperative follow-up evaluation, abdominal ultrasound was performed on the two cats with uterine abnormalities. Cat 1 was ultrasonographically within normal limits. Cat 2 was diagnosed with ipsilateral renal agenesis on the same side as the absent uterine horn.

Relevance and novel information The complexity of uterus unicornis and renal aplasia is demonstrated by this unique presentation of five related cats for ovariohysterectomy. This report raises questions regarding the genetic, environmental, hormonal or other underlying causes of this anatomic abnormality in cats that may spur additional research. This is the first publication describing uterus unicornis in gravid feline littermates, with one of the cats having ipsilateral renal agenesis. This is also the first publication to describe oviduct agenesis on the affected uterine horn in feline uterus unicornis.

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Case series description

Six cats, including four 1-year-old female littermates, along with the queen and tom, were presented to Mississippi State University's Mobile Surgical Unit for routine neuter. Each of the six cats were apparently healthy and surgery was performed without anesthetic or surgical complications. The cats were anesthetized using dexmedetomidine (Dexdomitor, 35 µg/kg; Zoetis), butorphanol (Torbugesic, 0.35 mg/kg; Zoetis) and ketamine (Ketaset 3.5 mg/kg IM; Zoetis). Carprofen (Rimadyl, 4.4 mg/kg; Zoetis) was administered subcutaneously for pain control. Two of the 1-year-old littermates (cats 1 and 2) were identified as having a uterine abnormality during surgery. At surgery, both cats had identifiable ovaries bilaterally, a thin cord of solid tissue at the site of one uterine horn and a more typical opposite uterine horn with intermittent bulges. The thin, cord-like uterine horn of cat 2 was incidentally detached

from the uterine body during surgery due to tissue friability. The gross diagnosis was uterus unicornis and pregnancy in the normal uterine horn. The reproductive tracts were surgically resected and set aside without opening the uterus, to prevent fetal suffering.¹ The reproductive tissues from both cats were submitted for

¹Department of Clinical Sciences, Mississippi State University College of Veterinary Medicine, Starkville, MS, USA

²Department of Pathobiology and Population Medicine, Mississippi State University College of Veterinary Medicine, Starkville, MS, USA

Corresponding author:

Wilson Cooper Brookshire DVM, MS, DACVPM, Mississippi State University College of Veterinary Medicine, 240 Wise Center Drive, PO Box 6100, Mississippi State, MS 39762, USA
Email: c.brookshire@msstate.edu



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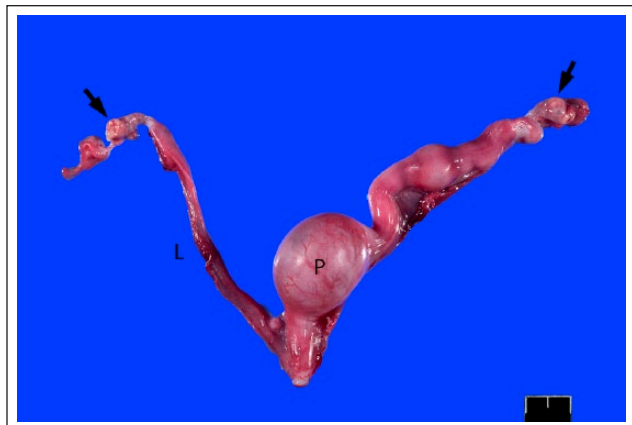


Figure 1 Uterus unicornis, reproductive tract, Cat 1. Left uterine horn (L) is replaced by solid cord of smooth muscle and vascularized loose connective tissue. Ovaries have corpora lutea (arrows). One site of placentation is prominent (P). Bar = 1 cm

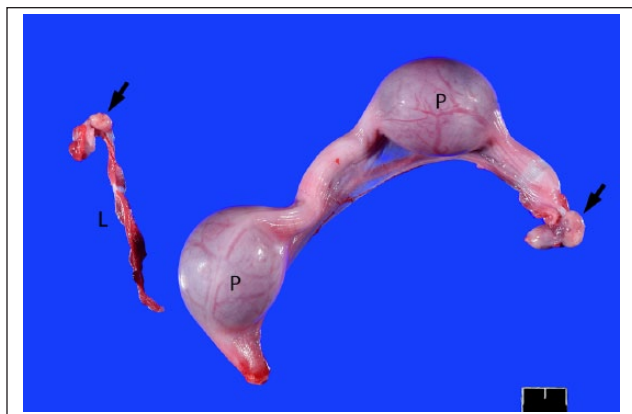


Figure 2 Uterus unicornis, reproductive tract, Cat 2. Left uterine horn (L) is replaced by solid cord of smooth muscle and vascularized loose connective tissue. Detachment occurred during surgery. Ovaries have corpora lutea (arrows). Sites of placentation are prominent (P). Bar = 1 cm

pathologic evaluation. Reproductive abnormalities were not identified during surgery for the two other 1-year-old littermates (both female tortoiseshell calico), queen (red-and-white tabby) or tom (red tabby). Cats 1 and 2 had similar red-and-white tabby color patterns.

The left uterine horn of cat 1 appeared as a string-like solid structure within the mesovarium and was 6 cm long and approximately 0.2 cm in diameter. The ovary on the left side was 0.6 cm in length and a 0.2 cm yellow body consistent with a corpus luteum was present. The right uterine horn grossly appeared normal with several circular bulges. The horn was 8.7 cm long and had two spherical swellings (0.8 cm and 2.3 cm in diameter, respectively). The largest spherical swelling was opened and contained an embryo

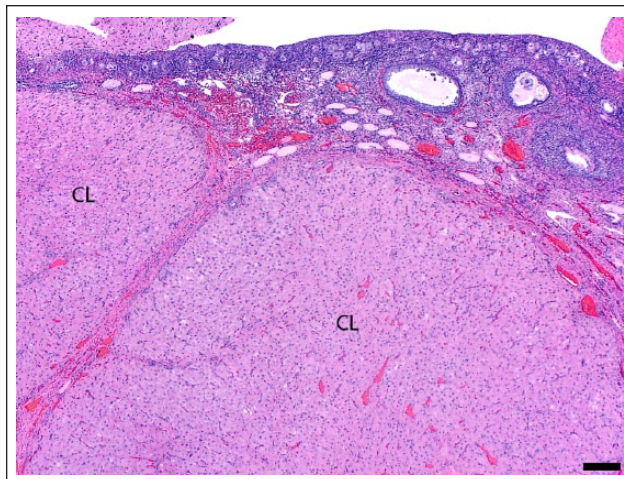


Figure 3 Numerous oogonia and 2 visible corpora lutea (CL), left ovary, Cat 1. This ovary is from the side of the uterus unicornis. HE, bar = 200 µm

(consistent with viability) of 0.6 cm length. The ovary on the right side was 0.8 cm in length with two 0.3–0.4 cm corpora lutea. The gross findings of cat 2 were nearly identical to cat 1.

Histologically, the left ovary of cat 1 had two corpora lutea, multiple atretic follicles, numerous oogonia within the cortex and an early Graafian follicle with two ova. No oviduct was identified in association with the left ovary. The right ovary had two corpora lutea, numerous oogonia within the cortex, multiple atretic follicles and at least one Graafian follicle. Fimbriae of the oviduct were normally developed. The cord of tissue at the site of the left uterine horn had a peripheral layer of smooth muscle and a central core of loose areolar and fatty tissue interspersed with numerous small arterioles and veins consistent with uterus unicornis.² No uterine lumen or any evidence of a ductular structure was present. The attached broad ligament was within normal limits. The right uterine horn and uterine body had hyperplastic endometrium in areas distinct from the bulging sections. Superficial endometrial epithelium was columnar and endometrial glands were moderately tortuous and lined by columnar epithelium. Luminal secretion was in many of the gland lumina. The larger (2.3 cm) bulging area was a site of placentation and had an identifiable intraluminal embryo consistent with viability and a normally differentiated and attached placenta. The smaller but identifiable bulging area was also a site of placentation, but the conceptus was not identified. The placenta was normally differentiated and no evidence of placental apoptosis or detachment was evident. A third, much smaller, area with a slight bulge was identified. However, this was not a site of placentation and consisted of a cluster of normally differentiated hyperplastic uterine glands within the endometrium.

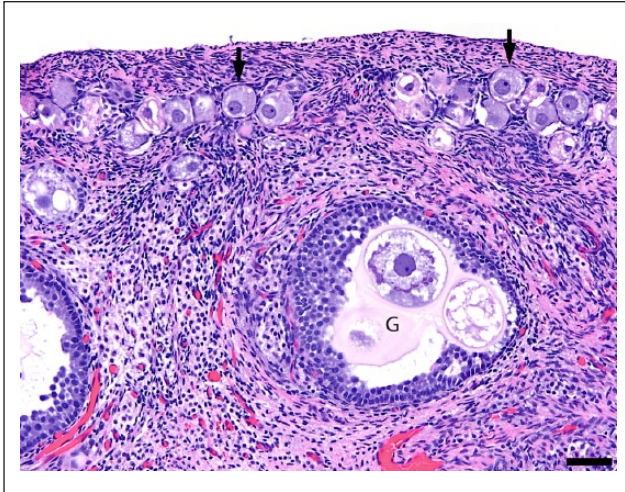


Figure 4 Graafian follicle (G) with multiple ova and numerous oogonia (arrows), left ovary, Cat 1. The ovary is from the side of the uterus unicornis. HE, bar = 50 μ m

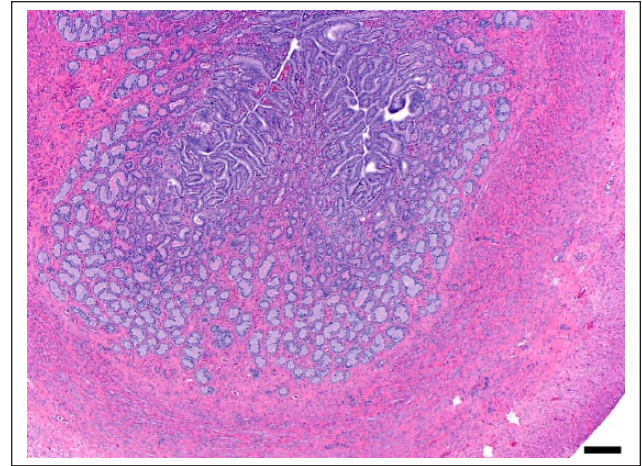


Figure 6 Uterus with physiologic hyperplasia of endometrium, right uterine horn, Cat 1. The endometrium reflects the expected finding in a pregnant cat. HE, bar = 200 μ m



Figure 5 Uterus unicornis, left uterine horn, Cat 1. Notice solid central core of loose areolar connective tissue with arteries, veins and lymphatics and peripheral smooth muscle. Part of the mesometrium is attached. HE, bar = 200 μ m

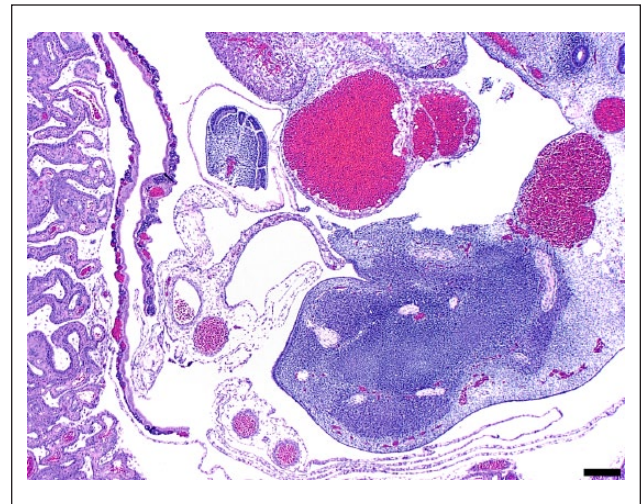


Figure 7 Placentation site and embryo, right uterine horn, Cat 1. The right uterine horn has an embryo and placenta consistent with viability. HE, bar = 200 μ m

The histologic findings in cat 2 were nearly identical to cat 1. Corpora lutea and oogonia were in both ovaries. The left uterine horn was a similar solid cord of peripheral smooth muscle and central loose areolar connective tissue interspersed with arteries and veins with no uterine lumen. The right uterine horn had hyperplastic endometrium in uterine sections between bulging areas. The bulging areas were identified as normal sites of placentation consistent with viable pregnancies. Oviduct tissue was not identified on the left side. Normal oviduct and fimbriae tissues were identified on the right side.

Both cats 1 and 2 presented to Mississippi State University College of Veterinary Medicine after surgery

for a follow-up evaluation. The surgical incision sites healed normally. Complete abdominal ultrasound was performed for both cats. No abnormalities were identified in cat 1. Ipsilateral renal agenesis of the left kidney was identified in cat 2. Neither renal tissue nor renal vasculature was visible on the left side.

Discussion

Uterine abnormalities are uncommonly encountered in veterinary medicine but have been identified in many species, including cats, dogs, cows, horses, deer, sheep, pigs, ferrets and alpacas. Prevalence of congenital uterine abnormalities in cats has been estimated to be 0.09%.

Uterine abnormalities in cats include uterus unicornis, segmental agenesis of one uterine horn and uterine horn hypoplasia. Uterus unicornis is defined as complete agenesis of one uterine horn. Normal ovaries and oviduct tissue are commonly reported as present on the agenesis side of the uterus in cats with uterine abnormalities.²⁻⁴ Ipsilateral renal agenesis is present in approximately 29% of cats with uterine abnormalities.² Mummified and ectopic fetuses have been reported in cats with uterus unicornis, but neither was identified in the cats in this case series.

In people, the prevalence of unicornuate uteruses is approximately 0.03–0.1%. Characteristic findings of a unicornuate uterus in women include a small cervix and a deviated 'banana-shaped' uterus connected to a single oviduct.^{5,6} Up to 70% of women with unicornuate uteruses have ipsilateral renal agenesis.⁷

Renal and uterine abnormalities often occur concurrently, and this can be explained by the interdependence between the tissues during embryologic development. Renal and uterine tissues are derived from common intermediate embryonic mesoderm. Embryonic mesoderm gives rise to paramesonephric ducts, which proliferate and differentiate rostro-caudally and form the oviduct, uterus, cervix and the cranial portion of the vagina. In contrast, the ovary develops from the gonadal ridge.^{2,8,9} This embryologic distinction between ovarian tissue and tubular reproductive tissues may explain why ovaries are typically present in mammals with uterine abnormalities.^{2,10} Despite having nearly identical uterine and ovarian tissues, only one of the affected sibling cats had concurrent ipsilateral renal aplasia. This discrepancy demonstrates the developmental complexity of uterus unicornis with ipsilateral renal agenesis.

It has been repeatedly suggested in veterinary publications that feline uterus unicornis is commonly associated with bilateral normal oviducts.²⁻⁴ In contrast to these publications, we did not identify normal oviduct tissue on the affected side of either cat described in this case series. Other published case reports describing uterus unicornis in cats, guinea pigs, horses and rabbits have also failed to describe normal oviduct tissue on the affected side.¹¹⁻¹⁵ Human literature describes unicornuate uteruses as having a single oviduct.^{5,6} However, multiple case reports describing segmental uterine aplasia in cats have described bilateral presence of oviduct tissue.^{16,17} Based on these reports and data presented in this case series, we suspect that cats with uterus unicornis likely do not have normal oviduct tissue, and cats with segmental aplasia likely do have normal oviduct tissue.

Many factors may be involved in uterine abnormalities, including genetic, hormonal, environmental or compromised blood flow.² There are no current definitive studies in the veterinary literature demonstrating

direct genetic linkages to congenital uterine diseases. Since the two siblings in this case report share the exact same uterine abnormality, a common cause could be suspected. Both cats were healthy, cycled normally at sexual maturity and established normal pregnancies. This may suggest that hormonal and environmental causes are unlikely, and that genetic factors may be the underlying cause. In the human literature, a case has been made for genetic linkages to congenital uterine abnormalities. It has been hypothesized that congenital uterine abnormalities, such as Mayer–Rokitansky–Küster–Hauser syndrome, may be transmitted as an autosomal dominant trait with incomplete penetrance coupled with variable expressivity of a single mutant gene.⁶ However, discovering genetic inheritance can prove difficult as relatives of women with uterine abnormalities may never show clinical symptoms despite having the abnormality.¹⁸ One such study was conducted and found a low frequency of affected relatives, thereby suggesting a cause dependent on many factors or multiple genes.¹⁹

Conclusions

This is the first publication to describe uterus unicornis in gravid feline littermates with only one of the cats having ipsilateral renal agenesis. This is also the first publication to describe oviduct agenesis on the affected uterine horn in feline uterus unicornis. The genetic and other underlying causes of uterine abnormalities are not known in dogs and cats. This case report demonstrates the complexity of uterine abnormalities since only half the littermates were affected and only one of the affected cats had ipsilateral renal aplasia. More genetic and epidemiologic studies are needed to explain the cause of uterine developmental abnormalities.

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