**Joint Pathology Center**
**Veterinary Pathology Services**

# WEDNESDAY SLIDE CONFERENCE
# 2020-2021

## Conference 16

**27 January, 2021**

Joint Pathology Center
Silver Spring, Maryland

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**CASE 1: MK1905835 (4151722-00)**

**Signalment:**
18-year-old female squirrel monkey, *Saimiri sciureus*

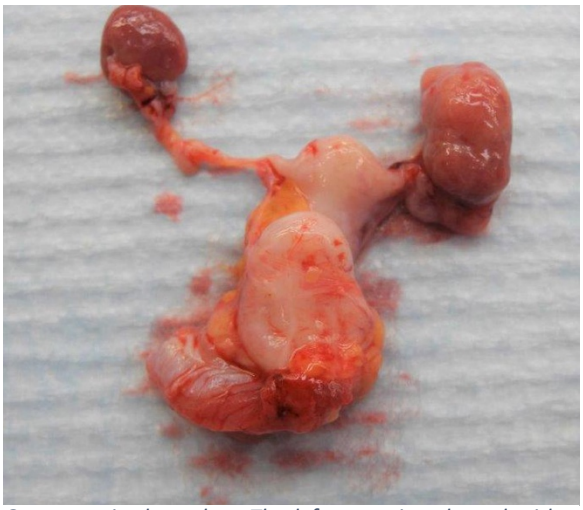
**History:**
Euthanized for because of cardiac enlargement and symptoms of heart failure.

**Gross Pathology:**
The heart was severely enlarged at 1.25% of body weight and thoracic and peritoneal effusion was present. The left ovary was found to be enlarged due to 7 mm diameter, firm, tan nodule with an irregular surface. The cut surface was solid.

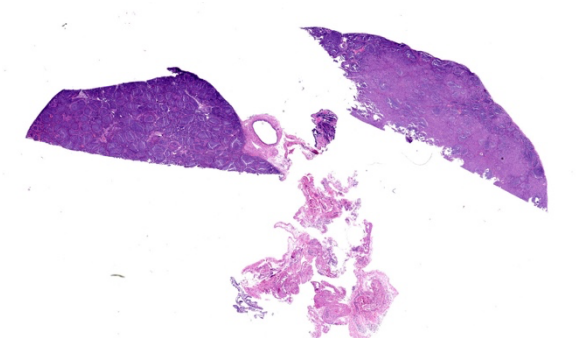
**Laboratory results:**
N/A

**Microscopic description:**
(Slides may have one or two sections of ovary) The tumor is well-demarcated and compresses adjacent ovary. It consists of widely separated follicle-like structures separated by bands of stroma. Most of the follicles are oval but some are irregular in shape. Some are cystic. Neoplastic cells line up perpendicular to the stroma; occasional rosettes are present. They are composed of cuboidal cells with scant eosinophilic cytoplasm. Nuclei are round to oval with inconspicuous nucleoli. PAS stain reveals some of the rosettes contain PAS positive material. The stromal cells are elongated. Stroma is composed of elongated spindle cells and numerous tubules. Mitotic figures are not observed.

Remaining ovary has hyperplasia of follicles the predominance of which lack ova and/or progression to antral follicles. The periphery of the ovary has small numbers of primary follicles. The uterus has normal endometrium myometrium.



*Ovary, squirrel monkey. The left ovary is enlarged with a 7mm nodule. (Photo courtesy of: NIH, Division of Veterinary Medicine, Diagnostic and Research Services Branch, 28 Library Drive, Bethesda, Maryland 20892)*



*Ovary, squirrel monkey: Two sections of the affected ovary and a section of fimbria are submitted for examination. (HE, 6X)*

**Contributor's morphologic diagnosis:**
Ovary: Granulosa cell tumor.
Ovary: Granulosa cell hyperplasia, senescent change.

**Contributor's comment:**
Ovarian tumors can arise from the outer epithelium (papillary cystadenoma, cystadenocarcinoma), the interior sex cords and stroma, and germ cells (dysgerminoma and teratoma). "Sex cord" is a term that denotes the possible embryologic origin of cells in the mesonephros.[14] SCSTs are the most commonly reported ovarian tumor in macaques.[4] They have been reported in rhesus, stump-tailed and bonnet macaques, baboons, gibbons and chimpanzees.[3,12]

Sex cord stromal tumors (SCST) are classified as either granulosa tumor (GCT), thecoma, or luteoma. GCT are often cystic and exude bloody fluid on cut section. They can be hormonally active and cause either hyperestrogenism or masculine behavior. They can develop from ovarian remnants. The follicular structures that they form often have rosettes with eosinophilic material in the center, (Call-Exner bodies). They can be either benign or malignant. GCT are commonly reported in cows, mares and dogs.[7,14] Inhibin produced by GCT which can cause atrophy of the opposite ovary.[16]

Other subtypes of SCST's include thecomas, luteoma, and Brenner's tumor (a type of epithelial stromal tumor). Thecomas have spindle shaped cells that are often vacuolated due to lipid. They tend to be solid. Luteomas have luteinized cells with abundant cytoplasm.[3,4,7,12] The latter two tumors are benign.

Also described in older squirrel monkeys is the proliferation of anovulatory follicle-like clusters of granulosa cells in the opposite ovary.[3] An early paper describes granulosa cell aggregates in both ovaries; this may have been the hyperplastic lesions that we see in this case.[14] A retrospective study of archived squirrel monkey ovaries found the granulosa cell proliferation was consistent feature starting at 8 years old. These occur prior to loss of reproductive ability and may be a feature of aging ovaries in this species. They are positive for anti-Müllerian hormone.[16]

In this case, the tumor is primarily solid with abundance of very cellular stroma suggests a granulosa-theca tumor. The ovary of a different, 17-year-old squirrel monkey has similar proliferation of anovulatory follicles.

**Contributing Institution:**
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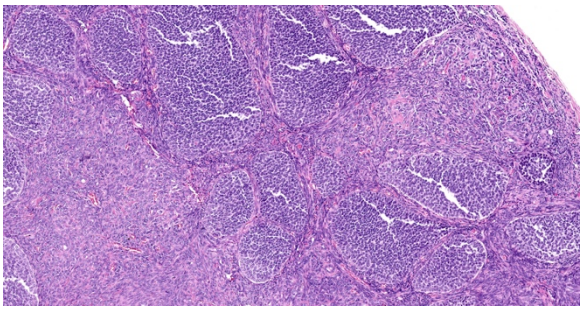
**JPC diagnosis:**
Ovary: Sex cord stromal tumor (granulosa-theca cell tumor).

**JPC comment:**
Granulosa cell tumor (GCT) is most common in the mare,[7,15] but also occurs with some frequency in the cow,[7,15] the queen,[2] the gerbil,[9] and nonhuman primates.[5] Less frequently, GCT has



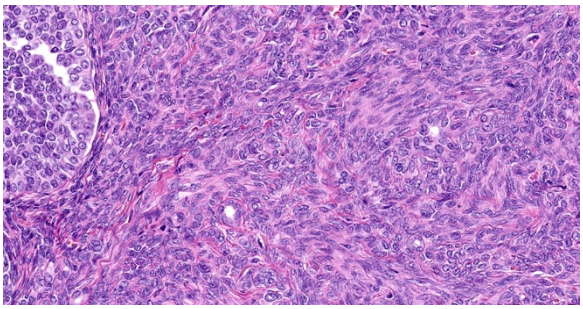
*Ovary, squirrel monkey. The neoplasm is composed of granulosa cells in two distinct patterns – large follicles and intervening nests and packets. (HE, 100X)*

been reported in the rock hyrax,[1] the Longjaw mudsucker fish (*Gillichthys mirabilis*),[8] and some prosimians (Lesser bushbaby, Pygmy slow loris, Slender loris).[11]

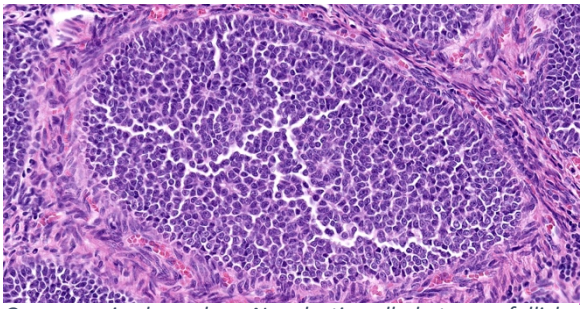
In humans, GCT are classified into two groups. The first primarily affects post-menopausal women and has an association with a mutation in *FOXL2*, and the second is a juvenile type that primarily occurs in children and young adults and is not associated with *FOXL2* mutation. Immunohistochemical stains such as inhibin, calretinin, steroid-factor-1 (SF-1), and FOXL2 are usually positive in sex cord-stromal tumors, while epithelial membrane antigen (EMA) is usually negative. However, the availability of validated products may limit their use in veterinary cases.[6]

With a variety of hormone receptors on granulosa cells, and the hormones produced by these cells, hormone therapy has been explored as a treatment modality. Previous methods have focused primarily on gonadotropin releasing hormone (GnRH) agonists/antagonists, estrogen antagonists, and synthetic progestins, but have met with limited success. Androgen antagonism has seen success in prostate, breast, and endometrial carcinoma, but has efficacy in the treatment of GCT has not yet been explored. Also recently explored is immunotherapy targeting the programmed cell death 1/programmed cell death ligand 1 relationship, with one study (NCT02923934) currently in Phase 2 trials.[12]

Epidermal growth factor-like domain-containing protein 7 (*EGFL7*) is a critical oncogene in the development of several cancers and its expression is a predictive biomarker for cervical cancer.



*Ovary, squirrel monkey: Follicles contain one or more rosettes (Call-Exner bodies) (arrows) (HE, 385X)*



*Ovary, squirrel monkey: Neoplastic cells between follicles are arranged in nest and packets on a fine fibrovascular stroma (HE, 380X)*

MicroRNA 126 (miR-126) embeds in the genomic region of *EGFL7*, silencing expression of this gene in pleural mesothelioma. Using fluorescent in situ hybridization (FISH), it was discovered that expression of miR-126 was significantly lower in malignant and benign GCT tissues than non-neoplastic ovarian cyst tissue. A mouse model with overexpression of miR-126 resulted in significantly smaller tumors than in control mice, suggesting the possibility of miR-126 as a new biomarker for GCT. This also may represent a future therapeutic avenue to explore.[16]

Conference discussion included the paraovarian cyst in section, and its possible origins. Cysts arising from the mesonephric tubules include cystic epoophoron, cyst rete ovarii, extraovarian rete cyst, and cystic paroophoron. Mesonephric duct cysts arise from peristent mesonephric ducts, and fimbrial cysts and hydatid of Morgagni arise from paramesonephric ducts.

This case includes a prominent thecal component, which is consistent with many canine sex cord stromal tumors. While often called simple granulosa cell tumors, in order to more fully capture the thecal component we prefer the diagnosis above.

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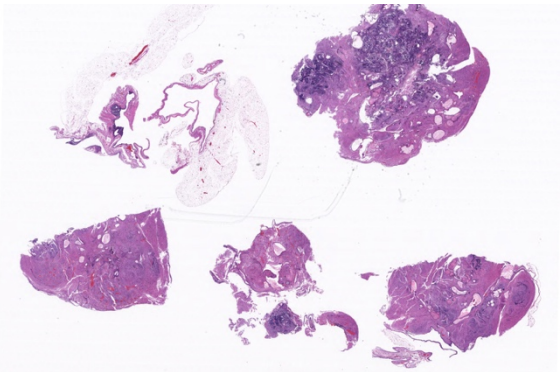
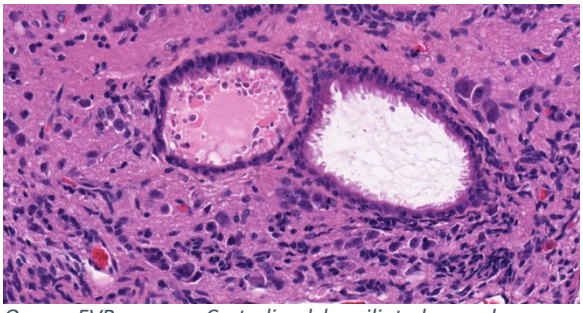
## CASE 2: 72739 (4155463-00)

**Signalment:**
16-week-old female FVB/N mouse (*Mus musculus)*

**History:**
50 female FVB/n mice were sedated with ketamine/xylazine and inoculated with Her2-positive mammary gland tumors (MGT) on the 4th right mammary fat pad. All animals were expected to develop MGT, however only 50% of animals did. Those that developed tumors took twice as long as normal to reach experimental manipulation size, and most had tumor regression approximately 2 weeks afterwards. 3/8 control animals had masses in abdominal cavity.



*Ovary, FVB mouse. Multiple sections of an ovarian mass are submitted for examination. With the exception of the most peripheral section at upper left, normal ovarian architecture is missing. (HE, 6.3X)*



*Ovary, FVB mouse. Cysts lined by ciliated ependyma are embedded in neuropil populated by small neurons, astrocytes, and oligodendroglia. (HE, 400X)*

**Gross Pathology:**
A 1.9 x 1.1 x 1.0 cm round, soft, tan to pink multinodular mass is present in the area of the left ovary.

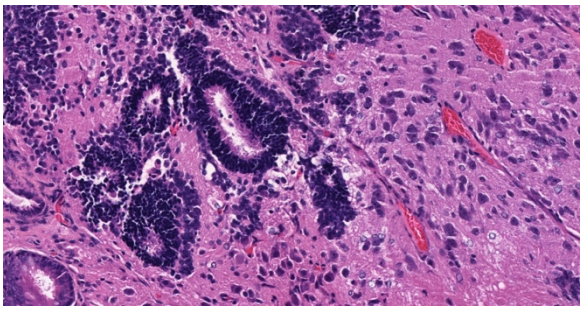
**Laboratory results:**
N/A

**Microscopic description:**
Ovary and oviduct. Effacing greater than 95% of the ovarian tissue is an infiltrative, unencapsulated, poorly demarcated, variably cellular and cystic, neoplasm composed of well-differentiated tissues from three primordial germ cell layers. Ectodermal elements include neural tissue comprised of neurons, glial cells, and clusters of small, hyperchromatic primitive neuroblastic cells embedded in neuropil, and numerous ependymal-lined cysts of varying size, up to 1 mm in diameter. These cysts are lined by columnar, ciliated cells and contain moderate amounts of basophilic material and degenerate cellular debris. Additional ectodermal elements include multiple cysts lined by stratified squamous epithelium with occasional keratohyaline granules that exhibit gradual and abrupt keratinization and contain variable amounts of lamellated keratin, debris, and degenerate cells. Endodermal elements include numerous variably sized cysts up to 3 mm in diameter which are lined by ciliated, pseudostratified columnar epithelium with interspersed goblet cells (respiratory epithelium), and mucous and serous mixed glands of variable maturity, arranged in haphazard acini along a larger duct. Cysts contain variable amounts of basophilic mucinous material to eosinophilic proteinaceous material, with scattered degenerate cells. Mesodermal elements include rare scattered bundles of smooth muscle and scattered foci of variably mature cartilage. Mitotic figures are rare. A few scattered ovarian follicles ranging from primordial to late primary maturity are present on the slide, as well as multiple cross sections of oviduct.

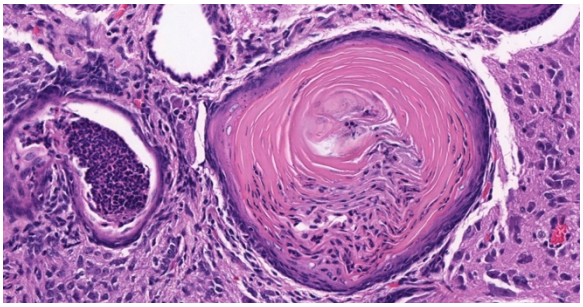
**Contributor's morphologic diagnosis:**
Ovary: teratoma

**Contributor's comment:**
Teratomas are a type of germ cell tumor that exhibit somatic cell differentiation with elements of at least two embryonic germ layers (ectoderm, mesoderm, endoderm).[1,3] Primordial germ cells must migrate within the embryo to reach the gonads, and as a result teratomas can arise anywhere along this migration path, in addition to presentation within gonadal tissue.[14] Teratomas of the ovary are rare in domestic animals but have been reported in many species, most commonly in the bitch and cow.[1,11]

FVB/N mice express the *Fv-1*$^{b}$ allele, which allows for susceptibility to the B strain of Friend Leukemia virus. This strain of mice is used for transgenic studies due to traits of super-fecundity, a large pronucleus in fertilized zygotes, and survivability of embryos following injection.[10,15] In studies of spontaneous pathology in FVB/N mice, ovarian teratomas have been reported at a rate of 2%, whereas male FVB/N mice are thought to be resistant to testicular teratomas.[5,7,10] However, these studies were conducted in aging mice and retired breeders, all at least 14 months of age. In this case, the animals were only 16 weeks old. Tumor frequency in this cohort was at



*Ovary, FVB mouse. Nests of primitive neuroepithelium, some differentiating to ependymal cysts, are embedded within the neuroepithelium. (HE, 400X)*



*Ovary, FVB mouse. Cysts of stratified squamous epithelium, filled with lamellated keratin and occasionally infiltrated by neutrophils (left) are scattered throughout the neoplasm (HE, 400X)*

least 4%, potentially higher but unable to be determined due to lack of availability of tissues.

Spontaneous ovarian teratoma development in mice is rare. In order to study the human condition, transgenic mouse models have been generated which have led to genetic associations with teratoma development. These include deficiency in c-mos, a serine kinase that is required for arrest of meiosis II. Lack of this enzyme is associated with development of parthenotes, which are thought to further progress to teratomas.[2,4] Bcl-2 is an outer mitochondrial membrane protein that acts to suppress apoptosis. In studies where transgenic mice overexpressed Bcl-2 in ovarian granulosa cells, there was increased teratoma development.[4,6] In a mouse model overexpressing alpha and beta chains of human chorionic gonadotropin, teratomas were thought to be a result of progression of luteomas, which occurred with increased frequency.[4,8] In a study investigating the role of signal transducer and activator of transcription 1 (STAT1), ovarian teratomas formed in a group of animals with an FVB/N background that were also overexpressing MMTV-neu, the rat homologue of mouse erbB2 oncogene. Animals with normal levels of STAT1 did not develop teratomas, nor did animals deficient in STAT1 that were of C57BL6 background that did not overexpress MMTV-neu.[4] Interestingly, the studies investigating BCL-2 and human chorionic gonadotropin also used mice with an FVB/N background.

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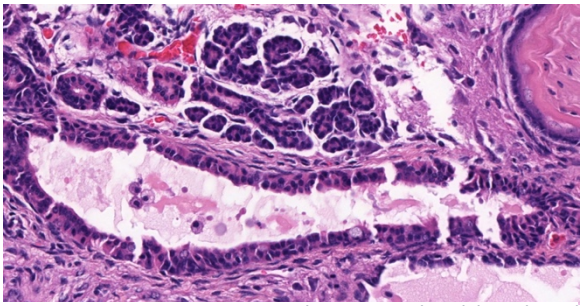
**JPC diagnosis:**
Ovary: Teratoma.

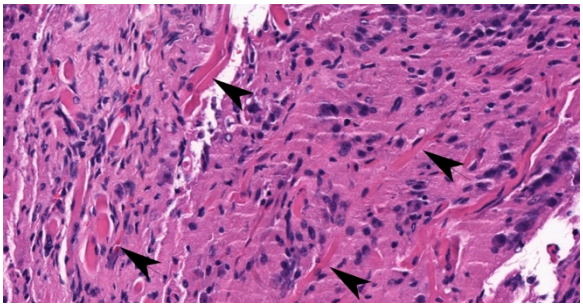
**JPC comment:**
Luckily, this entity is distinct from the 2014 movie "Teratoma", a 15-minute comedy from Poland. Teratomas are one of the more publicized tumors seen in humans, as the discovery of teeth and hair are surprising in the non-medical population. The word "teratoma" is derived largely from its root, terato-, which is Greek (*τέρας*) for "monster." While not monstrous themselves, their description can be a large task. Because they are derived from germ cells of the endoderm, mesoderm, and endoderm, knowing the lineage of different tissues is important. Potentially helpful mnemonics for derivatives of germ layers is offered.

ENDODERM: "endernal organs", a play on "internal". These include most internal organs and their linings, such as the gastrointestinal tract, liver, pancreas, and the respiratory system.

MESODERM: **M**uscle, **E**ndothelium, **S**pleen, **O**varies and other gonads, **D**ucts of genital



*Ovary, FVB mouse. Occasional cysts are lined by ciliated columnar respiratory epithelium throughout which are scattered mucin-containing cells. (HE, 400X)*



*Ovary, FVB mouse. Mesenchymal elements include isolated skeletal muscle fibers with peripheralized nuclei. (HE, 400X)*

system, **E**ndothelium of lymphatics, **R**enal, **M**ale gonads

ECTODERM (7E's): **E**pidermis, **E**pithelial linings of external orifices, **E**ar, eye, and nose sensory tissues, **E**namel of teeth, **E**xocrine glands, **E**ncephalon (CNS), **E**ye lens

This is by no means complete but may assist in the quick classification of tissues.

Teratomas are classified into either mature or immature, with a histologic grading criterion attached to the latter. Mature teratomas are exclusively composed of mature tissues and are most often cystic (mature cystic teratoma) but can be solid (mature solid teratoma). While most often benign, malignant transformation can occur. The immature teratoma is defined as containing variable amounts of immature (usually primitive/embryological neuroectodermal) tissues. Both a three-tier and two-tier grading schemes have been used for the immature teratoma, with good correlation between tumor grade and prognosis.[9]

Recent investigative efforts have focused on melanoma-associated antigen A2 (*MAGEA2*) and pre-mRNA processing factor 4 (*PRPF4*) genes in murine embryonal stem cells (mESC) and measured teratoma formation. *MAGEA2* is expressed exclusively in undifferentiated, differentiating, cancer cells, and embryonal stem cells. Early evidence suggests that increased *MAGEA2* expression is associated with increased proliferative and differentiation ability of stem cells. In knockout mice, teratomas were smaller and had fewer differentiated tissues within tumors.[12] Similarly, expression of *PRPF4* decreased with further tissue differentiation, and knockout mouse models resulted in decreased mESC pluripotency, but increased abnormal proliferation.[13] These studies, and similar studies, illustrate the complexity of embryologic tissue differentiation and our current limited understanding of the signals required for normal maturation.

The moderator mentioned that in the human literature, teratomas are starting to be classified as prepubertal or postpubertal, with prepubertal having more well differentiated tissues.

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## CASE 3: A19-7646 (4134509-00)

**Signalment:**
7 months, intersex, English Bulldog, *Canis familiaris*, canine

**History:**
A phenotypically female dog was presented for routine ovariohysterectomy. The surgeon/submitting veterinarian reported 'abnormal uterine structure' and submitted the spay specimen in formalin.

**Gross Pathology:**
The uterus was small for the age of the dog. Both uterine horns had segmental flattening or narrowing.

**Laboratory results:**
N/A

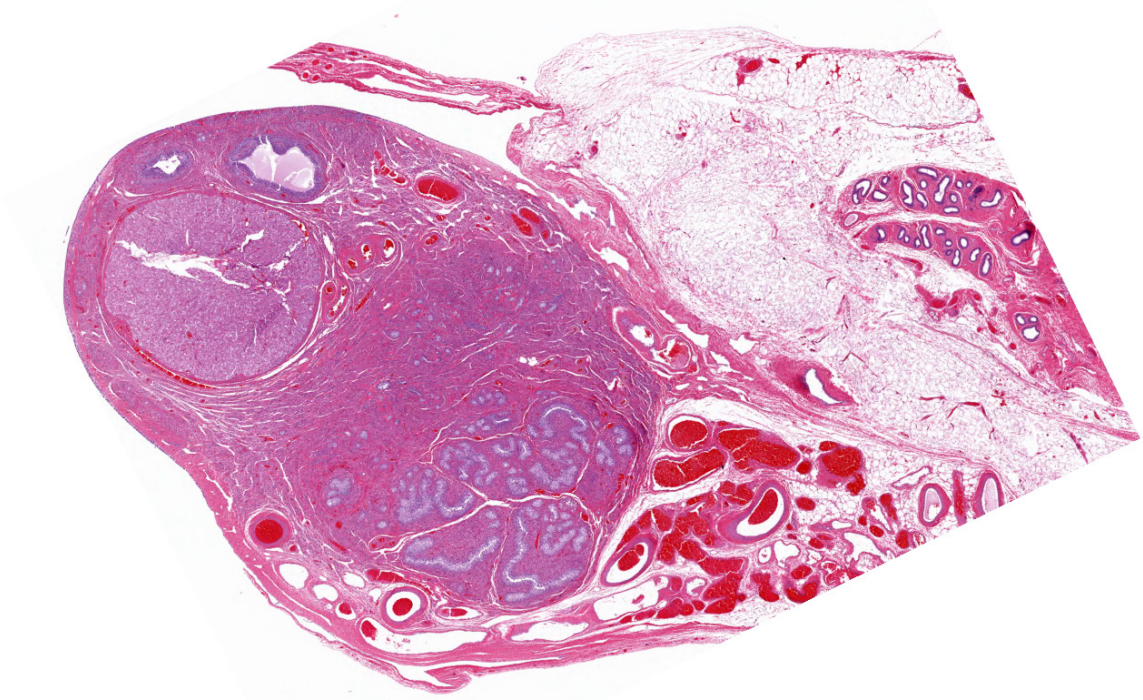
**Microscopic description:**
Both gonads were ovotestes. The ovarian component, toward one end of the section, included follicles in various stages of development and two small corpora lutea. The testicular component consisted mainly of interstitial cells with scattered seminiferous tubules lined exclusively by Sertoli cells. One gonadal section includes pampiniform plexus and epididymis. The uterus (not included in the submitted slide) was poorly developed with few endometrial glands and small diameter. Some segments of both uterine horns lacked an apparent lumen, depending on the plane of section.

**Contributor's morphologic diagnosis:**
Ovotestis

**Contributor's comment:**
This dog has ovotesticular disorder of sexual development (DSD). Both gonads were ovotestes. The uterus was hypoplastic. External genitalia were reportedly female. The sex chromosome type was not determined. Estrous cycle history was not provided, but the presence of corpora lutea indicates that ovulation had occurred. In contrast, spermatogenesis was not evident in the testicular component of the gonad.

Ovotestes have been reported in both XX and XY dogs, and in XX/XY feline chimeras.[7] They can be unilateral or bilateral, but the genetic basis for their development has not been determined in dogs.[3,4,7,11] Testicular or ovotesticular DSD has been identified in XX dogs of numerous breeds,[7] but apparently has not been reported in the English Bulldog. In reported cases, the diagnosis was made between 6 months and 4 years age.[1,2,5,6,9]

Ovarian tissue is usually in the cortex of the gonad at one end, with testicular tissue in the



*Gonad, dog. A single section of aberrant gonad is submitted for examination. Ovarian tissue at upper left includes two large follicles and a nodular corpus luteum; testicular tissue at lower life includes seminiferous tubules embedded in interstitial cells, and epididymal tubules at upper right. (HE, 9X)*

medulla at the opposite end.[3,4] In a study of gonadectomy specimens from ten phenotypic bitches with testicular or ovotesticular DSD, both gonads of 6 dogs were testes, 2 dogs had bilateral ovotestes, 1 had a testis and an ovotestis, and 1 had gonadoblastoma in one of two testes.[2] In that and other studies, the testicular component of the ovotestis was unremarkable except for the lack of spermatogonia or any evidence of spermatogenesis. In contrast, the ovarian component is typically functional with follicles in various stages of development and corpora lutea.

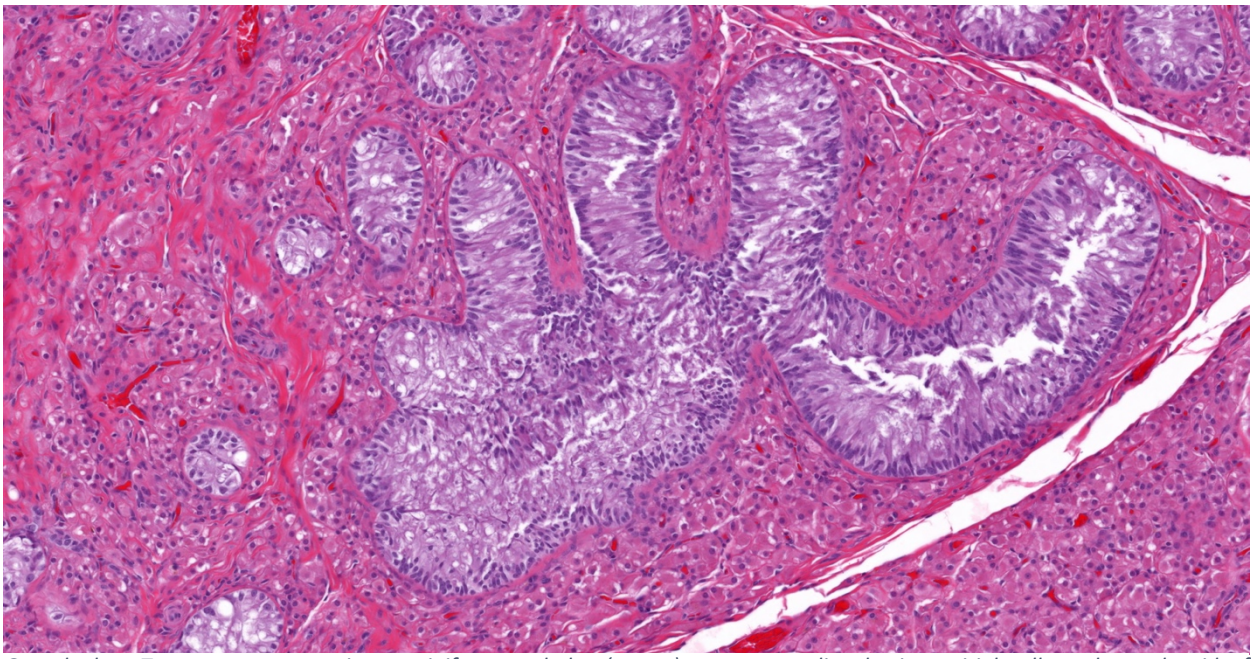
**Contributing Institution:**
Purdue University
Animal Disease Diagnostic Laboratory: http://www.addl.purdue.edu/
Department of Comparative Pathobiology: https://vet.purdue.edu/cpb/

**JPC diagnosis:**

1. Gonad: Ovotesticular disorder of sexual development.
2. Gonad: Ovarian hypoplasia.

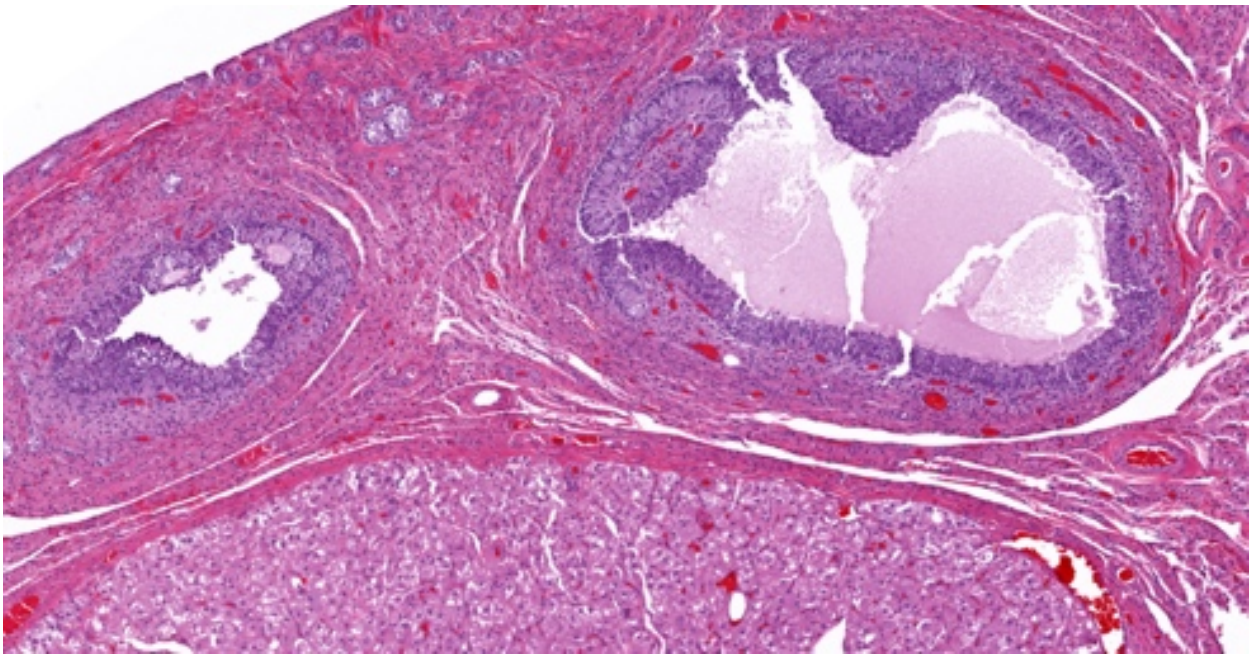
**JPC comment:**
This uncommon disorder of sexual development is not limited to canine species. While most cases of ovotestes are usually limited to having germ cells of either of one sex, there are rare reports of having male and female germ cells present. In a described case of ovotestis in a *Loxechinus albus* sea urchin, both spermatozoa and primary oocytes were present in close proximity to each other.[8] This condition appears to be rare in Echinodermata, but ovotestis is ubiquitous and normal in Mollusca. Pulmonates (snails and slugs) are hermaphrodites, using their ovotestis as the source of both oocytes and sperm. In the case of mating, body size is usually the determining factor for which snail supplies the ova or sperm, with larger snails acting as female and smaller snails acting as male.[10]

Endocrine disrupting chemicals (EDC) can have an extensive effect within populations of aquatic animals. These chemicals are part of a vast array of pharmaceuticals, plastics, household products, flame retardants, and accumulate within the aquatic environment through urban and agricultural run-off. One of the more potent

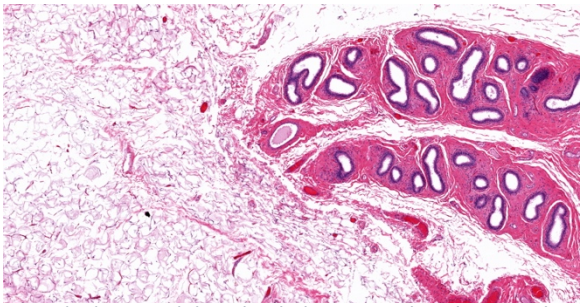


*Gonad, dog. Tortuous anastomosing seminiferous tubules (center) are surrounding by interstitial cells and are devoid of developing spermatogonia. (HE, 9X)*

EDCs is 17-α-ethinylestradiol (EE2), a synthetic analog of estrogen 17β-estradiol (E2). Observed effects in fish include decreased fertility, modulation of steroid levels, feminization, and cases of intersex presentation or sex reversal. Proteomic investigation using the mangrove rivulus (*Kryptolebias marmoratus*), one of only two hermaphroditic vertebrates capable of self-fertilization (sister species *K. hermaphroditus*), showed that early exposure to EDCs significantly changed the protein profile of the brain, liver, and ovotestes. Lower doses primarily affected brain and liver proteomes, but higher doses altered the ovotestis proteome with a dose-dependent



*Gonad, dog. Two follicles (upper right and left) and a corpora luteum are embedded among testicular interstitial cells (HE, 69X)*



*Gonad, dog. Epididymal tubules are reduced in number, embedded in testicular fat, and devoid of spermatozoa. (HE, 57X)*

response pattern. It is likely that estrogen-dependent pathways, such as lipid-metabolism, inflammation, and the innate immune system remain affected months after exposure to EDCs.[13]

Recent work with rabbits has yielded a potential animal model for DSD due to mutations in the *SRY* gene on the Y chromosome. Inducing clustered regularly interspaced short palindromic repeats (CRISPR)/Caspase 9-mediated mutation of the HMG region of *SRY*, rabbits developed ovotestis, testis, ovary, and uteri simultaneously. By demonstrating the ability to manipulate these genes, this may represent an avenue for further research of disorders of sexual development in animals and humans.[12]

The moderator emphasized the changes in terminology for classification of these disorders. True and pseudohermaphrodite and intersex are no longer preferred terms and are replaced by a collection of characteristics and traits. Disorders of sexual development are characterized by sex chromosome, *SRY* status, gonad type, tubular genitalia, and external genital phenotype. Unfortunately, karyotyping was not available in this case.

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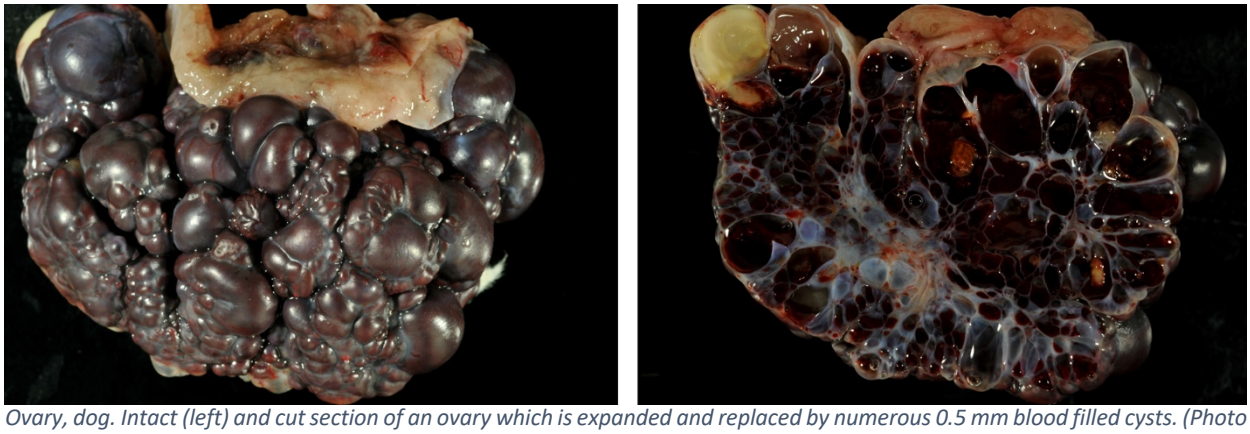


*Ovary, dog. Intact (left) and cut section of an ovary which is expanded and replaced by numerous 0.5 mm blood filled cysts. (Photo courtesy of: Institut fuer Veterinaer-Pathologie, Justus-Liebig-Universitaet Giessen, Frankfurter Str. 96, 35392 Giessen, Germany, http://www.uni-giessen.de/cms/fbz/fb10/institute_klinikum/institute/pathologie*

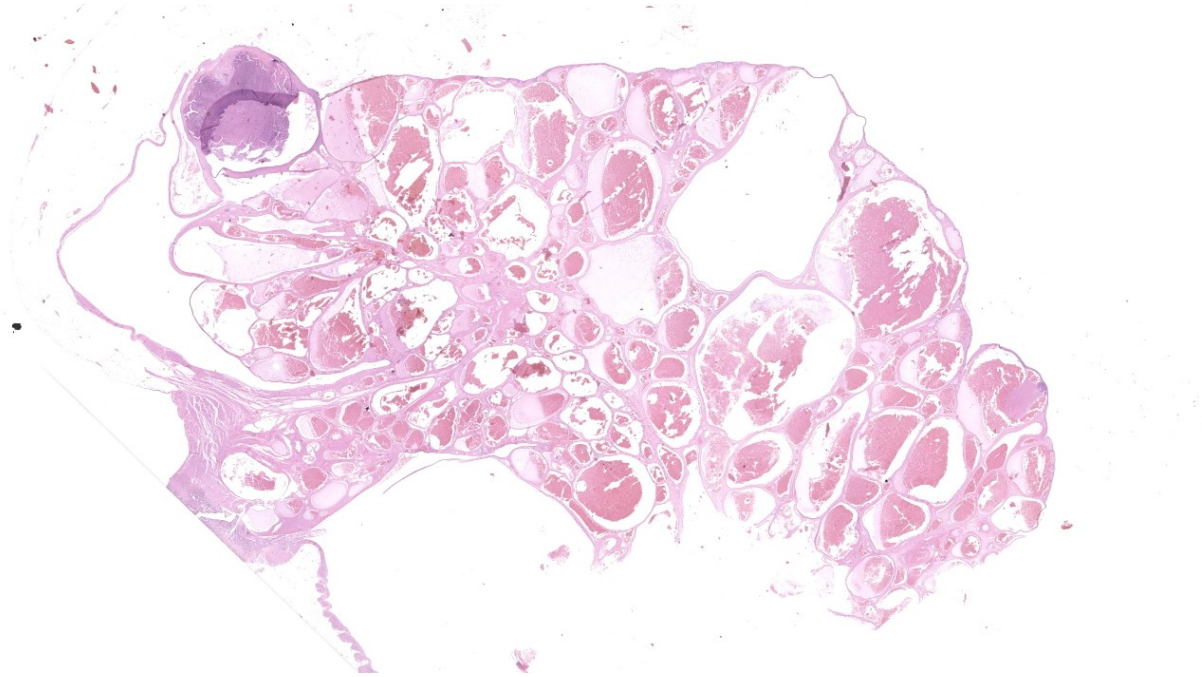
**CASE 4: T2303/14 (4068544-00)**

**Signalment:**
11 years old, female, Lowchen dog, *Canis familiaris,* canine

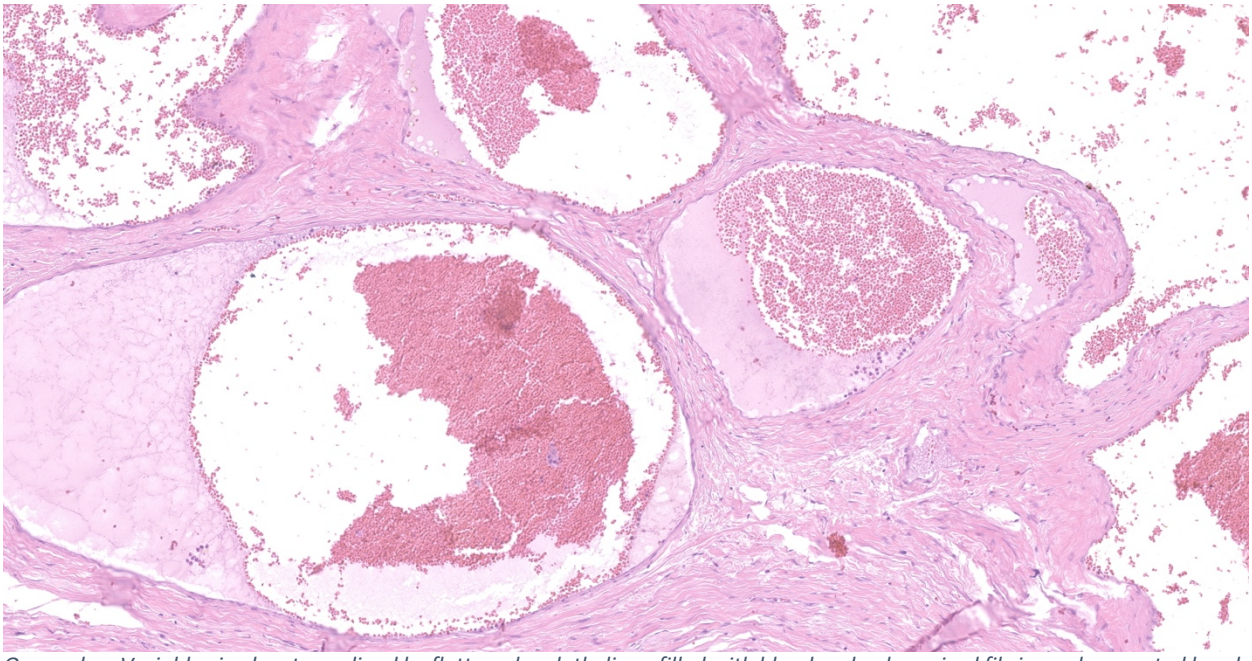
**History:**
The animal suffered from pyometra and during ovariohysterectomy one ovary appeared "quite abnormal". Both ovaries were formalin-fixed and submitted for histopathological examination.

**Gross Pathology:**
One ovary was 1.5 x 1.5 x 2 cm, with multiple small nodules and small cysts (histologically unremarkable with follicles and Corpora lutea in different stages, not submitted). The other ovary was 3 x 3 x 2 cm, with a bramble-like appearance. On cut surface multiple cyst-like structures filled with greasy brownish material were obvious.

**Laboratory results:**
Immunohistochemically endothelium was positive for von Willebrand factor and vimentin (not submitted).



*Ovary, dog. One section of ovary is submitted for examination. The ovary is effaced by numerous blood filled cysts, some contained within other empty cysts. The fimbriae of the oviduct are visible at bottom left. (HE, 6X)*



*Ovary, dog. Variably-sized cysts are lined by flattened endothelium, filled with blood and polymerized fibrin, and separated bands of dense collagen. (HE, 105X)*

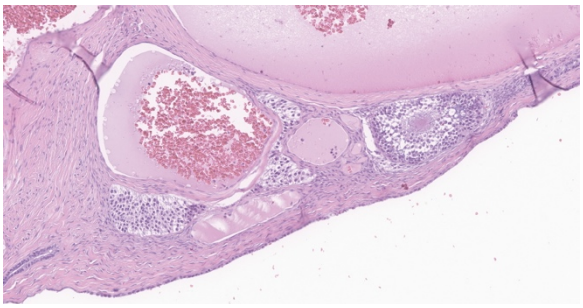
**Microscopic description:**
Ovary: Compressing and replacing normal ovarian tissue is a 3 x 2 cm, moderately cellular, well-demarcated, nodular, unencapsulated neoplasm composed of large blood-filled vascular spaces measuring up to 500 µm, separated by variably sized bands of fibrous connective tissue. Neoplastic cells lining the blood-filled spaces are flattened and spindeloid, with indistinct cell borders, scant amounts of fibrillar eosinophilic cytoplasm, elongate nuclei with finely stippled chromatin and indistinct nucleoli. Mitoses are less than 1 per high power field. Few vascular spaces contain thrombi measuring up to 0.5 µm, characterized by concentrically arranged fibrin with entrapped erythrocytes, completely or partially occluding the lumen. Multifocally fibrin and stromal collagen is replaced by granular basophilic material (mineralization).

**Contributor's morphologic diagnosis:**
Ovary, hemangioma, cavernous

**Contributor's comment:**
Ovarian neoplasia is a regularly found condition in dogs, but epidemiological data are rare. In a statistical analysis of cases of a private diagnostic laboratory in Germany the incidence of ovarian tumors was low (0.225 %) in a period of 10 years.[10] In the recently published Swiss Canine Cancer Registry (1955-2008) tumors of female reproductive organs account only for about 0.89 %.[1]

Ovarian neoplasia occurs more often in older animals. In dogs often owners note behavioral changes. Additionally, lactation, vaginal discharge or pyometra can be diagnosed. The most relevant tumors of the ovarian tissue are divided into three broad categories: deriving from the surface coelomic epithelium, from the gonadal stroma or from germ cells. Nongonadal stromal tumors (e.g. vascular, fibroblastic, smooth-muscle) are very uncommon in all species.[3,5,9]

Ovarian hemangioma is rare in domestic animals with the exception of mature and aged sows, in which hemangioma is the most common ovarian neoplasia. Tumors are described as globular, well circumscribed and tan to red-brown. They are located within the ovarian cortex and may occur bilaterally. The tumor is composed of well differentiated endothelium lining vascular spaces and clefts. There are no signs of malignancy.[2,6,8] Vascular hamartomas may also occur in the



*Ovary, dog: Variably-sized follicles, mostly atretic, are present within the remaining collagenous stroma. (HE, 181X)*

ovaries (observed in cows and sows) and a distinction between hemangioma and vascular hamartoma can be challenging.[9]

Hemangiomas are more common in dogs as benign mesenchymal skin tumors with distinct histological subtypes (e.g. cavernous and capillary).[10]

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**JPC diagnosis:**
Ovary: Vascular hamartoma.

**JPC comment:**
There was spirited debate about how best to classify this unusual lesion. The robust, fibrous nature of the separating connective tissue, and the few retained follicles within the affected tissue pushed the moderator and conference participants to diagnose vascular hamartoma over hemangioma. Unfortunately, additional unstained slides were not available for this case. However, a short discussion about ovarian hemangioma is provided.

Ovarian hemangiomas are rare occurrences, and while most often are discovered as an incidental lesion in humans, they may present in association with other ovarian neoplasms, or as their own primary lesion resulting in a mass, pain, ascites, and rarely widespread abdominal malignancy. Approximately 2/3 of ovarian hemangiomas are of the cavernous type, but capillary types are found either as the primary type or as part of a cavernous type.[6]

Human ovarian hemangiomas are most often found in the medulla or hilus but must also be differentiated from the numerous vessels of the ovarian medulla of older animals. Some ovarian hemangiomas have been associated with stromal luteinization, which would need to be differentiated from an ovarian steroid producing tumor with pseudo-vascular degenerative change. Other uncommon vascular tumors reported in the ovary include lymphangioma, infantile hemangioendothelioma, hemangiopericytoma, and glomus tumor.[4]

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