



WEDNESDAY SLIDE CONFERENCE 2008-2009

Conference 13

7 January 2009

Conference Moderator:

Dr. Don Schlafer, DVM, DACVP, DCVM, DACT, PhD

CASE I – 42029 (AFIP 3107596)

Signalment: Day of birth, gender undetermined, Friesian, *Bos Taurus*, Bovine.

History: The mass (figure 1) was attached to the placenta accompanying the assisted delivery of a normal full-term male fetus.

Gross Pathology: Attached to the placenta by a 15cm pedicle resembling umbilical cord was a soft, roughly circular (greatest diameter = 15cm) discoid mass with 'aerofoil' shaped cross-section (greatest thickness = 4cm), and weight of 0.316kg. The mass consisted of multiple lobules (0.5-2.5cm diameter) of fragile pink to grey tissue with a slightly granular appearance and without obvious differentiation into fetal tissues or variation in appearance from one lobule to another. Each lobule was surrounded by a thin, translucent external capsule that merged externally with the pedicle (**Fig. 1-1**).

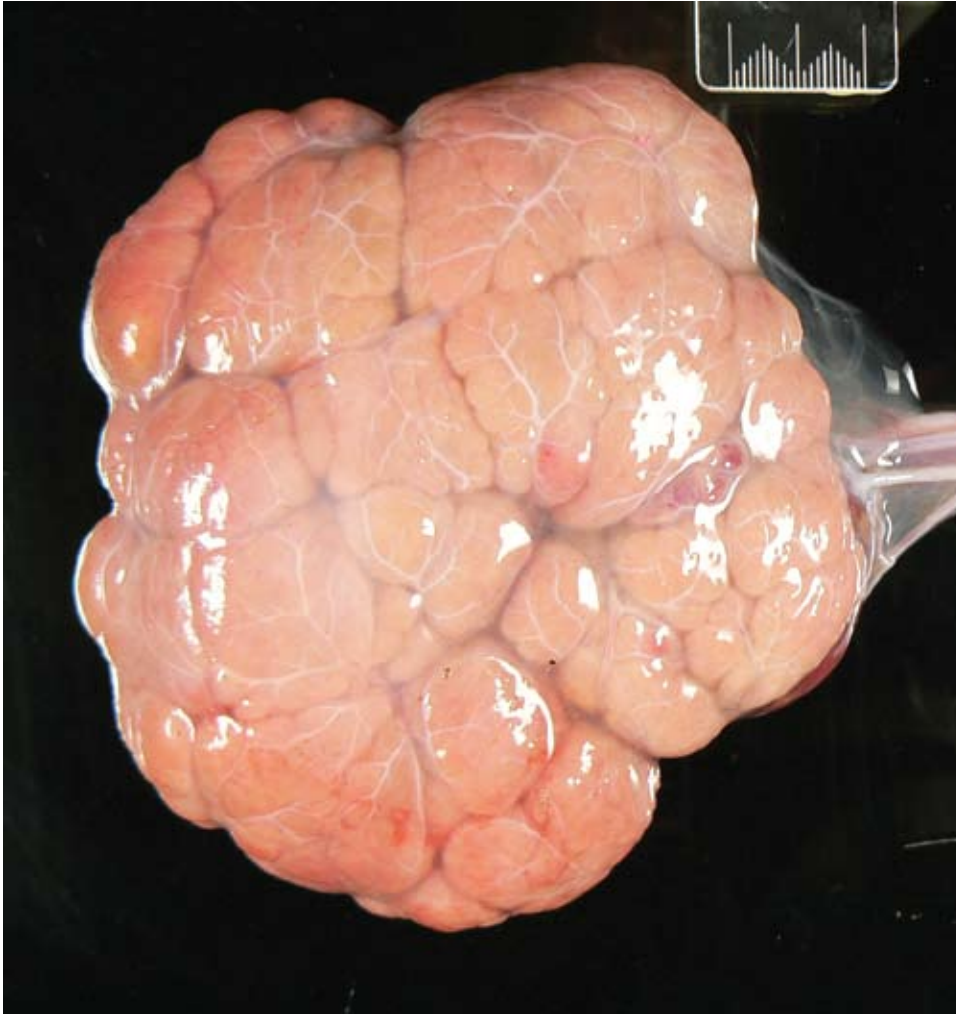
Laboratory Results: NA

Histopathologic Description: The discoid mass is formed from multiple lobules whose tissue elements

are essentially similar to those of normal cotyledon. However, the villi are more compact, often convoluted and anastomotic, and are separated from adjacent lobules by a discrete but thin fibrous capsule. Although the epithelium is hyperplastic, individual trophoblastic cells are cytologically normal, including many syncytial forms, with bi- and multinucleated forms present. They are attached to a basal lamina overlying the delicate fibrovascular stroma of the villus projections. In some areas, the interstitial region of the lobules is expanded by more extensive loose stroma, which is oedematous. Blood vessels appear normal. Small numbers of lymphocytes and plasma cells are present in the interstitial tissue throughout the mass.

Contributor's Morphologic Diagnosis: Placenta: Cotyledonary dysplasia with irregular villus hypertrophy and trophoblastic hyperplasia (trophoblastic non-hydatidiform mole), Friesian, bovine.

Contributor's Comment: The pedicle consisted of vascular, mesenchymal and epithelial (typical of the urachal extension) elements present in normal umbilical cord, while the similarity of the lobular tissue to chorionic villi of cotyledonary tissue was striking. No maternal elements were identified in any areas of the lesion.



1-1. Placenta, ox. Discoid mass attached to the placenta by a 15cm pedicle resembling umbilical cord. Photograph courtesy of Pathobiology Group, Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Palmerston North, New Zealand.

Mole is a term 'pirated' from the human literature which refers to the gestational trophoblastic diseases that are characterised by formation of an irregular mass of chorionic villi and varying degrees of trophoblastic proliferation, often with disruption of lymphatic drainage and subsequent cystic transformation of the mass.⁶ The latter form is referred to as hydatidiform. In bovid species, all forms of moles are rare, with fewer than 10 published reports. All of these reports have been associated with a co-twin and its own placenta.^{4,5} The absence of any detectable fetal structures such as skin distinguishes them from the more common amorphous globosus, which is often referred to as a fetal mole.³

Two forms of hydatidiform mole have been identified in humans: the complete mole and the partial mole. The former results from fertilisation of an unviable oocyst by one or more sperm. Thus, the genome of a complete hydatidiform mole comes entirely from the paternal side. Greater than 90% of such moles have a 46 XX diploid

karyotype.⁶ Partial moles, on the other hand, are nearly always triploid and usually result from fertilisation of an haploid ovum either by two sperm, or one sperm which duplicates its genome.¹ The rarity of the bovid condition has prevented similar detailed cytogenetic investigation in cows. In complete trophoblastic moles of humans, because of the absence of a viable maternally derived genome, no viable embryo is produced

and no fetal tissues develop. Instead, the paternally derived genome is able to dominate, resulting in excess development of the extra-embryonic tissues, particularly the placenta and its trophoblast. Thus, the mole becomes an hyperplastic mass of trophoblastic tissue.¹

In humans, 20% of patients with hydatidiform moles can be expected to develop malignant sequelae but such sequelae have not been reported in cattle.

AFIP Diagnosis: Placenta: Cotyledonary hyperplasia with irregular villus hypertrophy and trophoblastic hyperplasia (placental hamartoma)

Conference Comment: During the extensive conference discussion Dr. Schlafer was hesitant to call this particular lesion a hydatidiform mole. Dr. Schlafer and the contributor mentioned the paucity of moles reported in bovids, which added to the speculation that this entity is a true hydatidiform mole. A differential list for discrete

placental masses in bovids discussed during the conference included: amorphous globosus, adventitial placentation, and a co-twin that has died.⁷

In the human literature, a hydatiform mole is defined as a cystic swelling of chorionic villi accompanied by trophoblastic proliferation.² This description does not quite fit the histologic features of this lesion. The human literature further subdivides these moles into complete and partial moles. Complete moles are characterized histologically by diffusely edematous villi with diffuse trophoblastic hyperplasia, whereas partial moles have a mix of edematous and non-edematous villi with focal trophoblastic proliferation. The contributor mentioned the different karyotypes of these two moles. Because of the lack of female chromosomes, complete moles have no development of fetal parts. In contrast, partial moles can have development of some fetal parts because they have a karyotype with X and Y chromosomes allowing at least partial fetal development.²

In human medicine, it is extremely important to classify moles as either complete or partial because complete moles may precede choriocarcinoma.²

Contributing Institution: Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Palmerston North, New Zealand. Web site:www.massey.ac.nz

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Animals, ed. Maxie MG, vol 3., pp. 474-480. Elsevier Limited, Philadelphia, PA, 2007

CASE II – 08/14596 (AFIP 3106183)

Signalment: Male sheep (*Ovis aries*), Dorset poll breed. Age not specified.

History: Accreditation serology for *B. ovis* was inconclusive in this potential breeding animal.

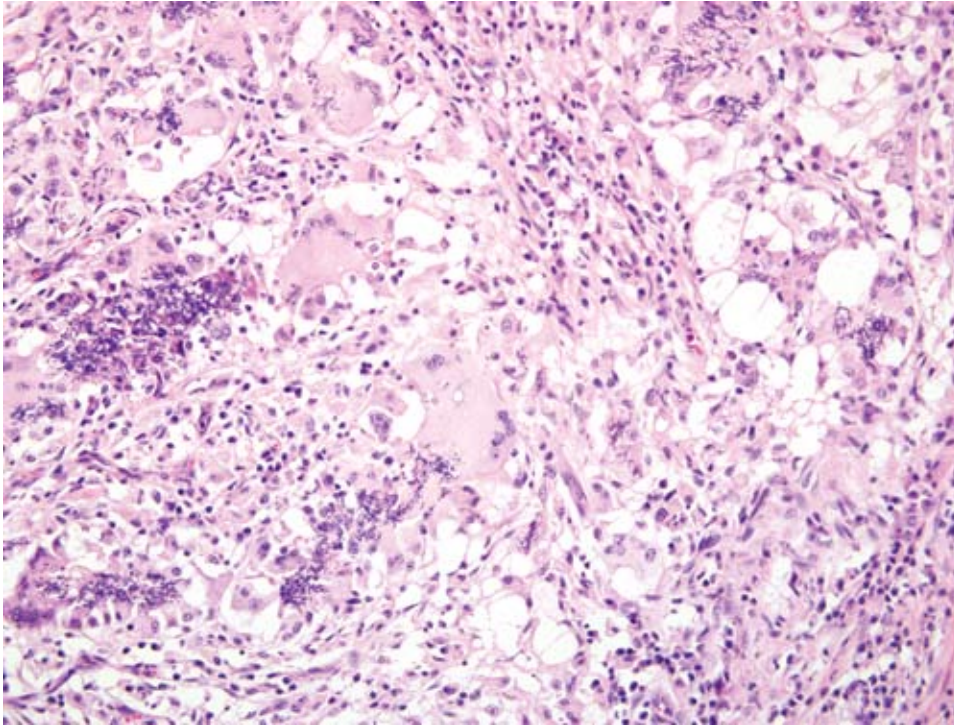
Gross Pathology: The animal was euthanized, and its entire genital tract was submitted for evaluation. The tail of the right testicle was noted to be firm and increased in size.

Laboratory Results: Cultures for *Histophilus somni*, *Brucella ovis* were negative. Modified ZN and Gram stains of impression smears made from the gonads indicated large numbers of Gram negative rods in the seminal vesicles. *Actinobacillus seminis* was cultured from both seminal vesicles and ampullae.

Histopathologic Description: There is a focal (in some sections multifocal) accumulation of histiocytes and multinucleated giant cells within the epididymal interstitium, surrounded by a collar of lymphocytes and plasma cells admixed with variable neutrophils (**Fig. 2-1**). In numerous sections, there is distinct mineralization and Splendore-Hoeppli like reaction at the center of the focus (foci). There are myriad fragments of spermatids noted at the center of the foci, often within histiocytes. There is compression of adjacent ducts, which occasionally have hyperplastic epithelium, and there is fibrosis of the interstitial connective tissue. Large numbers of sarcocysts are noted in the cremaster muscle.

Contributor's Morphologic Diagnosis: Multifocal or focal (depending on slide) granulomatous epididymitis with necrosis, interstitial fibrosis and epididymal epithelial hyperplasia (sperm granuloma).

Contributor's Comment: Spermatic granulomas are relatively common findings in rams¹ and are often associated with other conditions which induce leakage of spermatids into the interstitium. The testicle is an immunologically privileged site, and sperm are highly antigenic, containing cell walls rich in lipids and phospholipids. Epididymitis due to bacterial agents such as *Brucella ovis*, *Histophilus somni*, and *Actinobacillus*



2-1. Epididymis, sheep. Granulomatous inflammation characterized by numerous epithelioid macrophages, plasma cells, lymphocytes and few multinucleate giant cells. (HE 200X)

seminis often leads to spermatic granulomas as well as agent specific epididymitis and orchitis.

In this particular case, additional sections of epididymis, prostate gland and seminal vesicle displayed mild multifocal accumulations of neutrophils, which were presumed incited by ascending infection of *Actinobacillus seminis*.

AFIP Diagnosis: 1. Epididymis: Epididymitis, granulomatous, focally extensive, moderate with a sperm granuloma
2. Epididymis: Epithelial hyperplasia, multifocal, moderate

Conference Comment: Dr. Schlafer discussed the anatomy of the epididymis and the importance of grasping the basic anatomic features to help in identifying and understanding the pathogenesis of various entities that affect the male reproductive system.

Sperm are produced within the testes and inside the seminiferous tubules. Sperm travel through a plexus of channels called the rete testes. From the rete testes, numerous small efferent ductules transport sperm to the head of the epididymis. Within the head and body of the epididymis sperm undergo changes that transform them into fertile cells. Sperm traverse the head and body over a period of several days, and eventually reach the tail of

the epididymis for storage prior to ejaculation via the ductus deferens.² The contributor mentioned the highly antigenic nature of sperm; any release of sperm into the extratubular compartment leads to a foreign body type reaction. This is followed by a strong immune response resulting

in an accumulation of large numbers of plasma cells, CD4 and CD8 positive lymphocytes, and an up-regulation of MHC I in epithelial cells. As in the case of a foreign body, a chronic immune response leads to fibrosis and walling off of the lesion. This often leads to spermioistasis, a spermatocele, or a sperm granuloma.¹

The known causes of sperm granulomas were discussed; they include congenital duct anomalies, adenomyosis, trauma, and infections. Bacteria are implicated most frequently, as mentioned by the contributor, and the route of infection is via ascension from the urethra and accessory sex glands. The immunologically privileged site allows for the organism to proliferate unabated. This often leads to formation of a sperm granuloma and loss of fertility.¹

There was extensive slide variation with this particular case. The contributor mentioned "distinct mineralization and Splendore-Hoeppli like reaction at the center of the foci" which was not present on all of the submitted slides.

Contributing Institution: NSW Department of Primary Industries, EMAI Regional Veterinary Laboratory Woodbridge Rd, Menangle, 2568 Australia.

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CASE III – Case 1 (AFIP 3103339)

Signalment: Tissues are from a 4-year-old, intact male Poodle dog (*Canis familiaris*)

History: Kennel History:

The kennel has a 10-11 month history of infertility.

Three stud dogs and 11 bitches.

No litters from March until Jan 27, 2008. (One puppy born to a previously negative bitch was bred to a positive male in Nov. Her most recent *B. canis* test at Cornell for AGID month #2 in kennel eradication.) Tested 14 dogs, Jan 4, 2008, 8 of 14 positive at Cornell by AGID.

Euthanized 5 dogs Jan 30, 2008

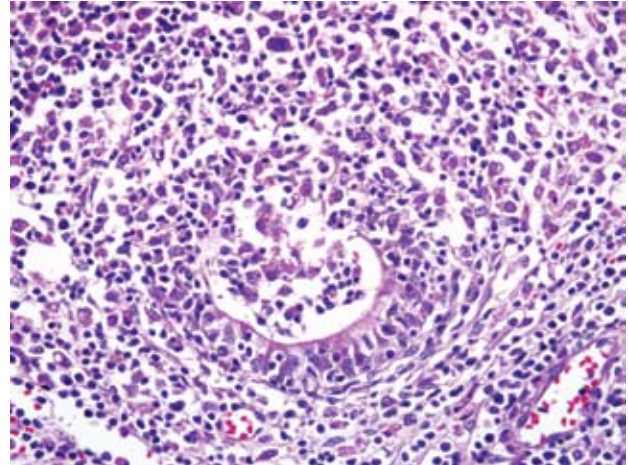
Spayed and neutered 2 dogs on Feb 1, 2008 and started on Doxycycline (28 days) and Gentamicin (7 days) unless culture and sensitivity reveal better options.

Patient History: Infertility. Small soft testicles with firm epididymis bilateral. Left testicle had a fluid filled lesion on ultrasound. Prostate enlarged, fluctuant and painful, straining to defecate and blood in stool. Mild conjunctivitis.

Gross Pathology: Significant findings were restricted to the genital system. The prostate gland is mildly enlarged, but symmetrical. The testicles are atrophied and soft. They are slightly yellow-tan colored and lack normal lobular appearance. The right testicle contains a central, 0.5cm area of cavitation containing exudates or sequestered necrotic tissue. The epididymis (bilateral) is slightly firm, but no gross lesions are noted when incised.

Laboratory Results: Bacteriology Results; Aerobic Culture; Tissue: Testicle; Organism ID: *Brucella canis*

Histopathologic Description: *Testicles:* There is diffuse, severe atrophy of the seminiferous tubules. In several areas, there are small clusters of remaining tubules that are small, hypocellular and have thickened hyalinized basement membranes. There is no evidence of spermatogenesis. Conspicuous clusters of interstitial cells are present within the testicle. There is diffuse lymphohistiocytic infiltration throughout the parenchyma.



3-1. Epididymis, dog. Cellular infiltrate composed of numerous lymphocytes, plasma cells, and fewer histiocytes that often transmigrate and segmentally replace ductular epithelium. (HE 400X)

In addition, there is one cavity containing ischemic necrotic tissue sequestrum surrounded by dense lymphohistiocytic infiltrates.

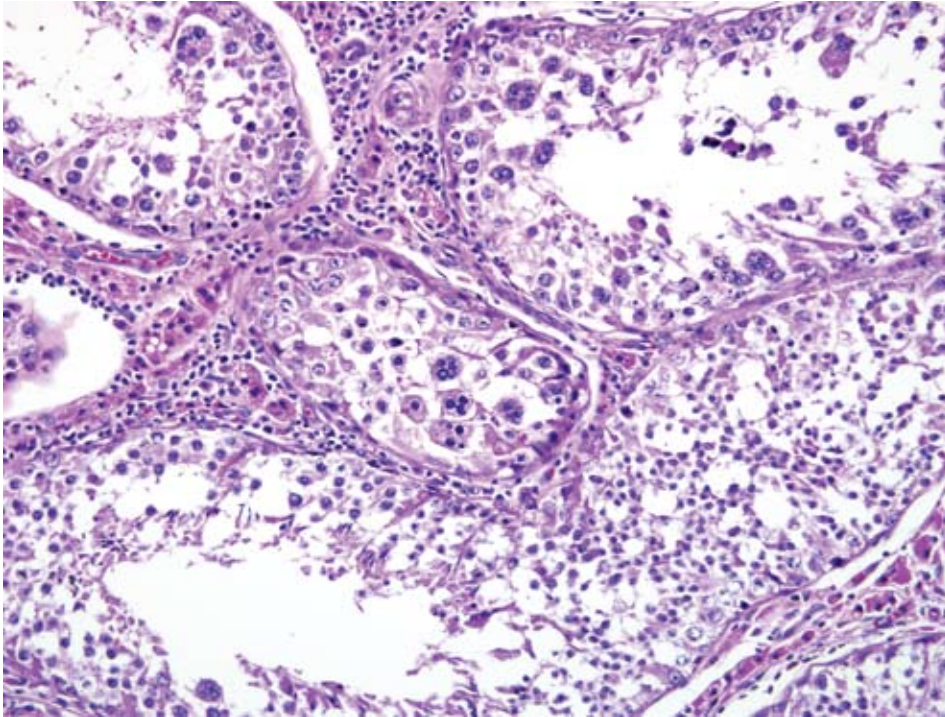
Epididymis: The lesions are similar to those in the testicle with diffuse, dense sheets of lymphohistiocytic cells, atrophic tubules, inflammatory cell infiltrates in tubular walls, plus intense lymphohistiocytic clusters within tubules (**Fig. 3-1**). There are no spermatids in epididymal tubules.

Prostate gland: The majority of the prostate gland examined is composed of hyperplastic acini lined with a single layer of tall, plump columnar epithelium with abundant eosinophilic cytoplasm. An occasional small lymphoid nodule is present within the interstitium of these areas. Within one lobe, there is marked acinar atrophy with reduction in the number of acini and diffuse, dense sheets of lymphocytes, plasma cells and macrophages. The remaining acinar walls are moderately infiltrated with primarily lymphocytes.

*** Sections submitted will contain either testicle, testicle and epididymis, or prostate gland.

Contributor's Morphologic Diagnosis: Testicles: Orchitis, lymphohistiocytic, chronic, severe, diffuse with marked seminiferous tubular atrophy and focal necrosis (**Fig. 3-2**)

Epididymis: Epididymitis, lymphohistiocytic, chronic, severe



3-2. Testicle, dog. Seminiferous tubules are degenerative characterized by thickened and undulating basement membranes, paucity of germinal cells, vacuolation and loss of Sertoli cells, and numerous intraluminal multinucleate cells. Lymphoplasmacytic inflammation expands the interstitium and surrounds tubules (HE 200X)

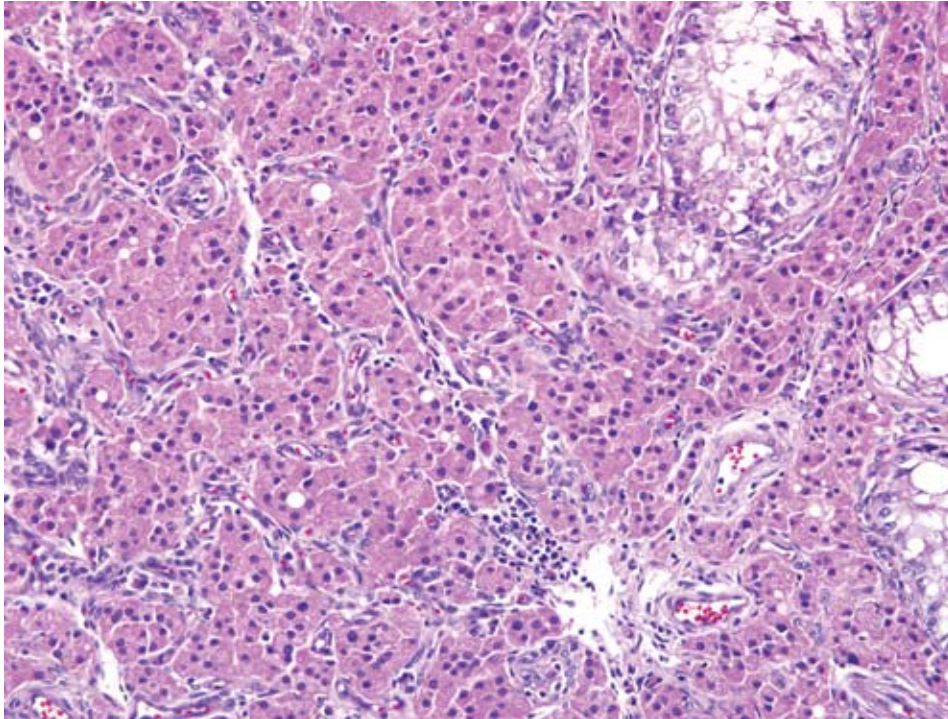
Contributor's Comment: This case represents one of several dogs seen from the same kennel with a history of infertility. Most of the patients either tested positive for *Brucella canis* by agar gel immunodiffusion or yielded positive bacterial cultures from either epididymis/testes, lymph nodes or prostate glands. In the male reproductive system, the classic appearance of canine brucellosis is a severe epididymitis that is accompanied by varying degrees of testicular atrophy. Inflammation of the testicles (orchitis) is infrequently seen. Therefore, the unique feature of this case is the level of inflammation/destruction in the testicle. When orchitis occurs secondary to *B. canis*, it can be severe and characterized by primarily lymphoplasmacytic infiltrates with destruction of seminiferous tubules and occasional foci of necrosis.^{1,3} Inflammation can extend into the vaginal tunic with draining ulcers from the scrotum.³

Brucellosis in dogs has been described with *B. melitensis*, *B. suis*, *B. abortus* and *B. canis*; however, only *B. canis* is considered epidemiologically significant.⁴ *B. canis* has been reportedly recovered from just about every bodily fluid and/or surface: vaginal secretions, semen, abortuses, milk, urine, saliva, ocular secretions and feces.⁴ The organism is transmitted through venereal and/or oral routes. Following entry, the organism is taken up by the mononuclear-phagocytic system and distributed to the lymphoid and genital compartment where the organisms multiply.⁴ Bacteremia develops and proliferation of the organism in the target organs results

in the lesions typical of the disease: uterine infection and abortion in females, epididymitis and prostatitis in males, lymphadenitis, discospondylitis, anterior uveitis, dermatitis, meningoencephalitis (refer to nice flow chart, pg. 197 of Ref. #4). Diagnosis is achieved through serology, agglutination tests, agar gel immunodiffusion, ELISA, and immunofluorescence; however, definitive diagnosis can only be made through retrieval of the organism from bacterial culture.⁴ Treatment is difficult, in part because of the intracellular nature of the organism. Many different drugs and drug combinations have been tried, but no combination has been found to be 100% effective.⁴ Combination drug treatments have shown better efficacy than single antibiotic therapies.⁴ Lastly, *B. canis* has zoonotic potential. The incidence of human infections is not known.⁴ People contract the disease through contact with the organism shed during abortions or in research laboratories where people work directly with the organism.⁴

AFIP Diagnosis: 1. Testicle: Orchitis, lymphohistiocytic, chronic, diffuse, severe, with marked seminiferous tubular atrophy and loss, and interstitial cell hyperplasia
2. Epididymis: Epididymitis, lymphohistiocytic, chronic, diffuse, severe
3. Epididymis: Epithelial hyperplasia, diffuse, marked

Conference Comment: Considerable time was spent discussing the changes within the interstitial cell



3-3. Testicle, dog. Interstitial hyperplasia markedly expands the interstitium and separates and surrounds degenerate seminiferous tubules. (HE 200X)

population (**Fig. 3-3**). Dr. Schlafer and the attendees discussed the proliferation of interstitial cells and debated hyperplasia versus neoplasia. The contributor mentioned a “conspicuous cluster of interstitial cells” when describing the proliferation, and at the end of the conference considerable disagreement still existed as to whether this change represented interstitial cell hyperplasia or an interstitial cell tumor.

Abortions caused by *B. canis* are normally late gestational abortions that occur after 50 days. As seen in this case, the usual sequelae to *B. canis* infection in male dogs is epididymitis and testicular degeneration. This often causes severe scrotal irritation and affected dogs often focus on this discomfort and lick the area until it is ulcerated. Lymphadenopathy of the mandibular and retropharyngeal lymph nodes is common. Placental lesions consist of necrosis of chorionic villi with a plethora of bacteria within infected trophoblastic cells. Infected females often discharge copious amounts of foul vaginal secretions after abortion, which is an excellent means of disease transmission. Fetal lesions are fatal and include pneumonia, endocarditis, and hepatitis.²

Brucella canis is caused by a mucoid strain of *Brucella* that is similar to *Brucella suis*. Because of its mucoid nature, *B. canis* lacks surface antigens that *B. abortus* and *B. melitensis* have, thus rendering conventional test methods ineffective.²

Contributing Institution: Oklahoma Animal Disease Diagnostic Laboratory and Center for Veterinary Health Sciences, Oklahoma State University, Stillwater, OK. www.okstate.edu

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CASE IV – 04-26927 (AFIP 2937766)

Signalment: Four-year-old, female, Labrador retriever, canine (*Canis familiaris*)

History: The patient was presented for a routine ovariohysterectomy.

Gross Pathology: The ovary was gray and shriveled.

Laboratory Results: None

Histopathologic Description: None

Contributor's Morphologic Diagnosis: Ovarian ganglioneuroma

Contributor's Comment: Neoplasms and hyperplasias of ganglionated plexuses outside the central nervous system are called ganglioneuromas and ganglioneuromatosis, respectively.¹⁻⁴ These lesions are rare and have been reported in a steer², a horse¹, a cat, and dogs.^{3,4} They are composed of variably sized neurons, nerve fibers, and connective tissue stroma. Ganglioneuromas tend to be solitary, unencapsulated but well demarcated masses. Mitotic figures are rare or absent. There are no reports of metastasis.⁴ Ganglioneuromatosis tends to be segmental,

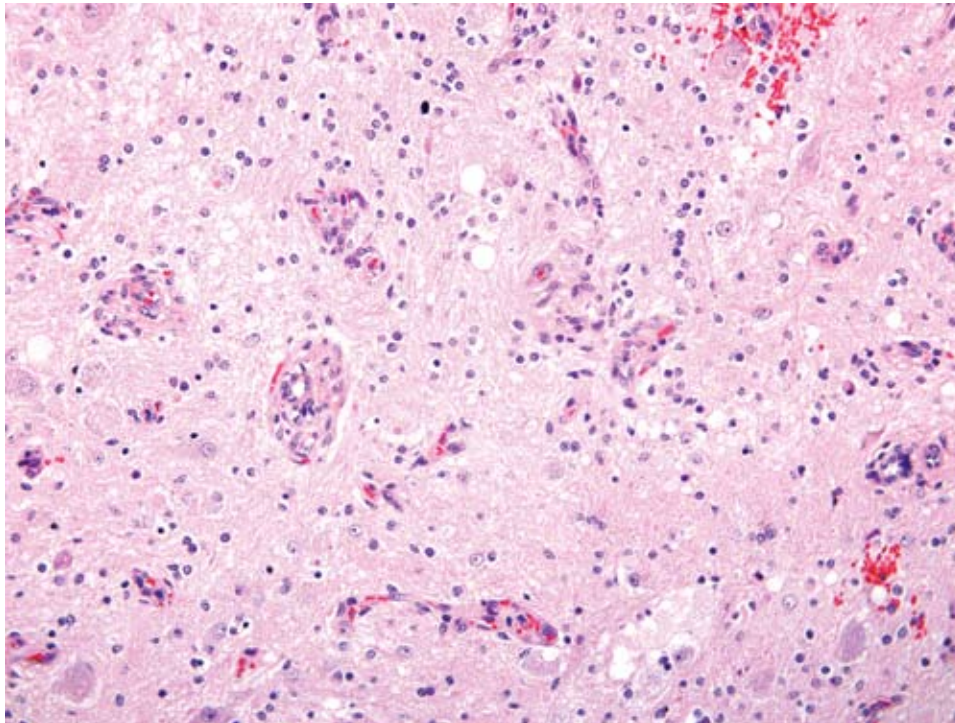
infiltrative and involve all layers of the intestine.² In human beings, ganglioneuromatosis has been associated with multiple endocrine neoplasia.

Diagnosis can be confirmed by a variety of methods to include transmission electron microscopy (TEM), histochemistry, and immunohistochemistry. TEM reveals dense core vesicles in ganglion cells and neuronal processes. Umyelinated axons are encased by Schwann cells. Histochemical stains for axons and myelin reveal that nerve fibers are nonmyelinated. Immunohistochemical stains reveal that ganglion cells are positive for NSE and Schwann cells are positive for S-100 and vimentin. Nerve fibers are positive for neurofilament protein.⁴

Neurogenic tumors of the canine ovary have not been described. The nerve supply to the ovary is via a sympathetic plexus that accompanies the ovarian vessels. This relationship may explain the numerous small vessels enmeshed in the tumor.

AFIP Diagnosis: Ovary: Teratoma, favor monodermal variant

Conference Comment: Our differential diagnosis for this neoplasm included ganglioneuroma and central nervous tissue component of teratoma. Ganglioneuromas consist of large ganglion cells separated by fusiform Schwann cells and collagen. The neurons in the present



4-1. Ovary, dog. The neoplasm is composed of neuroectodermal tissue which recapitulates neural tissue characterized by neuropil, neurons and glial cells. (HE 400X)

case were separated by a felt-like background of cellular processes resembling neuropil; this neuropil also contained cells resembling oligodendrocytes and astrocytes. We interpret this as central nervous tissue differentiation rather than peripheral nervous tissue differentiation, and therefore the neoplasm is consistent with the central nervous tissue component of teratoma. Differentiation along other embryonic cell layers is not evident in the sections examined during conference. Examination of other regions of the tumor is needed to confirm that differentiation along other embryonic layers is not present. Pathologists from the AFIP Departments of Gynecologic and Breast Pathology, Neuropathology, and Soft Tissue Pathology concurred with the diagnosis.

Although teratomas are usually defined as neoplasms composed of tissue derived from at least two germinal layers⁶, occasional ovarian tumors may be composed of cells from only one layer. In humans, these tumors are derived predominately or exclusively of endodermal or ectodermal tissue and are referred to as monodermal teratomas.⁷ Rarely these neoplasms are composed almost exclusively of neuroectodermal tissue, including astrocytes, oligodendroglial cells, and ganglion cells.⁷ Arguably such tumors may be hamartomas rather than true neoplasms.

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References:

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