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Department of Veterinary Pathology
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CASE I – A906 (AFIP 2935882).

Signalment: 23-year-old, female, Indian rhesus macaque (*Macaca mulatta*).

History: This macaque, born at the Tulane National Primate Research Center was part of the breeding colony from 1980 to 2002. A906 delivered her 13th infant in 2002, after which she was transferred to an aging project. In November 2003, A906 was found dead.

Gross Pathology: External exam - The animal was emaciated and dehydrated, with severe alopecia. The body weight at the date of the death was 6.5 kg.

Digestive system - The entire small intestine was necrotic with bloody fluid feces. The colon had two firm infiltrative masses, one of 2X2 cm located at 15 cm from the ileocecal junction and a second one of 1X1 cm located at 5 cm from the ileocecal junction.

Reproductive system - The left ovary was atrophic. The right ovary was enlarged, and was totally replaced by a multilocular cyst measuring 3X2.5 cm and lined by a thin wall. In some of the compartments of the cyst a sebum-like material was visible through the thin wall.

Contributor's Morphologic Diagnosis: Mature benign teratoma of ovary (Dermoid cyst).

Contributor's Comment: The cause of death established at necropsy was colon carcinoma with intestinal infarction. The ovarian teratoma presented here was an incidental finding.

On histologic examination, the cyst wall was composed of stratified epithelium with rare underlying sebaceous glands and hair follicles. Numerous cells situated in the cyst wall were producing melanin. A heterogeneous collection of structures from other germ layers were also identified, such as bone, cartilage, smooth muscle, adipose tissue, thyroid tissue and glandular structures. All these tissues lacked morphologic features of anaplasia. The lumen of the cyst contained amorphous material and necrotic cellular debris. As in most cases of teratoma in rhesus monkeys, this lesion was unilateral.[1] Ovarian teratomas have also been previously reported in an orangutan and an African green monkey.[2] While teratomas are often detected in the young and cause impaired fertility, the onset of neoplasia in this case was unknown and the reproductive history of this animal suggests no impairment in fertility.[3]

AFIP Diagnosis: Ovary: Teratoma, Indian macaque (*Macaca mulatta*), nonhuman primate.

Conference Comment: Teratoma is a germ cell neoplasm that arises from totipotential primordial germ cells and has disorganized elements of at least two of three embryonic germ layers (endoderm, mesoderm, ectoderm). Endoderm includes simple, stratified columnar, and cuboidal, ciliated or non-ciliated epithelium; goblet cells; and sebaceous or sweat glands. Mesoderm includes muscle, cartilage, bone, and blood vessels. Ectoderm includes keratinizing squamous epithelium, hair, teeth, and nervous tissue.[4,7]

Teratomas are classified as immature or mature. Immature (teratocarcinoma) contain less-differentiated embryonal tissues with some differentiated structures. Mature teratomas are composed of well-differentiated tissues. Most are well-differentiated and benign; however, malignant variants can occur and have been described in the bitch and mare. Teratomas can be solid or cystic. Cystic teratomas are often referred to as dermoid cysts and consist primarily of a cyst lined by skin.[4,5,6,7,9]

Teratomas in the dog and cat are usually ovarian and almost always benign. Teratomas in the horse are usually testicular and often occur in cryptorchid testicles. Benign and malignant teratomas occur in mice and occur spontaneously in certain strains such as B6C3F1LT/SV, CD1, and C3H mice. Adrenal and uterine teratomas have been reported in ferrets. Other species in which teratomas have been reported include, but are not limited to, cattle, swine, and sheep.[5,6,7,10]

Other germ cell tumors include dysgerminoma, choriocarcinoma, embryonal carcinoma, and yolk sac carcinoma. Dysgerminomas are the least differentiated

and resemble seminomas with solid sheets of round cells with vesiculate centrally placed nuclei and amphophilic cytoplasm. Choriocarcinomas undergo trophoblastic differentiation with large pleomorphic trophoblastic giant cells, syncytiotrophoblasts, cytotrophoblasts, and prominent blood-filled spaces. Embryonal carcinomas are rare and may contain multinucleated giant cells resembling syncytiotrophoblastic cells; however, cytotrophoblastic cells are absent. Yolk sac carcinomas differentiate into mesoblast and yolk sac endoderm composed of nests and ribbons of neoplastic epithelium in periodic acid-Schiff (PAS) positive material. Its characteristic histologic feature is a glomerulus-like structure composed of a central blood vessel enveloped by germ cells within a space lined by germ cells (Schiller-Duval body).[5,7,8]

Contributor: http://www.tpc.tulane.edu/

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CASE II – 756 (AFIP 2789028).

Signalment: Three late term caprine, *Capra* sp., fetuses with placenta.

History: In February of 2001, a newly established goat herd, assembled from multiple sources, experienced an abortion rate of over 10%.

Gross Pathology: No lesions were observed in the fetuses. The placenta exhibited a thick creamy reddish-brown exudate between cotyledons.

Histopathologic Description: There was moderate to marked suppurative inflammation of the intercotyledonary chorionic membrane, with moderate multifocal villar necrosis. Cotyledonary inflammation was most developed at the base of villi and was characterized by a superficial multifocal mixed cellular inflammatory infiltrate in which plasma cells predominated. Intracytoplasmic, blue foamy organisms were found in trophoblast cells throughout the arcade and were most numerous at the base of villi.

Contributor's Morphologic Diagnosis: Placentitis, necrotizing, subacute, multifocal, suppurative, plasmacytic with large numbers of foamy blue intracellular organisms, etiology consistent with *Coxiella burnetii.*

Contributor's Comment: Lesions typical of *Coxiella burnetii* were restricted to the placenta. Trophoblast cells were distended with intracytoplasmic, foamy blue organisms characteristic of *C. burnetii*. This was confirmed by PCR analysis of placental tissue. Since the affected goat herd was assembled from numerous sources, it is probable that both reservoir and naïve animals were purchased. Exposure of the naïve animals to organisms shed by the reservoir animals and/or organisms in the new farm environment likely preceded the abortion storm.

Coxiella burnetti is a rickettsial, obligate intracellular parasite with worldwide distribution. The organism is resilient in the environment and persists indefinitely in animal reservoirs such as dairy cows, sheep, goats and wildlife. Reservoirs shed the organism in milk, fetal fluids, urine and feces. The organism rarely causes systemic disease in infected animals other than abortion and stillbirth. *C. burnetii* is the cause of Q fever in humans, a zoonosis. Inhalation of contaminated dust or

ingestion of infected milk can lead to a clinical syndrome in man characterized by fever with or without pneumonia and hepatitis.

AFIP Diagnosis: Chorioallantois: Placentitis, subacute, diffuse, moderate, with multifocal necrosis and myriad intratrophoblastic organisms, etiology consistent with *Coxiella burnetti*, goat (*Capra hircus*), caprine.

Conference Comment: The contributor provides a general background overview of *Coxiella burnetti*.

Typical light microscopic findings include an acute, diffuse, suppurative placentitis with extensive necrosis of cotyledonary villi and intercotyledonary epithelium. The placentitis is most severe in the intercotyledonary areas. A lymphoplasmacytic infiltrate is usually present in the chorioallantoic interstitium. As pointed out by the contributor, hypertrophic trophoblasts containing the organisms have a characteristic foamy appearance with multiple unstained vacuoles within a finely granular blue cytoplasm. Vasculitis is not usually a feature.[1,3]

Grossly, the intercotyledonary chorioallantois is thick, leathery, yellow, and covered with surface exudates. Cotyledons may have multiple areas of gray discoloration in areas of inflammation and necrosis. Gross fetal lesions are nonspecific.[1,3]

The differential diagnosis for a necrotizing placentitis associated with intra-trophoblastic organisms includes:[1,3]

1. *Brucella ovis* – vasculitis common
2. *Chlamydophila abortus* – vasculitis common, more severe cotyledonary inflammation, coccoid organisms
3. *Toxoplasma gondii* – primarily affects cotyledons

As pointed out by the contributor, *C. burnetii* is a zoonosis causing Q fever in man. The organism is extraordinarily virulent in man and a single organism can result in disease. Infections occur primarily in abbatoir employees and personnel working in research centers. Clinical syndromes associated with Q fever include a self-limited febrile illness, pneumonia, hepatitis, endocarditis, osteomyelitis, and neurologic manifestations. The majority of infections are mild self-limited febrile illnesses.[2]

Contributor: BCMAF Animal Health Centre, Abbotsford, BC, Canada

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CASE III – 4075-10-02 (AFIP 2940308).

Signalment: Fetus, gestational age about 7 months, female, Ayrshire, bovine.

History: The fetus was stillborn. Conception was by embryo transfer. The heifer had retained placenta but showed no other clinical signs at the time of abortion. The farm had had several abortions during the previous 2 months. The farm was free of bovine leucosis (BVL), infectious bovine rhinotracheitis (IBR) and bovine virus diarrhea (BVD).

Gross Pathology: The fetus had moderate interstitial oedema of the lungs. The liver was swollen and brick-red. The cotyledons were necrotic and oedematous. Intercotyledonary areas were thickened and leathery. The amnion was markedly thickened and oedematous with a leathery aspect.

Laboratory Results: Bacteriology and PCR: *Ureaplasma diversum* was isolated from the placenta and abomasal contents and identified by nested PCR. No other specific bacteria were isolated. Mycology: No fungal growth.

Histopathologic Description: Necrotizing placentitis with multifocal mineralization was present in the chorioallantoic placenta. In the liver there was diffuse moderate centrilobular degeneration. In the lung there was marked multifocal necrotizing alveolitis.

Contributor's Morphologic Diagnosis: Placenta, allantoamnion, amnionitis, necrotizing, diffuse, chronic, severe with vasculitis and mineralization.

Contributor's Comment: The macroscopic and histological findings are characteristic but not pathognomonic of ureaplasma infection.[1,2,3] Definitive diagnosis requires isolation and identification of the bacterium. The strain was identified by nested polymerase chain reaction.[4] *Ureaplasma diversum* can be

spread via artificial insemination and embryo transfer as well as via natural breeding. The infection is often subclinical in chronically infected herds.[5] In central Finland there appeared to have been an epidemic of virulent *U. diversum* infection during 2002-2003. Numerous farms in that area experienced problems ranging from early embryonic death and vulvitis to abortions in the 2nd and last trimester. *U. diversum* has recently been reported as an important pathogen causing reproductive problems in Brazil.[6]

AFIP Diagnosis: Placenta: Placentitis, necrotizing, subacute, diffuse, severe, with vasculitis, thrombosis, and mineralization, Ayrshire (*Bos taurus*), bovine.

Conference Comment: *Ureaplasma diversum* is an important cause of reproductive failure and abortion in cattle. *U. diversum* belongs to the family Mycoplasmataceae, the smallest free-living parasites capable of autonomous growth. It is frequently present on the mucous membranes of the nasal passages, vulva, and vagina of the cow, the sheath of bulls, and in semen and embryo transfer fluids.[5,7]

Virulent strains of *U. diversum* can cause abortion, embryonic death, birth of dead or weak calves, and vulvitis. Grossly, the amnion is typically the most severely affected with patchy thickening and yellow discoloration, fibrosis, edema, inflammation, necrosis, and mineralization. The fetus is usually well preserved.[5,7]

Histologically, fibrosis and interstitial necrosis of the placenta are extensive; there is often a mononuclear inflammatory infiltrate. A mild arteritis is typically present. Erosive conjunctivitis with prominent goblet cell formation is present in the fetus as well as a nonsuppurative pneumonia with prominent peribronchiolar lymphoid tissue.

Some slides contained vessels partially occluded by fibrin thrombi.

Contributor: National Veterinary and Food Research Institute (EELA), http://www.eela.fi

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CASE IV – AFIP #1 (AFIP 2983846).

Signalment: Adult Holstein cow.

History: Placenta from an adult, multiparous Holstein cow is presented for examination after abortion of an approximately 120-day-gestation fetus.

Gross Pathology: Tissue representing approximately ½ of a bovine placenta is examined. The tissue is diffusely edematous. The chorionic surface is covered by variably sized (0.5 to 3.0 cm diameter), individual and coalescing raised, firm, ovoid, dark red plaques thickening intercotyledonary spaces. A few grossly normal cotyledons are present.

Histopathologic Description: Dark red plaques consist of multifocal, raised, well demarcated primitive placental villus structures that replace and widen intercotyledonary stroma. Structures are composed of variably sized, thin walled vessels aligned perpendicularly to the chorionic surface, supported within a dense fibrous stroma. These vessels extend to the tissue surface which is occasionally covered by thin layers of mineralized material. In many of the plaques, vessels are separated by vertically linear pools of free erythrocytes. Surrounding stroma is edematous. Moderate numbers of plasma cells are among villous structures in some sections.

Contributor's Morphologic Diagnosis: Adventitial placentation, multifocal, placenta

Contributor's Comment: Adventitial placentation is the development of additional sites of placentation between adjacent placentomes, as the result of inadequate development of existing placentomes. In ruminants, development of such structures is a mechanism used for compensation of inadequate placentation.[1]

The condition generally results from an insufficient number of caruncles resulting either from congenital disorders of endometrial organization (too few caruncles) or more commonly by the loss of caruncles due to inflammation/scarring following repeated episodes of endometritis.[2] Primitive villus attachments between the chorion and endometrium attempt to compensate for inadequate placentation.[1]

Cows normally have 75-120 caruncles in the uterus, and ewes and goats have 40-125. Not all caruncles are utilized in a normal single pregnancy.[2] When adventitial placentation becomes diffuse, pregnancy cannot proceed beyond midterm. Hydrallantois is a common complication.[1]

In most cases, the compensatory effort leads to placental insufficiency and abortion. However, one case of successful live birth of a healthy cloned calf found to have been supported by an atypical placenta affected with severe adventitial placentation is reported.[3]

AFIP Diagnosis: Chorioallantois: Adventitial placentation, multifocal, with edema and minimal lymphoplasmacytic placentitis, Holstein (*Bos taurus*), bovine.

Conference Comment: The contributor provides a concise summary of the causes of adventitial placentation. As mentioned by the contributor, hydrallantois is a common complication that is characterized by excessive fluid in the allantoic sac. The quantity of fluid present may exceed 150 liters verses a normal 15-20 liters of fetal fluid present between the amnion and allantoic sacs. Common sequelae to hydrallantois, if the fetus is not aborted early, include dystocia, uterine atony with retained fetal membranes, and metritis. Additionally, adventitial placentation is often seen in cloned fetuses and is also thought to be an age-associated change as it is often seen in cows with a higher parity.[1,2,4]

Grossly, additional sites of placentation are visible in intercotyledonary areas and appear as red plaques, sometimes with villi that extend from cotyledons. Corresponding changes are visible in the endometrium.[4]

Contributor: Utah Veterinary Diagnostic Laboratory (UVDL), Utah State University, ADVS Dept., Logan, UT 84322, www.usu.edu/uvdl

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