

## **2017 Northeast Veterinary Pathology Conference – Joint Pathology Center April 1-2**

### **Case Submission Form**

#### **NEVPC CASE #11**

**IDENTIFICATION NUMBER ON SOURCE MATERIAL:** Cornell University 65180-15

**INSTITUTIONS:** Cornell University, College of Veterinary Medicine, Department of Biomedical Sciences, Section of Anatomic Pathology, Ithaca, NY

**SIGNALMENT:** 3-5 year old, female mixed breed dog

**HISTORY:** A 3-5 year old, female mixed breed dog was rescued from a SC animal shelter by a NY rescue organization. Upon arrival she was treated for heartworm infection. When she tested negative for HW antigen 6 months later, she presented for ovariohysterectomy (OHE). During OHE two firm egg-sized mass were noted cranial to the left ovary, approaching the left kidney and small intestine. Multiple sesame seed-sized masses extended in the broad/suspensory ligaments from the area of the reproductive tract to near the small intestine. There were similar, less severe changes noted adjacent to the right ovary.

#### **GROSS FINDINGS:**

Variably sized masses were present in the mesenteric attachments of the uterus and ovaries as described in the clinical history. A thin cord-like structure was present within the broad ligament connecting the left ovary to the described egg-shaped mass. Representative sections are taken through both uterine horns, ovaries, and masses.

#### **HISTOPATHOLOGIC FINDINGS:**

**Uterine and ovarian vessels:** There are multiple variably sized anastomosing vessels which are frequently dilated (up to 3cm) with multiple lumens present on cross-section. Dilated vascular spaces (aneurysm) are filled with blood and variably organized thrombi which are surrounded by altered arterial walls. Other vessels have blood filled clefts within the wall (dissections). The largest aneurysms correspond with the “egg sized masses” within the suspensory ligament near the left ovary. The lumen of altered vessels is lined by flattened endothelial cells with moderate to marked diffuse intimal expansion by fibrosis with scattered fibroblasts and variable inflammatory cells including hemosiderophages. The internal elastic lamina is not evident in most vessels. Thrombosed vessels have loss of the endothelial lining and imperceptible merging of intimal connective tissue with thrombi. Several thrombi contain areas of mineralization and clusters of hemosiderin laden macrophages or organized to completely recanalized thrombi. The tunica media is diffusely peripheralized, compressed, wrinkled, scrolling and disrupted with variable splitting, fragmentation, and condensation of elastic fibers. Adjacent to large aneurysms there are multiple smaller aneurysmal congested dilations. Around the largest aneurysm there are multifocal to coalescing infiltrates of lymphocytes and plasma cells and adventitia and arterial wall. In the uterus (not in provided sections), there are small foci of endometrial glands within the myometrium layers extending approximately two thirds out towards the serosal surface (adenomyosis). Diffusely, the endometrium along both horns is moderately hyperplastic and tortuous. The luminal surface and superficial two thirds of the

endometrial glands are lined by tall columnar epithelial cells (estrogen influence). Within the stratum compactum there are moderate numbers of scattered hemosiderin laden macrophages.

#### Special histochemical Stains:

The following histochemical stains were applied to uterine/ovarian vessels:

Masson's Trichrome (for collagen): The stain highlights vascular wall disruption, increased collagen expanding the intima, and narrowed lumen. Also, this stain demonstrates the expansion the media and intima of large vessels with fragmentation of elastin, and highlights the occasional smaller vessels occluded by intimal proliferation.

Movat's Pentachrome (for connective tissue): Similar to the Trichrome, staining highlights vascular wall disruption, increased collagen expanding the intima, and narrowed lumen as well as highlighting mucinous deposits in the expanded intima. This stain also highlights elastic fibers and emphasizes the scrolling expanded redundant tunica media.

### **MORPHOLOGIC/ETIOLOGIC DIAGNOSES:**

Suspensory ligament around left and right ovaries: Intimal fibrovascular dysplasia with multiple arterial aneurysms, thrombosis, and dissection

### **DISCUSSION:**

The described masses around both the left and right ovaries, as well as within the mesenteric connective tissues extending towards the kidney, and small intestine correspond with arterial aneurysms, the largest of which have attenuated walls and contain large thrombi. The thrombi show varying stages of chronicity with some mostly composed of erythrocytes and fibrin while others are completely recanalized and contracted. These aneurysms are present within the vascular plexuses around the ovaries which are equivalent to the pampiniform plexuses of the male testes. Interestingly, blood vessels within the myometrium of the uterus appeared normal. Vascular malformations can result in abnormal blood flow which predisposes to the formation of thrombi and aneurysms with the potential to rupture.

Aneurysms are defined as segmental enlargement of a vessel 1.5X larger than the adjacent vessel and are defined by the nature of the aneurysm wall (true, dissecting, false). A dissecting aneurysm is a tear in the vessel wall with blood collection between the vessel layers. A false or pseudo-aneurysm is a hematoma present outside a vessel wall. There are both congenital and acquired causes of true aneurysms. Congenital causes include the connective tissue disorders (Marfan, Loeys-Dietz, Erler's-Danlos syndromes), neurofibromatosis (type I), and anomalous vessels. Aneurysms of the aorta are associated with bicuspid aortic valve. Acquired causes of aneurysms in humans include hypertension, atherosclerosis, non-infectious vasculitis (e.g. polyarteritis nodosa), arterial mediolysis (idiopathic), infection, trauma, or fibromuscular dysplasia.<sup>1</sup> Fibromuscular dysplasia (FMD) encompasses a group of idiopathic vascular abnormalities primarily affecting arteries which causes thickening and distortion of the vessel wall. With imaging (angiography), areas of alternating stenosis and dilatation impart a "string-of-beads" appearance to affected arteries (multifocal FMD). Structural changes are most frequent in medium and large vessels with three forms recognized based on the layer involved: medial, intimal and adventitial. Medial fibromuscular dysplasia is the most common form while both

intimal and adventitial are uncommon. Intimal fibromuscular dysplasia is characterized by non-inflammatory proliferation of smooth muscle cells, myofibroblasts and fibroplasia which disrupt the internal elastic lamina (preserved in the medial form) and infiltrate into the intima.<sup>2</sup> Vessel wall changes can result in stenosis/occlusion, aneurysm, or dissection with clinical signs reflecting the involved vessel. In humans, fibromuscular dysplasia most frequently involves the renal arteries, carotid/vertebral arteries, and less frequent involvement of intracranial vessels; however, fibromuscular dysplasia is recognized to cause local disease in extra-renal and extra-cervical arteries.<sup>5</sup> Involvement of the renal arteries is associated with renovascular and systemic hypertension. Although evidence supports a genetic basis for susceptibility to FMD, the genetic basis of and predisposing factors for fibromuscular dysplasia are unknown.<sup>5</sup> In The United States Registry for Fibromuscular Dysplasia, 91% of registrants were female.<sup>4</sup>

These findings in this case are consistent with fibromuscular dysplasia, specifically the uncommon intimal form of fibromuscular dysplasia. Fibromuscular dysplasia has previously reported affecting the coronary arteries in a dog.<sup>3</sup> After the diagnosis of FMD, CT angiogram was performed on this dog to evaluate for other vascular malformation which revealed: 1. segmental aplasia of the hepatic caudal vena cava with right azygos continuation and, 2. segmental abdominal vena cava dilation and severe left hydronephrosis and segmental proximal left hydroureter. Vascular abnormalities were not noted in the thorax. In this dog, FMD appears to be localized to vessels adjacent to the reproductive tract. Surgical excision of these aneurysms is considered curative but the presence of other vascular malformations in this dog cannot be ruled out. Ovarian varices, which have only been reported in humans and can be a bilateral change is a differential; however, the section demonstrate arterial alterations.<sup>6</sup>

#### References:

- 1 Burke A, F. Tavora: *Practical cardiovascular pathology : an atlas*. Philadelphia: Wolters Kluwer Health, 2011.
- 2 Harrison EG, Jr., McCormack LJ: Pathologic classification of renal arterial disease in renovascular hypertension. *Mayo Clin Proc* 1971;46(3):161-167.
- 3 Mete A, McDonough SP: Epicardial coronary artery fibromuscular dysplasia, myocardial infarction and sudden death in a dog. *J Comp Pathol* 2011;144(1):78-81.
- 4 Olin JW, Froehlich J, Gu X, Bacharach JM, Eagle K, Gray BH, et al.: The United States Registry for Fibromuscular Dysplasia: results in the first 447 patients. *Circulation* 2012;125(25):3182-3190.
- 5 Olin JW, Gornik HL, Bacharach JM, Biller J, Fine LJ, Gray BH, et al.: Fibromuscular dysplasia: state of the science and critical unanswered questions: a scientific statement from the American Heart Association. *Circulation* 2014;129(9):1048-1078.
- 6 Tarazov PG, Prozorovskij KV, Ryzhkov VK: Pelvic pain syndrome caused by ovarian varices. Treatment by transcatheter embolization. *Acta Radiol* 1997;38(6):1023-1025.