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Conference Moderator:

Dr. Kathleen Gabrielson, DVM, PhD, Diplomate ACVP

CASE I: H-8379 (AFIP 3103222).

Signalment: 11-year-old, male owl monkey (*Aotus nancymaae*).

History: This monkey was euthanized due to cardiac and renal failure. Echocardiogram showed dilated cardiomyopathy with left ventricular hypertrophy, pericardial effusion, ascites, and abnormal kidneys.

Gross Pathology: At necropsy, the pericardial sac was filled with serosanguineous fluid; the heart was enlarged with multiple white streaks (degeneration/fibrosis) in the ventricular walls. The ascending aorta was “double-barreled,” having apparently two lumina; the latter tracked into the abdominal aorta near the kidneys. Several linear yellow streaks (plaques) were observed in the thoracic and abdominal aorta. The kidneys were light brown with black and red speckling (nephropathy); the liver was enlarged (hepatomegaly).

Laboratory Results: Hematocrit 19.6% ↓; RBC $2.66 \times 10^6/\mu\text{l}$ ↓; BUN 45 mg/dl ↑; creatinine 1.4 mg/dl ↑

Histopathologic Description: The aorta is oval-shaped and measures 4-5 mm in diameter; associated with the tunica media of the aorta is a second oval-shaped channel of slightly larger diameter that partially encircles the aorta. The wall of the aorta is approximately 300 μm thick versus approximately 500 μm for the second channel; the wall of the latter has an irregular endothelial lining and contains fibromuscular proliferation, degeneration/necrosis, and granulation tissue.

Contributor's Morphologic Diagnosis: Aorta: dissection, tunica media with fibromuscular proliferation, degeneration/necrosis, and granulation tissue.

Contributor's Comment: The aortic dissection in this owl monkey started in the ascending aorta and extended to the level of the kidneys. The dissection presented as a “double-barreled aorta” with a false channel. The false channel was partially endothelialized, suggesting it was a chronic change. Mention should be made of terminology in reference to aortic dissections. That is, while aortic aneurysm is used as a general term by many, a distinction is made by others between an aneurysm and a dissection.⁽³⁾ A “true” aneurysm is considered an abnormal dilatation of a blood vessel wall that is bounded by arterial wall components. A “false” aneurysm involves an interruption in the vessel wall and the development of an extravascular hematoma that communicates with the vessel lumen. On the other hand, a dissection develops when blood enters the wall of an artery (e.g. via intimal tear), dissecting between layers, as in the aorta of this monkey. Other terms used to describe aortic dissections include dissecting hematoma and dissecting aortic aneurysm.

In general, the incidence rates for aortic aneurysms in nonhuman primates appear to be low; however, spontaneous lesions have been reported in the gorilla and squirrel, howler, capuchin, patas, spider, and owl monkeys.⁽¹⁾ In contrast, aortic aneurysms are not uncommon in the owl monkey, with an incidence rate of 8.6% (N=257) in one report. The majority of the aneurysms in this report were classified as dissecting with only three others termed saccular aneurysms. Aortic plaques were seen in some of these animals, as was chronic nephropathy, cardiomegaly, left ventricular hypertrophy, pericardial effusion, pleural effusion, pulmonary edema, hemothorax, hemoperitoneum, hepatomegaly, and cholelithiasis. More females than males were affected.

Hypertension is a major risk factor for aortic dissection in human males aged 40-60 years. Degenerative changes in the tunica media of the aorta may also be important. Inherited connective tissue disorders that lead to abnormal vascular structure (e.g. Marfan syndrome) fall into the latter category. Complications following arterial cannulation and pregnancy have also been associated with aortic dissection in humans. Interestingly, atherosclerosis and medial scarring due to diseases such as syphilis are not usually associated with dissections. Following the particular predisposing factor(s), an intimal tear develops with hemorrhage into the wall of the aorta.(3) Conversely, the initiating event may be a ruptured vasa vasorum with bleeding into media.(5) The pathogenesis of the aortic dissection in this monkey was not determined.

AFIP Diagnosis: Fibroelastic artery, aorta: Aortic dissection lined by endothelium, fibromuscular proliferation, cystic medial degeneration, and mucinosis.

Conference Comment: This interesting case was reviewed in consultation with the AFIP Department of Cardiovascular Pathology. During the conference, participants discussed the nomenclature pertinent to this case, with a focus on the distinction between an aneurysm and a dissection; inappropriate interchangeable use of the terms aneurysm and dissection may be culpable for undue perplexity when reviewing case reports in the literature. A true aneurysm is a localized abnormal dilation of a blood vessel or the heart, and can be further classified by its overall shape and size, with saccular (i.e. focal, bulging, asymmetrical outpouching) and fusiform (i.e. segmental to diffuse, circumferential) types being described. By contrast, a false aneurysm, also referred to as a pseudo-aneurysm, results from a vessel wall defect and extravasation of blood into a hematoma within the extravascular connective tissue that communicates freely with the vascular space (i.e. “pulsating hematoma”). Like a false aneurysm, a dissection is characterized by the extravasation of blood; however, the blood in a dissection accumulates between layers of the vessel wall, rather than in the extravascular connective tissue as occurs in a false aneurysm. Blood usually extravasates via an intimal tear, as with a false aneurysm, but a dissection may also occur by rupture of vessels of the vasa vasorum within the media. Dissections may be aneurysmal (i.e. present within a vessel that is also abnormally dilated), but are not always so; therefore, use of the term “dissecting aneurysm” may be inappropriate.(3)

The most important risk factor for aortic dissection in humans is hypertension; less commonly, aortic dissection is associated with abnormal vascular extracellular matrix (ECM) due to inherited or acquired connective tissue disorders.(3) Participants reviewed one such disorder, Marfan syndrome, an inherited defect in the extracellular glycoprotein fibrillin-1 which results from a mutation in the *FBNI* gene. Fibrillin-1 is a major component of the ECM microfibrils that provide the scaffolding on which tropoelastin is deposited to form elastic fibers. Fibrillin-1 abnormalities result in defective mechanical properties of the ECM in the cardiovascular system and eyes, resulting in aortic aneurysm, aortic dissection, and lens subluxation or dislocation. Moreover, since normal microfibrils sequester transforming growth factor β (TGF- β) and control its bioavailability, Marfan syndrome is characterized by excessive activation of TGF- β ; this not only further contributes to the altered vascular ECM integrity, but likely accounts for other clinical manifestations of the syndrome not attributable to ECM abnormalities (e.g. bone overgrowth).(2) These observations are supported by studies in a mouse model of Marfan syndrome in which *Fbn1*^{+/-} mice developed myxomatous mitral valve and aortic lesions that were prevented by the administration of TGF- β antibodies, demonstrating the importance of TGF- β in the pathogenesis of the lesions and indicating that elevated TGF- β may be primarily responsible for the development of mitral valve prolapse in children with Marfan syndrome.(4)

While in most cases of aortic dissection no specific underlying pathology is identified in the aortic wall, the most frequently detected lesion is cystic medial degeneration in the absence of inflammation. In this case, some participants noted areas of cystic medial degeneration and therefore considered, in addition to Marfan syndrome, other causes of vascular ECM abnormalities, including Ehlers-Danlos syndrome, vitamin C deficiency, and defects in copper metabolism.(3) Some participants noted the presence of foam cells and rare cholesterol clefts, reminiscent of atherosclerosis; however, their subadventitial location is not consistent with atherosclerosis, and as mentioned by the contributor, while atherosclerosis is among the most important predisposing factors for aneurysms (along with hypertension), dissections are unusual in the presence of atherosclerosis, presumably because of medial fibrosis precluding propagation of the dissection.(3) Nevertheless, the gross description of yellow plaques within the aorta is consistent with atherosclerosis and participants could not exclude it as a causal or contributory factor in this case. Finally, some participants noted striking microscopic resemblance to a stented vessel, and dissection can occur iatrogenically due to complicating arterial cannulations.(3)

Contributor: University of Texas MD Anderson Cancer Center, Michale E. Keeling Center for Comparative Medicine, 650 Cool Water Drive, Bastrop, TX 78602

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CASE II: 47928 (AFIP 3135954).

Signalment: 13-year-old, 2.83 kg, female, spayed Persian cat (*Felis catus*)

History: This cat presented to the cardiology service with a history of collapse, pericardial effusion and chronic renal disease. Thoracic radiographs revealed cardiomegaly, and echocardiography identified a mass at the heart base and pericardial effusion. Due to the cat's declining condition, euthanasia was elected.

Gross Pathology: Based upon fat stores and muscle mass, the cat was assessed to be in fair to good body condition. At the base of the heart, between the aorta and pulmonary artery, adjacent to and compressing the right atrium, a 2.5 x 2.0 x 1.3 cm multi-nodular, pale tan to white, soft, slightly bulging mass was adhered to the epicardial surface of the right atrium. The pericardial sac contained 18 mL of non-clotted, serosanguinous effusion and 23 mL of serosanguinous effusion were noted in the pleural space. The lungs exhibited moderate to severe, diffuse congestion and pulmonary edema. Multifocally throughout the cortex and medulla of the right and left kidneys were thin walled, fluid filled cortical and medullary cysts. The liver also contained few multifocal cysts, grossly interpreted to involve the biliary tree. Additional findings included mandibular prognathism with glossal protrusion.

Laboratory Results: T4 values were normal; potassium levels were decreased at 2.55 mmol/L (3.5-5.3 mmol/L); and BUN was mildly elevated at 36 mg/dL (15-34 mg/dL).

Histopathologic Description: Examined is a section of heart that displays the left ventricular outflow tract including the left ventricle, interventricular septum, right ventricle, mitral valve, aortic valve, aorta and epicardium (visceral pericardium). At the base of the heart, adjacent to the aorta and compressing the right atrium, there is a well demarcated, expansile, densely cellular, nodular mass, composed of round to polygonal cells arranged in packets and separated by a fine fibrovascular stroma ("zelballen structures"). Neoplastic cells are mildly pleomorphic with abundant finely vacuolated eosinophilic to amphophilic cytoplasm and indistinct cell borders. Nuclei exhibit mild pleomorphism, are central to peripheral with finely stippled chromatin and a single, variably distinct nucleolus. Anisocytosis and anisokaryosis are mild and there are 0-1 mitotic figures per 400x field. At the periphery of the mass, small, mildly infiltrative lobules of neoplastic cells are noted adjacent to ectatic vessels, but no direct vascular invasion is observed. Small numbers of lymphocytes are scattered throughout the neoplastic populations. Within the mass, there is a focal paucity of neoplastic cells in which fibrocytes are situated amongst a stroma of loosely arranged connective tissue, separated by clear space (edema) and infiltrated by scattered lymphocytes and macrophages (region of previous necrosis, presumptive).

Focally, there is a large aggregate of lymphocytes within the epicardium, and few ectatic vessels contain clusters of neoplastic cells (intracardiac metastasis, not present on every slide). Diffusely, mesothelial cells of the epicardium are enlarged (hypertrophy) and the epicardium contains moderate numbers of inflammatory cells composed of lymphocytes, macrophages, neutrophils and eosinophils, admixed with eosinophilic acellular fibrillar material (fibrin) and occasionally plump fibroblasts. Macrophages multifocally contain golden brown granular pigment (hemosiderin, confirmed with iron stain). Small numbers of inflammatory cells extend into the underlying

myocardium. Diffusely, the mitral valve is moderately expanded by increased mucinous matrix and there is mild multifocal interstitial fibrosis within the interventricular septum and left ventricular myocardium. The endocardium of the left atrium is irregular and is diffusely expanded by fibrous connective tissue (endocardial fibrosis). There is also minimal to mild, multifocal myofiber disarray noted within the left ventricular myocardium. Multifocally, the tunica media of small and moderate sized arterioles is thickened by hypertrophic smooth muscle cells (arteriosclerosis).

Neoplastic cells exhibit diffuse, strong cytoplasmic staining for synaptophysin and chromogranin A, diffuse weak cytoplasmic staining for neuron specific enolase (NSE), and negative staining for thyroglobulin, cytokeratin, vimentin and calcitonin. Positive and negative controls were run and stained appropriately. Intracardiac metastatic foci stain strongly positive with synaptophysin and chromogranin A. Reticulin stains highlight the connective tissue stroma and enhance the packeted pattern of the neoplasm.

Contributor's Morphologic Diagnosis: 1. Heart (base between aorta and pulmonary artery): Focal chemodectoma with multifocal epicardial metastasis.
2. Heart: Moderate multifocal chronic ongoing lymphohistiocytic, neutrophilic, fibrinous epicarditis with mesothelial cell hypertrophy, hemosiderosis and fibroplasia.
3. Heart: Moderate diffuse mitral valve myxomatous degeneration (consistent with valvular endocardiosis) and left atrial endocardial fibrosis.
4. Heart: Moderate multifocal arteriolar tunica media hypertrophy (arteriosclerosis), mild multifocal myocardial interstitial fibrosis, and minimal to mild, multifocal ventricular myofiber disarray.

Contributor's Comment: Chemodectoma, also referred to as aortic body tumor or extra-adrenal non-chromaffin paraganglioma, is a primary neuroendocrine tumor of chemoreceptor cells in the region of the heart base.(4,5) Primary tumors of the heart and pericardium (including the great vessels) are rare in cats, with a reported incidence of 0.03%.(1,5) Chemodectomas are particularly uncommon in cats, with limited reports in the literature.

Chemoreceptor tissue is composed of parenchymal cells (chemoreceptors and glomus cells) and sustentacular cells and aids in the regulation of respiration and circulation.(2,4) Chemoreceptors are sensitive to changes in arterial partial pressure of carbon dioxide and oxygen, blood pH and temperature, and stimulation of chemoreceptors may result in adaptive modifications in respiratory rate and/or arterial blood pressure.(2,4,6) In mammals, the chemoreceptor system is part of the parasympathetic nervous system, leading to the terminology "non-chromaffin paragangliomas".(6) Neoplasms of the chemoreceptor cells most commonly arise within the aortic or carotid body and less frequently the glomus pulmonale, glandula suprarenalis or in ectopic sites.(2,4,6) Aortic body tumors are more common than carotid body tumors in animals, though carotid body tumors are more often malignant than aortic body tumors.(2) Chemodectomas typically form a single mass or multiple nodules within the pericardial sac near the base of the heart and have been reported to occur between the aorta and pulmonary artery, between the pulmonary artery and left auricular appendage, or below the aorta and right auricular appendage.(2,4-6) The mass in this cat was located at the base of the heart, adjacent to the right atrium and auricle between the aorta and pulmonary artery.

Though chemodectomas are non-functional in animals, clinical signs can be attributed to the neoplasm acting as a space occupying lesion, causing compression of multiple adjacent structures.(2,5,6) The tumors can vary greatly in size (0.5 - 12.5 cm) and are often associated with accumulation of serous, often blood tinged, fluid in the pericardial sac.(2) Pericardial effusion (as noted in this cat) can result from lymphatic invasion of neoplastic cells at the base of the heart or the compression of small pericardial veins, and may cause impairment of normal cardiac function and decompensation, depending on the speed and volume of accumulation.(2,5,6) Obstruction of the thoracic duct and/or cranial vena cava may lead to pleural effusion, pericardial effusion, ascites, and subcutaneous edema, particularly of the head, neck and forelimbs, while obstruction of blood return to the atria may manifest as systemic congestion.(2,5) Airway and esophageal compression may be clinically evident as dyspnea or coughing and vomiting, respectively.(2) Non-specific signs of systemic illness, including debilitation, anorexia and lethargy may also be noted.(2,5,6) Gross and histologic evaluation of the lungs in this case revealed moderate to severe, diffuse congestion, pulmonary edema and a moderate amount of serosanguinous pleural effusion. These findings are interpreted to be secondary to the compressive effects of the neoplasm. Pericardial effusion is likely secondary to compression, vascular invasion, and hemorrhage within the neoplasm. The associated inflammation in the epicardium of this cat is suspected to be secondary to the pericardial effusion.

Chemodectomas are typically well demarcated and comprised of round to polygonal cells with indistinct cell borders, scant cytoplasm and central round nuclei with fine chromatin and prominent nucleoli.(4) In our case, positive reticulin and trichrome staining demonstrated the small lobules delineated by fine fibrovascular stroma, which is a typical feature of this neoplasm.(4) Mitoses are rare, and occasionally there may be small amounts of scattered T-lymphocytes throughout the mass.(4,6) Lymphocytes were identified within the neoplasm in this case, but were not further characterized.

In our case, neoplastic cells exhibited diffuse, strong cytoplasmic staining for synaptophysin, chromogranin A, diffuse weak staining for neuron specific enolase (NSE), and negative staining for thyroglobulin, vimentin, cytokeratin and calcitonin, consistent with a diagnosis of chemodectoma. Chemodectomas are known to exhibit positive immunohistochemical reactivity for synaptophysin, chromogranin A and NSE.(4) Synaptophysin is considered to be a specific marker for neuroendocrine tumors because it is not detected in non-neuroendocrine cells or neoplasms.(3,4) Chromogranin positive granules are also typical of neuroendocrine tumors.(4) Occasionally, as noted in this tumor, staining of neoplastic cells for NSE may be weak, hypothesized to result from rapid autolysis of chemoreceptor cells and subsequent loss of immunoreactivity.(4) Neoplastic neuroendocrine cells also commonly exhibit argyrophilic cytoplasmic granules when stained with Churukian-Shenk or Grimelius silver stains (not performed in this case). Differential diagnoses for a heart based tumor in a cat include lymphosarcoma, ectopic thyroid adenoma/carcinoma, ectopic parathyroid chief cell adenoma, and thymoma.(2,6) Tumors of ectopic thyroid tissue may exhibit a similar histologic appearance and immunohistochemistry may be helpful in distinguishing such tumors. Ectopic thyroid tumors should stain positively for cytokeratin and thyroglobulin, while C cell tumors should stain positively for calcitonin.(4)

Because chemodectomas are so rarely identified in cats, biological behavior is essentially unknown.(5) Extrapolating from behavior in other species, aortic body tumors tend to be more benign than carotid body tumors and grow slowly by expansion.(2) Advanced lesions may be associated with neoplastic invasion of the adventitia of the great vessels, atrial myocardium, and as in this case, epicardial vessels, consistent with intracardiac metastasis.(5) Willis et al (2001) reported metastasis in 22% of canine chemodectomas and 2 of 6 (33%) of the reported feline cases.(6) In 2 of 2 cases of feline chemodectoma reported by Tilley et al (1981), tumor emboli were noted in blood vessels, with metastasis to the pericardium, epicardium and myocardium.(5) Multifocal thoracic metastatic foci, with spread to local lymph nodes (mediastinal, sternal) and/or the lungs has also been reported in the cat.(3,5) In this case, there was a site of extracardiac metastasis within tissue that was histologically most compatible with remnant thymic tissue. The highly vascularized stroma frequently associated with chemodectomas may facilitate metastasis via the bloodstream.(5) Chemodectomas may also secrete angiogenic substances, leading to the development of a collateral blood supply that can involve the local vasculature.(6) Long term prognosis is typically guarded to poor, as the tumor is often diagnosed at an advanced stage, though one cat is reported to have lived 13 months post-diagnosis.(5,6) In humans, surgical excision is the treatment of choice and is frequently associated with good success.(6) However, surgical intervention has had limited success in dogs and complete removal is rarely possible.(5,7)

This cat exhibited mandibular prognathism with glossal protrusion, consistent with brachycephalic conformation. Chronic hypoxia is likely involved in the pathogenesis of chemodectoma development, as increased prevalence of this tumor is noted in humans and cattle living at high altitudes, humans with emphysema and brachycephalic dogs.(2,4,6) However, a definitive link with chronically low oxygen tension has not been established in the cat. Ventricular myofiber disarray was minimal to mild. This finding can occur with myocardial hypertrophy, but echocardiographic evaluation revealed that wall thickness was within normal limits. In the absence of additional gross or histologic evidence of hypertrophic cardiomyopathy, the clinical significance of this lesion is not known. The cause for the left atrial endocardial fibrosis is unknown. Mitral insufficiency secondary to valvular myxomatous degeneration is a possible consideration; however, mitral valve abnormalities were not indicated on the echocardiography report.

This cat also had multiple cysts in the kidneys, which may be consistent with polycystic kidney disease, an autosomal dominant congenital disease of a variety of species and breeds of animals, including Persian cats. Mutations in PKD-1 and/or PKD-2 genes leading to altered function of related proteins polycystin-1 and polycystin-2. Polycystin-1 is involved in normal cell proliferation and apoptosis pathways and mutations allow cells either to enter a differentiation pathway that results in tubule formation or to become susceptible to apoptosis, both of which contribute to tubular cyst formation, while polycystin-2 is involved in plasma membrane calcium channels. As cysts enlarge, they compress adjacent parenchyma, leading to secondary changes (compression necrosis and fibrosis of tubules and glomeruli) and when extensive regions are polycystic and impaired, there may be clinically

evident renal dysfunction. In this case, the renal cysts are a likely contributor to the chronic renal disease noted in the history. Congenital forms of polycystic kidney disease are also often associated with cystic bile ducts and bile duct proliferation in the liver (as noted in this case) and/or pancreatic cysts (not seen in this cat). In addition, congestion and degenerative changes were noted within the centrilobular regions of the liver, likely secondary to right-sided heart insufficiency due to compression of the heart by the mass.

AFIP Diagnosis: 1. Heart base: Chemodectoma.
2. Heart, epicardium: Epicarditis, fibrinous, diffuse, chronic, mild.
3. Heart, atrioventricular valve: Degeneration, fibromyxomatous, focally extensive, mild.

Conference Comment: The contributor provides a comprehensive review of the entity. Participants reviewed the predilection sites for chemodectoma in animals, and the moderator reiterated the point that most are nonfunctional. In contrast to many neoplasms of neuroendocrine origin, chemodectomas exert their detrimental effects on affected animals via their space occupying nature rather than a specific secretory product. In addition to the immunohistochemical stains noted by the contributor, electron microscopy is useful for distinguishing “heart base tumors” of ectopic thyroid follicular cell origin from those of aortic body chemoreceptor cell origin. While the former contain large lysosomal dense bodies, they lack the small membrane-bound secretory granules that are characteristic of aortic and carotid body chemoreceptor cells. Moreover, the number of granules may be further useful for distinguishing chemoreceptor adenomas (in which they are more numerous) from carcinomas.(2)

Contributor: The Animal Medical Center, Department of Pathology, 510 East 62nd Street, New York, NY 10065
<http://www.amcny.org/>

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CASE III: 16665/9D (AFIP 3139391).

Signalment: 2-year-old, female wild boar (*Sus scrofa*).

History: An adult wild boar was caught during boar hunting.

Gross Pathology: On post mortem examination, the boar was in good body condition with adequate muscle mass and body fat stores. Within the ventricular walls and the interventricular septum there were numerous, multifocal to coalescent, well demarcated, unencapsulated, white to pale pink, from 3 mm to 2 cm, irregularly round to oval nodules that expanded and replaced the myocardial tissue and that elevated the epicardium and the endocardium, protruding within the ventricular cavities. On cut surface the nodules were homogeneous in color and diffusely firm.

Histopathologic Description: Heart: Within the ventricular wall there are multiple, focally extensive, well-demarcated, not infiltrating, irregularly round to oval, intramuscular and subepicardial, from 3 mm to 1 cm in size nodules that expand and replace the normal myocytes, composed of haphazardly disposed, irregularly shaped myocytes with markedly distended cytoplasm characterized by single or multiple, clear, up to 200 um diameter vacuoles occasionally containing a moderate amount of finely granular, eosinophilic material. The small amount of remaining cytoplasm and the compressed nucleus are displaced to the periphery of the cells. There are numerous cells characterized by a centrally located, up to 40 um in size, irregularly round nucleus, with one or two

indentations, margined chromatin and a prominent nucleolus. These cells have abundant finely granular eosinophilic cytoplasm. Minimal, diastase-labile, PAS-positive granules confirmed the presence of intracytoplasmic glycogen within many of the cells. The anisocytosis and anisokaryosis are moderate. The mitotic index is less than one. Multifocally within the nodules there are minimal inflammatory infiltrates composed of lymphocytes, macrophages and plasma cells. There is mild diffuse edema and hyperemia. At the periphery of the nodules there are multifocal hyper eosinophilic myocytes with fragmented cytoplasm and pyknotic or absent nuclei (necrosis).

Contributor's Morphologic Diagnosis: Heart, myofibers: severe, multifocal myofiber vacuolar degeneration consistent with glycogen deposits, and myocyte dysplasia compatible with multiple cardiac rhabdomyoma (rhabdomyomatosis), wild boar, suid.

Contributor's Comment: Cardiac rhabdomyoma is a lesion characterized by large vacuolated myocardial cells containing glycogen, and synonymously “rhabdomyomatosis”, “congenital glycogen tumor”, “circumscribed glycogenic storage disease”, “nodular glycogenic degeneration”, “nodular glycogenosis” and nodular glycogenic infiltration are used for the lesion.(2) This kind of lesion typically occurs in children less than one year old, in pigs, and rarely in cattle, sheep, dogs and deer.(3)

In swine it is an incidental finding and occurs most commonly in the left ventricle of the heart. Some authors suggest a familial predisposition for cardiac rhabdomyomas in red wattle and red wattle-cross piglets.(4) Animals of all ages are affected and the occurrence of this lesion in animals as young as three weeks old suggests a congenital condition. The etiology and pathogenesis are not known and it is thought to be a hamartoma or malformation rather than a true neoplasm. Ultrastructural and immunohistochemical studies in swine suggest it is a congenital dysplasia of cardiac muscle and/or Purkinje cells. In fact, cardiac rhabdomyoma cells share ultrastructural features of both cardiac myofibers and Purkinje cells, creating uncertainty as to their histogenesis.(4) The relative paucity of poorly oriented myofibrils, abundant glycogen, binucleation, and desmosomal intercellular junctions in rhabdomyomas are characteristics of Purkinje cells (4), but intercalated discs, which are exclusive to cardiac myofibers, are also present in some rhabdomyoma cells.(4) This combination of ultrastructural features has led to the hypothesis that cardiac rhabdomyomas arise from either two types of fibers or a pluripotential embryonic cell.(4)

Affected animals are usually asymptomatic but in affected dogs chylopericardium and right-sided congestive heart failure have been reported.(2) The occurrence of cardiac rhabdomyomas in stillborn and neonatal red wattle piglets in the absence of heart failure concurs with previous reports of the congenital and incidental nature of these lesions in pigs.(4) However, the absence of concurrent disease in one red wattle piglet suggests that cardiac rhabdomyomas may potentially cause sudden death, perhaps by interfering with normal myocardial conduction, as occurs in people. (4) Grossly the lesions appear as irregular, pale, white, pink or tan myocardial foci or streaks varying in diameter from barely visible to 3 cm in swine.

AFIP Diagnosis: Heart, myocardium: Cardiomyocyte swelling and glycogen-type vacuolar change, nodular, multifocal, moderate to marked (rhabdomyomatosis).

Conference Comment: In humans, cardiac rhabdomyomas occur most often in pediatric patients with tuberous sclerosis, a hereditary autosomal dominant syndrome that results from mutations in the gene *TSC1* or more commonly, *TSC2*, characterized by the development of a variety of hamartomas and benign neoplasms. The gene products, hamartin and tuberin, combine to form an inhibitor of the kinase mTOR, an important regulator of protein synthesis, anabolic metabolism, and cell size. Interestingly, the tumors associated with tuberous sclerosis (e.g. giant-cell astrocytomas and cardiac rhabdomyomas) are noted for having voluminous cytoplasm.(1)

During tissue processing, the loss of glycogen from affected cells creates a distinctive and helpful histologic artifact: “spider cells,” so named because of the radial arrangement of residual sarcoplasm that extends from the nucleus.(5) Conference participants briefly discussed glycogen storage diseases in the differential diagnosis for this lesion.

In addition to the histopathologic findings described by the contributor, some sections reviewed by conference participants contained few sarcocysts.

Contributor: Servizio Diagnostico di Anatomia Patologica e Patologia Veterinaria, Dipartimento di Sanità Pubblica, Patologia Comparata e Igiene Veterinaria, Facoltà di Medicina Veterinaria di Padova, Viale dell'Università, 16, 35030 Legnaro, Padova, Italy
<http://www.sanitaveterinaria.unipd.it/>

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CASE IV: 0130/09 (AFIP 3140226).

Signalment: 2-year-old, male, castrated Maine coon cat (*Felis catus*).

History: The cat was brought to a veterinary clinic with a history of episodic dyspnea and a 2-week history of cough. On presentation, the cat had a heart rate of 180 beats per minute (tachycardia), with a gallop rhythm on auscultation. Lung sounds were difficult to evaluate. Ultrasound examination with echoradiographs showed a mild dilatation and hypertrophy of the left ventricle, and several fibrous strands between papillary muscles of the ventricle wall and the septum wall. A mild dilatation of the left atrium could also be seen. A diagnosis of restrictive cardiomyopathy of endomyocardial fibrous type was made. The cat also had moderate hydrothorax and lung edema and the owners elected euthanasia.

Gross Pathology: The heart was moderately enlarged with an elongated left ventricle, comprising a ventricular remodeling with rounded apex. Marked fibrotic structures (ventricular scar) bridged the ventricular septum (from the papillary muscle) and the free wall. The left atrium was moderately enlarged; however, the right atrium was normal and the right ventricle was only mildly hypertrophied.

Histopathologic Description: Tissue from myocardium including endocardium: A severe thickening of the endocardium with fibrotic strands is present. These fibrotic structures are comprised of fibroblasts in a dense matrix. Lobule-like structures intermingled with parallel streaks can be seen. The extracellular matrix consists of red collagen and bluish chondroid tissue. The fibroblasts are elongated to, in some areas, round (i.e. more chondrocyte-like) in appearance. In one subendocardial area, a lipid rich tissue is found. The underlying myocardium is characterized by a diffuse, moderate interstitial fibrosis.

Contributor's Morphologic Diagnosis: Endomyocardial fibrosis with myocardial interstitial fibrosis, left ventricle, eccentric hypertrophy of left ventricle, compatible with a restrictive cardiomyopathy of endomyocardial fibrous type.

Contributor's Comment: Many feline cardiomyopathies are classified as idiopathic.(2) In a retrospective study of 106 cats with cardiomyopathy, 57.5% had hypertrophic cardiomyopathy (HCM), 20.7% had restrictive cardiomyopathy (RCM), 10.4% had dilated cardiomyopathy (DCM) and unclassified cardiomyopathy (UCM) was found in 10.4%.(2) None of the described cardiomyopathies in that study showed the severe endomyocardial fibrosis with crossing fibrous strands in the left ventricular lumen, which characterized the heart of the Maine coon cat in this case.

Cats with RCM present with diastolic dysfunction and increased myocardial stiffness. The etiology is unknown.(3) Two basic forms of RCM in man have been reported: myocardial and endocardial RCM. These two forms are also described in the cat. The feline myocardial form, a myocardial disease with restrictive filling and severe atrial dilatation, is idiopathic. The endomyocardial form, endomyocardial fibrosis (EMF), is characterized by marked fibrosis of endocardium and endomyocardium. The etiology of EMF is not known but different backgrounds have been discussed. In human RCM, associations with hypereosinophilic syndrome, endomyocarditis or vasculitis have been suggested.(1) Many cases of human EMF have been reported from the tropics; hence a search for infectious or nutritional causes has often been pursued.

Familial HCM has been reported in Maine coon cats.(4) However, the lack of severe concentric hypertrophy and atrial dilatation is not consistent with a diagnosis of HCM in this case. An association with endomyocarditis and left ventricular endocardial fibrosis has been reported in the cat.(6) The lack of active inflammation in the present case does not rule out a viral or immune-mediated endomyocardial injury with secondary reparative fibrous tissue formation. The ultrasonographic, macroscopic and microscopic findings in the present case are compatible with a diagnosis of restrictive cardiomyopathy of endomyocardial fibrous type. This was based on the presence of many fibrous bands crossing between the papillary muscles and the septum wall. Secondary lung edema with hydrothorax had also developed.

AFIP Diagnosis: Heart: Endocardial fibrosis, diffuse, marked, with chondroid metaplasia, mild multifocal chronic endomyocarditis, interstitial edema, and myofiber disarray.

Conference Comment: Among the cardiomyopathies of domestic animals, the feline cardiomyopathies are probably the best characterized, and include an assortment of idiopathic cardiovascular disorders. In decreasing order of prevalence, the feline cardiomyopathies are summarized below:(5)

Feline Cardiomyopathies			
Classification	Key Gross Findings	Key Microscopic Findings	Summary
Hypertrophic (HCM)	Cardiomegaly with either symmetric concentric ventricular hypertrophy or asymmetric hypertrophy of the LV and a slit-like LV lumen; LA dilation; +/- atrial thrombi, multifocal ventricular fibrosis, endocardial fibrosis in the LV outflow tract	Hypertrophied myofibers with vesicular nuclei; myofiber disarray in the LVFW and IVS; diffuse interstitial fibrosis (particularly in the inner aspect of the LFFW); focal endocardial fibrosis	Most common CM in cats; autosomal dominant inheritance in Maine coon and American shorthair cats; impaired diastolic ventricular filling (due to diminished LV lumen) with usually normal systolic function; distinct from hyperthyroidism, which also may cause concentric myocardial hypertrophy
Restrictive (RCM)	Severe endocardial thickening; mural thrombosis; marked LA dilation +/- thrombosis; thickened LVFW with diminished LV volume	Replacement of myocardium and endocardium by granulation tissue and fibrosis; histiocytic, and/or lymphoplasmacytic endomyocarditis	Includes the myocardial form and the endomyocardial form; also termed "LV endocardial fibrosis", which may be preceded by endomyocarditis, of which <i>Bartonella</i> sp. has been suggested as a cause; occurs primarily in older cats; impaired diastolic ventricular filling with usually normal systolic function
Dilated (DCM)	All heart chambers enlarged; ventricles dilated, flaccid, and thin-walled; atrophy of papillary muscles and trabeculae; +/- subendocardial fibrosis	Usually minor microscopic lesions; moderate myofiber hypertrophy with mild, diffuse interstitial fibrosis; +/- myofiber loss and replacement with fibrosis; usually no myofiber disarray	Distinct from and rare in comparison to taurine-deficiency myocardial failure (TDMF), which causes identical gross and microscopic lesions and systolic dysfunction resulting in bilateral congestive heart failure
Excessive moderator bands (false tendons)	Numerous pink-white bands spanning the LV lumen and papillary muscles, usually connecting the cranial and caudal papillary muscles to the IVS; LV dilated or thickened	Abnormal moderator bands composed of Purkinje cells and dense collagen covered by endothelium; LV myocyte atrophy or hypertrophy; fibrosis; intramural coronary arterial intimal thickening, medial hyperplasia, perivascular fibrosis, and luminal narrowing	Occurs in mature cats but is considered a congenital defect; clinical signs of left-sided congestive heart failure

LV = left ventricle; LVFW = left ventricular free wall; IVS = interventricular septum; CM = cardiomyopathy

Cardiomyopathy is a diagnosis of exclusion and, by strict definition, should be used only to describe idiopathic primary myocardial disease. Therefore, myocardial dilation due to taurine deficiency (i.e. taurine-deficiency myocardial failure [TDMF]) and concentric hypertrophy attributed to hyperthyroidism are distinct from dilated and hypertrophic cardiomyopathies, respectively. In cats with HCM, DCM, RCM, and myocarditis, the detection of feline panleukopenia virus genome by PCR suggests a possible causal role, but a definitive etiology for these conditions remains elusive.(5)

As alluded to by the contributor, this case may represent the chronic sequel of feline endomyocarditis, which can ultimately progress to left ventricular endocardial fibrosis, one of several idiopathic feline cardiovascular diseases grouped together clinically as RCM.(5,6) Some conference participants considered primary endocardial fibroelastosis (EFE) in the differential diagnosis; this congenital anomaly is exceedingly rare in domestic species, and is best documented in Burmese kittens, in which the condition results in microscopically detectable endocardial lymphedema at as early as one day of age. After 20 days of age, diffuse endocardial deposition of collagen and elastin is evident grossly; this may progress to involve Purkinje fibers, which undergo degeneration. Endocardial or myocardial inflammation are not features of EFE.(5)

The moderator emphasized the importance of echocardiography in correctly classifying feline cardiomyopathies clinically. Gross examination at necropsy is often less rewarding than antemortem echocardiography, and microscopic evaluation may be even less helpful, as evidenced by the overlap in microscopic findings between the various cardiomyopathies listed above and the usual paucity of significant microscopic lesions in feline DCM, specifically. A common sequel, observed in up to one third of affected cats, is unilateral or bilateral hindlimb ischemia due to iliac thromboembolism.(5,6)

Contributor: Department of BVF, Division of Pathology, Toxicology & Pharmacology, SLU (Swedish University of Agricultural Sciences), Box 7028, SE-750 07 Uppsala, Sweden
www.slu.se

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