CASE I – A22 512297 (AFIP 2812387).

**Signalment:** Rat, *Rattus rattus*, ACI/Seg, male, 10 months of age at study initiation.

**History:** The ACI-rat strain is an established animal model that develops malformations of the urogenital system.\(^2\) The ACI/Seg substrain has a propensity to develop adenocarcinoma of the prostate.\(^1,4\) ACI/Seg male rats (Harlan Sprague-Dawley) were evaluated during an approximately 22-month study to determine the background incidence of prostatic changes; none of these rats were exposed to any xenobiotics. One group of male rats was castrated at approximately 8 months of age, 2 months prior to study start and a second group served as controls. An unexpected finding was that approximately 10-30% of the rats (from both the surgically treated and control groups) developed unilateral facial (periorbital) swelling with or without exophthalmia and/or corneal opacity. Affected rats developed facial swelling as early as Study Week 8 and subsequently died or were sacrificed beginning in Study Week 18. This change continued to develop in select rats throughout the duration of the study.

**Gross Pathology:** The facial lesion was generally localized adjacent to the eye/orbit or the cervical areas and described as an irregular/nodular mass which contained yellow, caseous to granular material. Some facial lesions were locally extensive, involving the skin, bone, skeletal muscle, and/or nerves in the affected area, as well as the Harderian gland and orbit.

**Laboratory Results:** Bacteriological culture of the affected tissue(s) generally yielded pure isolates of coagulase positive *Staphylococcus aureus*. 
**Contributor’s Morphologic Diagnosis:** Facial area, soft and osseous tissues-pyogranulomatous inflammation.

**Contributor’s Comment:** Pyogranulomatous inflammation involving soft and osseous tissues of the facial area of rats is an unusual change in our experience. Based on available data, it seems that the oral cavity is the likely source of the organism. However, none of these rats had any experimental manipulations of the oral cavity (i.e. no oral gavage) and there was no history of trauma to the oral cavity.

We are unaware of similar occurrences being reported in rats, although an outbreak of botryomycosis was reported in a colony of urokinase-type plasminogen activator (uPA) deficient mice.³ The majority of lesions occurred in the head and neck region, and *Staphylococcus aureus* was isolated from all mice sampled for bacterial culture.

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**AFIP Diagnosis:** Head, cross section, at the level of the olfactory bulb: Myositis, cellulitis, pharyngitis, osteomyelitis, and meningitis, pyogranulomatous and necrotizing, multifocal to coalescing, severe, with Splendore-Hoeppli material and large colonies of cocci, ACI/seg rat (*Rattus rattus*), rodent.

**Conference Comment:** Botryomycosis is a chronic granulomatous disease caused by non-filamentous non-branching bacteria surrounded by eosinophilic, acellular material that forms radiating clubs (Splendore-Hoeppli material) and affects the skin, and rarely, the viscera. The term “botryomycosis” is technically incorrect as it implies that the disease is caused by a fungus; however, the term has persisted since the lesions closely resemble fungal granulomas. Synonyms include bacterial pseudomycosis, bacterial pseudomycetoma, and bacterial pseudogranulomas. Bacterial pseudomycetomas are primarily caused by staphylococcal bacteria (usually coagulase-positive *Staphylococcus aureus*) as in this case; however, other causes alone or in conjunction with *S. aureus* include *Streptococcus* sp., *Proteus* sp., *Pseudomonas* sp., and *Actinobacillus* sp. Bacterial pseudomycetomas occur in cattle, sheep, horses, dogs, cats, pigs, and rodents among other species.⁵-⁹

The pathogenesis is unclear, but most likely results from an imbalance between host resistance and organism virulence. The host can isolate and contain the infection but cannot eliminate it. Infections are usually initiated by local trauma to the skin while some infections are associated with a foreign body which provides a nidus for granule formation. There is a possible genetic predilection, as pointed out by the contributor; certain strains of mice are more susceptible than others.
Immunodeficiency may also play a role. Bacterial pseudomycetomas have been reported in humans with HIV infection and chronic granulomatous disease.5,10

Typical gross findings include firm nodules with draining fistulous tracts that exude purulent exudate that may contain small white granules (grains). Infection involves the deep dermis and subcutis, and occasionally extends to the muscle, adjacent bone, and rarely the viscera.5,6,8,9

Typical light microscopic findings include nodular to diffuse pyogranulomatous dermatitis and panniculitis. The pyogranulomas are characterized by a central core of compact bacterial colonies (tissue granules or grains) surrounded by amorphous eosinophilic material that often forms radiating clubs (Splendore-Hoepppli material) further bounded by many neutrophils, epithelioid macrophages, lymphocytes, plasma cells, multinucleate histiocytic giant cells, and variable amounts of fibrosis. Splendore-Hoepppli material is thought to represent a localized antigen-antibody reaction.5,6,8,9,11

Differential diagnosis include eumycotic mycetoma, actinomycosis, nocardiosis, systemic mycosis, dermatophytic pseudomycetoma, foreign body reactions, opportunistic fungi and algae, and chronic bacterial abscesses.5,7,9

Botryomycotic mastitis occurs in cattle, pigs, and sheep. Actinobacillus lignieresii (wooden tongue) is a form of botryomycosis in cattle. The neck and pectoral region (“breast boils”) are common sites of botryomycosis in horses and the stub of the spermatic cord in geldings is a common site. In pigs, castration wounds are also a common site. In rats and mice, botryomycosis typically results in swelling of the head, abscessation, and visceral lesions. In nude mice, periorbital abscesses and nasal furunculosis result due to sparse protective pelage, distorted vibrissae and hair shaft growth, and impaired T-cell function. B6 mice are especially prone to ulcerative dermatitis associated with S. aureus. Pulmonary botryomycosis is a rare condition in horses, guinea pigs, and cattle. There is a single report of mammary botryomycosis in an African elephant.6,8,11,12,13

Gram stains performed at the AFIP revealed myriad Gram positive cocci.

**Contributor:** Merck Research Laboratories, Department of Safety and Assessment, West Point, PA

**References:**
1. Isaacs JT: The aging ACI/Seg versus Copenhagen male rat as a model system for the study of prostatic carcinogenesis. Cancer Res 44:5785-5796, 1984
10. Scott DW, Miller WH: Equine Dermatology, pp. 245-249. Saunders, St. Louis, Missouri, 2003

CASE II – UTMDACC AFIP WSC H-7663 (AFIP 3031561).

Signalment: 17-year-old, female, rhesus macaque, Macaca mulatta.

History: Presented 3 days prior to death with 2-day-old infant, moderate weight loss, and post-partum bleeding, non-responsive to supportive therapy, found non-responsive in cage with vomit, CPR attempts unsuccessful.
Gross Pathology: Multifocal aspiration pneumonia; dilatation of esophagus, stomach, and jejunum; mid-jejunal constrictive mass; fatty liver

Histopathologic Description: Jejunal mass – The ring shaped fibrous constriction observed histologically is evident on low magnification examination of the microscope slide. The mucosal tissue is expanded forming elongated crypts and cystic glands. The lamina propria is invaded by cells proliferating as tubes and cords. A prominent fibrous connective tissue stroma is present supporting the invading epithelium. The neoplastic cells vary from tall columnar to short cuboidal and have variable amounts of cytoplasm. Crypts in the mucosa vary from having a single layer of columnar epithelium to having highly stacked pseudostratified columnar cells. As the cells invade atypia increases with an increase in nuclear to cytoplasmic ratio, increased anisokaryosis, and the presence of obvious small angular amphophilic single or double nucleoli. Mitotic index is variable from 1-5 per 40X field with abnormal mitoses being observed.

Contributor’s Morphologic Diagnosis: Jejunum, adenocarcinoma, locally invasive with stricture

Contributor’s Comment: Small intestinal neoplasia has been reported in rhesus macaques as a report on a series of necropsies and in a case report. The colonic adenocarcinoma of the aging rhesus macaque is better known and published. The incidence of intestinal neoplasia in rhesus has a strong affinity to the cecocolic junction, with virtually all of the cases reported in the literature occurring at this site and are associated with clinical histories including chronic diarrhea. Small intestinal tumors such as this case are not adequately represented in the literature to determine if this is a typical presentation and location. This animal had an unremarkable medical history, had been a good producing female in the breeding colony and her weight had fluctuated between 8 and 10.5 kg. The weight loss terminally wasn’t appreciated until the prolonged post-partum bleeding was noted and she was brought out of the group housing area she had been in. Rapid decline with terminal aspiration resulted in death. Post-mortem examination indicated that the partial obstruction of the intestinal tumor caused proximal dilatation of the gastrointestinal tract with ileus and a third space fluid accumulation phenomenon. Histologic examination revealed a moderately well differentiated locally invasive neoplasm that had extended to the intestinal serosal; although, no distant metastasis was noted.

AFIP Diagnosis: Jejunum: Adenocarcinoma, rhesus macaque, Macaca mulatta, nonhuman primate.
Conference Comment: Intestinal adenocarcinoma is rare in most animal species except cotton-top tamarins and New Zealand, Australian and European sheep. Cotton-top tamarins are a model for ulcerative colitis and associated carcinoma in humans.5,6

Adenocarcinomas are divided into four histomorphologic types. More that one type is typically present and classification is based on the predominant cell type:

1. Acinar (Tubular): Irregularly branching tubules lined by flattened to columnar cells, embedded on a fibrous stroma, that infiltrate the submucosa and muscularis.
2. Papillary: Papillary projections lined by multiple layers of anaplastic columnar cells with little stroma; mitotic index tends to be high.
3. Mucinous: Acinar or irregular crypts, filled or distended with mucin, which replace at least 50% of the tumor. Mucin may be intracellular and extracellular.
4. Signet-ring: Isolated cells or nests of cells that contain intracellular mucin that displaces the nucleus to the periphery.

Some classifications include a solid type composed of solid sheets of large, anaplastic, or pleomorphic cells with little stroma and no evidence of squamous or glandular differentiation. Desmoplasia is a prominent feature of all types except for papillary adenocarcinomas. Generally, all types, with the exception of the papillary type, metastasize widely via the lymphatics to the regional lymph nodes.5,7,8

Grossly, adenocarcinomas appear as nodular or annular, firm, gray-white stenotic areas that are frequently transmural. There is often intestinal dilation/muscular hypertrophy proximal to the stenosis or tumor obstruction. Although adenocarcinomas typically do not project into the intestinal lumen, papillary types do form intraluminal masses.5

Most primary neoplasms of the intestines in the dog are adenocarcinomas and are more common in the large than the small intestine. The duodenum and colorectum are the most common sites. Some investigators have reported a breed predisposition in boxers, collies, and German shepherd dogs.5,7,8

Adenocarcinoma is the third most common intestinal neoplasm in cats after lymphoma and mast cell tumors. The jejunum is the most common site of intestinal adenocarcinoma in cats and Siamese are predisposed. Stromal osteochondroid metaplasia is a common feature of feline intestinal adenocarcinomas.5,7,8

The incidence of intestinal adenocarcinoma in cattle and sheep varies by region. In some countries, intestinal adenocarcinoma of cattle is rare and the jejunum is most
commonly affected. In other countries, bovine intestinal adenocarcinoma is more common and is associated with ingestion of bracken fern in animals with bovine papillomavirus-4 infection. These lesions are multiple and range from adenomas to carcinomas throughout all levels of the small intestine. Metastasis to regional lymph nodes, omentum, and liver most commonly occurs with rare metastasis to extra-abdominal lymph nodes and lung. In countries in which ovine adenocarcinoma is common, ingestion of bracken fern and herbicide use have been incriminated as possible etiologies. Unlike cattle in high prevalence areas, lesions in sheep are mid-jejunal and solitary with marked desmoplasia. Metastasis occurs via lymphatics to the draining lymph nodes and diaphragm, and rarely hematogenously to the lung and liver. In pregnant ewes, the altered position of the uterus allows transcoelomic metastasis to the reproductive organs.5,7,8

Intestinal adenocarcinoma in horses is rare, but involves the cecum and large colon 3 times more often than the small intestine. There is often marked desmoplasia in which cartilaginous and osseous metaplasia can occur. As in felines, intestinal lymphoma is more common in horses.5,7,8

Intestinal adenocarcinoma is extremely rare in pigs and is most commonly seen in the jejunum. Desmoplasia and inflammatory cells, predominantly eosinophils, are characteristic. Infiltration into the mesentery and regional lymph node metastasis are common.5,7,8

Adenocarcinoma of the colon is uncommon in most nonhuman primates; however, the laboratory maintained cotton-top tamarin has a high incidence of colonic adenocarcinoma that arises in animals with chronic idiopathic colitis resembling ulcerative colitis in humans. These adenocarcinomas are typically mucinous and highly invasive. A novel Helicobacter sp. has been isolated from the colon of cotton-top tamarins that may be involved in the pathogenesis of ulcerative colitis and colonic adenocarcinoma.6,9

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References:

CASE III – R06-0251 (AFIP 3027375).

Signalment: 2-year-old, intact male, Hartley guinea pig (Cavia porcellus).

History: The animal had been maintained for hands-on training. Enrichment treats including rolled oats, dehydrated vegetables (Veggie-Bites) and supplements high in vitamins C and D3 (Supreme Mini-Treats, PRIMA-Treats, Fruit Crunchies and Turf Foraging Crumbles) were administered frequently. There was a history of repeated colonic impaction starting 2 months prior to death which intermittently resolved with supportive therapy including a laxative (Laxatone) and electrolyte replenisher (Prang). The animal was found dead in his cage 3 weeks after the last bout of colonic impaction had resolved.

Gross Pathology: The thoracic cavity contained 15 ml of serosanguineous and fibrinous pleural effusion and the lungs were mildly atelectatic (Figure R06-0251-G1). The pericardial sac contained 10 ml of hemorrhagic effusion (Figure R06-0251-G2). A pale tan, soft to firm, beaded to verrucous mass was present on the epicardium of the dorsal aspect of the right heart (Figure R06-0251-G3). The liver was mottled dark red (Figure R06-0251-G4). Bilaterally, the kidneys were mottled.
pale tan to dark brown with a pitted capsular surface (post-formalin fixation, Figures R06-0251-G5 and R06-0251-G6).

**Histopathologic Description:** Slide consists of a sagittal section of heart including bilateral atria, ventricles, atrioventricular valves and the interventricular septum. Randomly distributed throughout the myocardium are multifocal, small areas of metastatic mineralization (confirmed by von Kossa histochemical staining) and fibrosis (confirmed by Masson’s trichrome histochemical staining) associated with myofiber degeneration, atrophy and loss. Infrequent capillaries and small arterioles throughout the myocardium are also mineralized. Some slides also include sections of pulmonary artery and/or aorta. These great vessels have multifocal areas of mineralization affecting the internal elastic lamina, subintima and/or the tunica media including individual elastin fibers. The epicardium is variably thickened by moderate amounts of collagen, fibrin and fibroblasts as well as scattered lymphocytes, histiocytes and fewer heterophils. Epicardial neovascularization, particularly at the base of the heart is prominent. In multifocal areas, there is also hyperplasia of mesothelial cells on the epicardial surface. In some slides, the section includes the epicardial mass noted grossly. Histologically, this mass is composed of organizing fibrin within which are scattered fibroblasts, endothelial cells and aggregates of erythrocytes.

Mineralization was also documented in the trachea, lung, kidney, stomach, colon, seminal vesicles, liver, spleen and various vessels within skeletal muscle, mesentery/peritoneum, lung, tongue, stomach and choroid plexus. Myofiber degeneration, atrophy and fibrosis were also noted in skeletal muscle from the hindlimb.

**Contributor’s Morphologic Diagnoses:**
1. Heart, myofiber and vascular mineralization, chronic, multifocal, marked with multifocal degeneration, atrophy, loss and fibrosis.
2. Great vessels, intimal and medial mineralization, multifocal, marked.
3. Epicardium, epicarditis, fibrinous to fibrosing, chronic, multifocal to widespread, marked with lymphohistiocytic inflammation and mesothelial hyperplasia.

**Contributor’s Comment:** The systemic mineralization present in numerous tissues is consistent with metastatic or soft tissue calcification of guinea pigs. It is most common in guinea pigs older than 1 year of age and affects males more often than females.\(^1,3,5,6,8,9\) Although the condition is typically asymptomatic, the clinical signs exhibited include weight loss, muscle and joint stiffness, renal failure and sudden death.\(^2,3,5,6\) The condition was previously referred to as ‘wrist stiffness syndrome’ since mineralization was often restricted to soft tissues around the elbows.\(^4,5,7\) However, mineralization can also be more widespread as in this case.\(^3,6,8,9\) This
syndrome is attributed to a dietary imbalance of magnesium, calcium and phosphorus rather than a deficiency of a single mineral.\textsuperscript{1-9} Excessive phosphorus and calcium impede absorption and utilization of magnesium. The condition can be minimized or prevented by feeding diets that contain 0.3-0.4\% magnesium, 0.9-1.1\% calcium, 0.6-0.7\% phosphorus, 0.4-1.4\% potassium, \leq 6 IU of vitamin D/g and a calcium:phosphorus ratio of 1.5:1.\textsuperscript{9} The imbalance in this guinea pig was likely due to excessive dietary enrichment with treats high in vitamin D\textsubscript{3} leading to hypercalcemia.

No evidence of colonic impaction was noted at necropsy. Historical reports of colonic impaction in this guinea pig could be attributed to metastatic mineralization of the colon. However, published reports documenting an association between these two conditions in humans or animals were not found.

The cardiac and skeletal muscle lesions are also likely consequences of the metastatic mineralization. However, guinea pigs also develop vitamin E/selenium responsive myopathies as well as a poorly understood syndrome known as ‘myocardial and skeletal muscle degeneration with mineralization’.\textsuperscript{6} Contributing factors for the latter condition have not been clearly identified; although, vitamin E and selenium levels are typically within normal limits and genetic factors are usually implicated. Animals are typically asymptomatic without gross lesions; histologic lesions include degeneration of cardiac and skeletal myofibers with variable mineralization and mononuclear infiltration.

The cause of death in this case is ascribed to the extensive myocardial lesions resulting in acute congestive heart failure characterized by pleural effusion. The guinea pig’s condition was also exacerbated by hemopericardium and cardiac tamponade which were likely secondary to vascular rupture of a mineralized vessel into the pericardium.

We cannot completely rule out concurrent renal failure in this case since renal failure can be a complicating condition of metastatic mineralization. Pre-existing underlying renal disease independent of metastatic mineralization cannot be discounted either since aging guinea pigs also develop segmental nephrosclerosis.

**AFIP Diagnoses:**
1. Heart: Epicarditis, proliferative, chronic, diffuse, moderate, with multifocal myocardial fibrosis and mineralization, Hartley guinea pig (\textit{Cavia porcellus}), rodent.
2. Heart, great vessels: Mineralization, intramural, multifocal, moderate.
Conference Comment: The contributor provides a thorough overview of metastatic or soft tissue calcification of guinea pigs as well as touching on the differentials of vitamin E/selenium deficiency, and the “myocardial and skeletal muscle degeneration with mineralization” syndrome. As pointed out by the contributor, concurrent renal failure could not be completely ruled out as a potential cause of the metastatic mineralization in this case.

Metastatic calcification occurs in otherwise normal tissue and almost always results from hypercalcemia secondary to a disturbance in calcium metabolism. The pathogenesis of metastatic calcification involves the entry of large amounts of calcium ions into cells where they precipitate on organelles, especially mitochondria. The four causes of metastatic calcification in order of their importance in veterinary medicine are listed below:

1. Renal failure – retention of phosphates induces secondary renal hyperparathyroidism and hypercalcemia. Calcium is deposited in the kidneys, alveolar septa, gastric mucosa, and pleura.

2. Vitamin D toxicosis – ingestion of calcinogenic plants (Cestrum diurnum, Tricetum flavescens, Solanum malacoxylon) by herbivores results in severe soft tissue mineralization primarily involving the aorta, heart (endocardium of right and left atria and left ventricle), and lungs. Acute vitamin D toxicosis in dogs and cats is commonly caused by ingestion of cholecalciferol containing rodenticides. The intestinal mucosa, vessel walls, lung, and kidneys are mineralized.

3. Parathormone (PTH) and PTH-related protein – primary hyperthyroidism is rare. Elevated levels of PTH-related protein and hypercalcemia can be associated with canine lymphoma and adenocarcinoma of the apocrine gland of the anal sac. Mineralization occurs in the intestinal mucosa, vessel walls, lung, and kidneys.

4. Destruction of bone by primary or metastatic neoplasms.10,11,12

Metastatic calcification may occur widely throughout the body; however, it principally occurs in the interstitial tissues of the gastric mucosa, kidneys, lungs, systemic arteries, and pulmonary veins. All of these tissues lose acid and therefore have an internal alkaline compartment predisposing them to metastatic calcification. The deposition of mineral salts usually does not result in clinical dysfunction; however, on occasion, massive involvement of the lungs or kidneys can cause respiratory deficits and renal damage respectively.10,11

Contributor:
http://www.mskcc.org
http://www.med.cornell.edu;
http://www.med.cornell.edu/research/rea_sup/mouse_phenotyp.html
References:
1. Galloway JH, Glover D, Fox WC: Relationship of diet and age to metastatic calcification in guinea pigs. Lab Anim Care 14:6-12, 1964

CASE IV – Rat 9550 (AFIP 3026801).

Signalment: 10- to 12-week-old, female, F344 rat (Rattus norvegicus).
History: The rat arrived at our research institution at six to eight weeks of age and was group housed in standard rat caging. Four weeks after arrival, a large tumor was noted by caretakers. Physical exam revealed a large, firm, multilobulated tumor, firmly attached to the body wall on the left caudal thorax. She was in otherwise normal body condition and was demonstrating no other clinical signs. Due to the extent of the tumor, the rat was humanely euthanized.

Gross Pathology: A firm, well-demarcated, unencapsulated multilobular mass was present, arising from the left thoracic wall. The mass was 5.5 cm in maximal dimension and encompassed the left caudal ribs, invading the thoracic cavity (Figures 9550-G1, G2, G3: R denotes rib cage; thoracic side of mass shown). No other gross pathologic changes were observed.

Histopathologic Description: There is a multilobular well-demarcated and infiltrative mass that has effaced the majority of the left caudal and lateral rib cage (Figures 9550-HE-1 – 5) and extends into the plural cavity. The mass is characterized by large irregular nodules and sheets of highly pleomorphic cells supported by a fine vascular stroma. Neoplastic cells vary markedly in size and shape from elongate to round or angular and contain one or more round to elongate markedly pleomorphic euchromatic nuclei with one or more prominent nucleoli and variable amounts of finely stippled to deeply eosinophilic cytoplasm. Large multinucleated giant cells and mitotic figures are common. Occasionally, large vacuolated cells (“spider” cells) may also be present. Neoplastic cells are red with Masson’s Trichrome-stained sections of tumor (9550-MaTri-1), and fibrillar cross-striations are observed in phosphotungstic acid hematoxylin (PTAH) –stained sections of tumor (9550-PTAH-1,2,3).

Immunohistochemistry (See figure panel): The neoplastic cells are uniformly negative for Cytokeratin 7 and GFAP. The neoplastic cells are uniformly positive for Desmin. However, the neoplastic cells are variably positive for alpha smooth muscle actin. In some regions of the tumor there is strong positive cytoplasmic staining and in other areas the neoplastic cells are negative.

Although sections of this tumor were evaluated by electron microscopy (not shown), the images obtained were suboptimal due to preservation of the tissues in Bouins fixative. Regardless, we were able to visualize filament structures and Z-lines, further supporting the diagnosis of rhabdomyosarcoma.

Contributor’s Morphologic Diagnosis: Thorax: Rib: Rhabdomyosarcoma, pleomorphic, Fischer 344 rat (Rattus norvigicus).

Contributor’s Comment: Rhabdomyosarcoma is an uncommon malignant neoplasm that can arise in skeletal muscle or from nests of primitive mesenchymal cells.
located in tissues that lack striated muscle. Based on the human classification scheme, tumors can be categorized into one of the following types: embryonal (juvenile), botryoid, alveolar and pleomorphic (adult). These four types of tumors differ in gross presentation, histological appearance, prognosis, and age of onset.¹,²

Rhabdomyosarcomas are often difficult to diagnose due to the variable and pleomorphic nature of the neoplastic cells. The presence of elongated cells containing visible striations (“strap cells”) are often helpful, but striated cells are commonly absent or difficult to see in these tumors. Special stains, including phosphotungstic acid-hematoxylin (PTAH) and immunohistochemical staining, as well as electron microscopy, are useful and often necessary to perform in order to conclusively diagnose rhabdomyosarcoma.¹-⁴ Immunohistochemistry results are somewhat dependent upon the tumor type, as some cells vary in staining based on differentiation. The following table, extracted from Cooper, et. al., demonstrates the typical staining patterns of rhabdomyosarcomas:

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vimentin</td>
<td>- or weak +</td>
</tr>
<tr>
<td>Cytokeratin</td>
<td>-</td>
</tr>
<tr>
<td>Desmin</td>
<td>+</td>
</tr>
<tr>
<td>Muscle-specific actin</td>
<td>+</td>
</tr>
<tr>
<td>Smooth-muscle actin</td>
<td>-</td>
</tr>
<tr>
<td>Sarcomeric actin</td>
<td>+</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>+</td>
</tr>
</tbody>
</table>

The immunohistochemistry results for alpha SMA in this rat are interesting. Most rhabdomyosarcomas are negative; however, it has been reported that some human and domestic animal rhabdomyosarcomas occasionally express smooth muscle actin.⁵

Electron microscopy is another useful tool for diagnosing rhabdomyosarcoma. Though there is some disagreement about the specific criteria used to diagnose the tumor, general components of the sarcomere should be recognized. Z lines, A—H—M band complexes or cross sections of thick and thin filaments in a hexagonal array are examples of these ultrastructural characteristics.³

Rhabdomyosarcomas occur in a variety of anatomical locations in humans and animals. The heart and lower extremities are the two most commonly affected regions in animals, though many other areas have been reported, including the ear, kidney, lung, urinary bladder, and uterus.² Rhabdomyosarcomas have been most commonly diagnosed in the dog; in this species, laryngeal rhabdomyosarcoma and botryoid rhabdomyosarcoma of the urinary bladder are recognized as distinct
The embryonal form is the most common form reported in the dog, while alveolar seems to be the least common, as with humans. In rats, spontaneous primary rhabdomyosarcoma has been reported in the mandible, ear pinna, left forelimb and axillary region, left hind limb, ventral abdominal wall, and the thoracic and abdominal cavities. In addition, metastatic lesions have been found in the mediastinum, lungs, diaphragm, and the base of the right ear.

As with other species, rhabdomyosarcomas in rats are rare; in Fischer 344 rats specifically, the incidence is less than 1%. Case reports have described tumors occurring in a wide age range, though it is thought that rhabdomyosarcoma is predominantly a disease of older rats. This is in contrast to other species, where rhabdomyosarcoma is more frequently diagnosed in younger animals. It has been suggested that rhabdomyosarcomas of young rats are a distinct entity from that in the older animals, with the disease in young rats being characterized by a low incidence and the presence of highly differentiated tumors. Consistent with case reports in young rats, this tumor demonstrates a high degree of cellular differentiation.

In humans, rhabdomyosarcoma is the most common soft tissue sarcoma in children. Primary thoracic rhabdomyosarcomas are rare but can develop within the lung, mediastinum, heart, and chest wall. Males are most commonly affected, and presentation generally occurs either during childhood or the 5th to 7th decades of life. In children with chest wall tumors, involvement of the ribs is rare, compared to other primary sarcomas of the chest wall, though focal invasion is common. The tumor in this rat is similar to thoracic wall rhabdomyosarcoma in children in that it is a focally invasive tumor that encompasses, but does not invade, the ribs.

AFIP Diagnosis: Skeletal muscle: Rhabdomyosarcoma, Fischer 344 rat (*Rattus norvigicus*), rodent.

Conference Comment: The contributor provides a thorough summary of rhabdomyosarcomas to include the four types of rhabdomyosarcoma, the histomorphologic appearance, useful special stains, immunohistochemistry, and ultrastructural characteristics.

As pointed out by the contributor, rhabdomyosarcomas occur infrequently in many animal species. The histomorphologic appearance varies from well-differentiated neoplasms that resemble immature striated muscle to highly undifferentiated forms with pleomorphic cells that frequently contain giant, bizarre, multiple nuclei. There may be small or abundant amounts of cytoplasm that may be extensively vacuolated (spider cells). Rhabdomyosarcomas are prone to outgrow their blood supply which leads to deep necrosis.
Botryoid rhabdomyosarcoma of the urinary bladder is an uncommon, distinct entity of the dog. It presents as a botryoid mass typically at the trigone area of the bladder in juvenile large-breed dogs, especially Saint Bernards. In cats, rhabdomyosarcoma is a rare variant of postvaccinal sarcomas.\textsuperscript{11,12,13}

The benign form, rhabdomyoma, is virtually unknown in animals. Nearly all of the benign muscle tumors seen in animals are congenital rhabdomyomas of the heart and been reported in neonatal or juvenile pigs, cows, sheep, and dogs suggesting the tumors arise in utero. Less common sites of origin include the larynx, tongue, and dermis. The tumor is composed of large pleomorphic mononuclear or binucleated cells with abundant eosinophilic granular cytoplasm. Mitotic figures are rare; however, cytoplasmic cross-striations are frequently found. Many cells contain abundant cytoplasmic glycogen demonstrable by PAS staining.\textsuperscript{11,12,13}

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References:

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