CASE I – 02-6330 (AFIP 2910172)

Signalment: Adult male SD rat *Rattus norvegicus*.

History: On 10/30/02 the rat presented to veterinary services for noisy breathing. Rat had cranial surgery 6 weeks prior to clinical presentation. Head submitted by clinical veterinarian for examination of sinuses.

Gross Pathology: Not reported.

Laboratory Results: Mycoplasma and SDA serology (ELISA) were both negative.

Contributor’s Morphologic Diagnosis: Chronic focally extensive moderate neutrophilic, necroulcerative, exudative, and lymphoplasmacytic rhinitis with edematous lymphoplasmacytic adenitis and intralesional fungal ball composed of concentric layers of mycelium (hyphae and conidia) morphology consistent with *Aspergillus fumigatus*.

Contributor’s Comment: Aspergillomas, or fungal balls, form in the paranasal sinuses of humans and have been reported in rats. Concentric layers of hyaline mycelium create the fungal ball. The superficial layers are viable and often have conidial heads. *Aspergillus* hyphae measure 3-6um in width, are regularly septate, have parallel walls, and progressive dichotomous branching at acute angles. Hyphal morphology is best demonstrated with GMS or PAS stains. The fruiting body of *A. fumigatus* is relatively characteristic with a golden-brown dome-shaped terminal vesicle, covered by uniseriate phialides which are elongated cells that produce columns of spherical conidia. Conidial heads are produced when the
Aspergilli are exposed to air such as in sinuses, pulmonary cavities, cutaneous infections and otomycosis. Note: conidial heads may not be present in all sections.

**AFIP Diagnosis:** Nasal cavity: Rhinitis, ulcerative and suppurative, multifocal, moderate, with aspergilloma, Sprague-Dawley rat, rodent.

**Conference Comment:** *Aspergillus* sp. are ubiquitous environmental saprophytes that are not usually pathogens, but can cause opportunistic infection. Infection occurs in debilitated or immunosuppressed animals, or those on prolonged antibiotic therapy. While *Aspergillus fumigatus* is most frequently diagnosed as the cause of Aspergillosis in mammals and birds, *A. flavus, A. niger, A. nidulans*, and *A. terreus* are also associated with disease in animals. Respiratory infections are common and inhalation of spores is the primary means of establishing infection. Since *Aspergillus* is angio-invasive, hematogenous spread can lead to infection in multiple sites. *Aspergillus flavus* and *A. parasiticus* can produce aflatoxins, the most significant of which is aflatoxin B1, a potent hepatotoxin.

The manifestation of *Aspergillus* infection varies among species. In birds, it causes granulomatous pneumonia and air sacculitis. In horses, *Aspergillus nidulans* is most often associated with guttural pouch mycosis. *Aspergillus* sp. causes mycotic placentitis and abortion in cattle and mares, with mycotic dermatitis in aborted calves, and sometimes in aborted foals. Damage to the ruminal mucosa by lactic acidosis, mechanical injury, or administration of antibiotics may predispose to mycotic rumenitis, with which *Aspergillus* sp. are associated. *Aspergillus fumigatus* is the most common cause of canine nasal aspergillosis. Disseminated aspergillosis also occurs in dogs but most cases occur in German Shepherd Dogs, and is caused by *A. terreus*.

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**References:**
CASE II – N98-75 (AFIP 2893182)

Signalment: Adult feral pig.

History: Tissue collected from one of several feral pigs slaughtered at a local meat processing plant. The pigs were heavily infested with various metazoan parasites.

Gross Pathology: The lungs were mottled pink and tan with irregular shaped, pale, hyperinflated areas in the caudal lung lobes and variably sized gray-tan nodular foci. On cut surface of these areas, the lumen of small to medium sized airways often contained one or multiple white, threadlike, 2-5 cm long nematode parasites.

Laboratory Results: None reported.

Contributor’s Morphologic Diagnoses:
1. Lung, airways: Bronchitis, bronchiolitis and peribronchiolitis, lymphoplasmacytic and eosinophilic, multifocal, moderate with intraluminal adult nematodes.
2. Lung: Pneumonia, subacute to chronic and eosinophilic, multifocal, mild.

Contributor’s Comment: Prominent hypertrophy of bronchiolar smooth muscle is evident in some sections. Several airways contain cross and tangential sections of male and female adult nematodes with morphologic features characteristic of swine lungworms (*Metastrongylus* sp.). Metastrongyluses have the typical strongylid intestine composed of few multinucleate cells with microvillus border similar to true strongyles and trichostrongyluses but they differ from these other strongyle subgroups in having coelomarian musculature\(^1\). Other features seen in these sections include lateral chords and female reproductive tracts with eggs containing developing larvae.

There are three important species of *Metastrongylus* found in the bronchi and bronchioles of swine: *M. apri*, *M. pudendotectus*, and *M. salmi*\(^2\). They are common parasites of swine throughout the world, especially feral populations and farmed pigs kept on soil or pastures. The female worms lay thick-shelled eggs containing...
L1 larvae in the airways where most are coughed up and pass out in the feces. When ingested by the intermediate host, earthworms, the parasite continues its development to the infective L3 stage. These larvae can survive in the earthworm for several years and the life cycle is then completed only if the earthworm is eaten by a pig. L3 larvae migrate across the gut wall and travel via lymphatics to mesenteric lymph nodes where they develop into L4 larvae. These larvae migrate through the lymphatics and vessels to the pulmonary arteries where they penetrate into alveoli and then migrate to bronchioles and bronchi. The migration through alveoli may result in areas of bronchopneumonia. Adult worms may be found in all lobes but often have a predilection for the ventro-caudal portions of the caudal lung lobe. Although lesions are not normally as severe as seen in ruminants infected with *Dictyocaulus*, lungworms in swine can produce a chronic catarrhal bronchitis and bronchiolitis with multifocal hyperinflated areas in the diaphragmatic lung lobes. Large lymphofollicular aggregates are evident grossly as 1-3 mm grayish subpleural nodules. Larvae and eggs may provoke a granulomatous inflammatory reaction in the alveoli. A persistent cough and poor growth rate are common clinical signs in infected pigs. Lungworms not only predispose pigs to secondary bacterial pneumonias, but may also play a role in the transmission of swine flu and hog cholera viruses.

Other parasites discovered at necropsy in these feral swine included spargana in the subcutaneous tissues, *Stephanurus dentatus* (the kidney worm) in the perirenal connective tissue, and intestinal worms *Ascaris suum* (large roundworm) and *Macracanthorhynchus hirudinaceus* (thorny-headed worm).

Many different nematodes have adapted to live in the lungs of mammals including *Filaroides hirthi* in dogs, *Crenosoma vulpis* in foxes, *Aelurostrongylus abstrusus* in cats, *Dictyocaulus* sp. in ruminants and equids, *Muellerius capillaris* and *Prostrongylus rufescens* in sheep and goats, *Parafilaroides* sp. in sea lions, and *Filaroides sp.* and *Filariopsis sp.* in monkeys. *Angiostrongylus cantonensis*, the rat lungworm, is a cause of eosinophilic meningoencephalitis in people.

**AFIP Diagnosis:** Lung: Bronchopneumonia, eosinophilic and lymphoplasmacytic, multifocal, moderate, with intra-airway adult metastrongyles, etiology consistent with *Metastrongylus* sp., breed not specified, porcine.

**Conference Comment:** This case was reviewed in consultation with Dr. Chris Gardiner, parasitology consultant to the Armed Forces Institute of Pathology, Department of Veterinary Pathology. The contributor provides a concise overview of *Metastrongylus*, its life cycle, and the comparative pathology of lungworms.
Smooth muscle hypertrophy and hyperplasia of the bronchial-associated lymphoid tissue are present on some slides. The possibility of a *Mycoplasma hyopneumoniae* infection was discussed in conference because of the peribronchiolar lymphocytes.

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**References:**

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**CASE III – Fi01-03 (AFIP 2890205)**

**Signalment:** Fish, grayling (*Thymallus thymallus*), 55 cm, age unknown, female.

**History:** Wild fish from a small river, found dead.

**Gross Pathology:** Whitish mass, 6 cm in diameter, cranial of the caudal fin, not ulcerated, in cut section whitish color and firm consistence, severe infestation with *Saprolegnia* sp.

**Laboratory Results:** None reported.

**Contributor’s Morphologic Diagnosis:** Skin: Iridophoroma.

**Contributor’s Comment:** Chromatophoromas are pigment cell tumors arising from dermal chromatophores in the skin of fish, amphibians and reptiles. The four chromatophore classes commonly found in fish are: melanophores with black or brown pigment (melanin), iridophores with colorless pigment (purines), erythrophores with red pigments, and xanthophores with yellow pigment. Erythrophores and xanthophores both contain carotenoids, pteridines and flavins.
Chromatophores are common fish tumors and large epizootics have occurred worldwide in marine and freshwater fish.\textsuperscript{3,4} While the majority of chromatophoromas are benign and restricted to the dermis, some of the largest are malignant as evidenced by increasing anaplasia, invasion and occasionally metastasis to liver or gill.\textsuperscript{5}

Iridophoromas are characterized by the presence of olive-green granular pigment, which is birefringent with polarized light. Ultrastructurally, in unstained sections, iridophoromas have stacked arrays of reflecting platelets.

Although the etiology for the majority of chromatophoroma epizootics is unknown, epidemiologic surveys from many studies are at least suggestive for a possible exposure to anthropogenic carcinogens.\textsuperscript{5} However, other potential etiologies like oncogenic viruses, genetic predisposition or ultraviolet radiation have to be evaluated.

AFIP Diagnoses:
1. Scaled skin and skeletal muscle: Iridophoroma, European grayling (\textit{Thymallus thymallus}), piscine.
2. Skin: Ulcer, focally extensive, with superficial zoosporangia, etiology consistent with \textit{Saprolegnia} sp.

Conference Comment: Chromatophores are contractile pigment cells of cold-blooded vertebrates that produce rapid color changes of the skin used for camouflage, sexual attraction, and protection. Color change is induced by intracellular aggregation and dispersion of pigment granules. These cells originate in embryonic neural crest cells and migrate to all tissues. Neoplasms of chromatophores are reported in snakes and fish.\textsuperscript{5,6,7}

The contributor mentions the four types of chromatophores in fish: melanophores, iridophores, xanthophores, and erythrophores. Iridophores are not true pigment-containing cells, but have birefringent intracytoplasmic particles that refract and reflect light, giving the appearance of color. Melanophores, xanthophores, and erythrophores contain true pigment.\textsuperscript{5,7}

\textit{Saprolegnia} is an oomycete, or water mold, and is an opportunistic pathogen that causes infection in fish secondary to immunosuppression or environmental stress, but can occur as a primary pathogen. The two species most commonly isolated from fish are \textit{S. parasitica} and \textit{S. diclina}. The typical gross appearance is a white to gray proliferative cotton-like growth on the skin or gills. Histologically,
there may be epidermal erosion, ulceration, necrosis, and edema, with broad colorless aseptate hyphae.\textsuperscript{8,9}

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http://www.vetmed.unibe.ch/itpa/Fiwi.htm

**References:**
9. Noga EJ: Fish Disease: Diagnosis and Treatment, pp. 116-120. Mosby, St. Louis, Missouri, 1996

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**CASE IV – NIAH No.1 (AFIP 2888761)**

**Signalment:** 6-year-old, female, Holstein, *Bos taurus*, bovine.

**History:** In December 2001, a 6-year-old Holstein cow developed a fever (41.3 C) a few days after parturition, and stopped milking with mammary consolidation. Despite treatment with antibiotics and ointment for mastitis, the cow died 15 days after parturition.
**Gross Pathology:** At autopsy, no lesion was seen in the skin of the udder or the teats, though the lower surface of the udder had turned dark green. Palpation of the udder revealed moderate consolidation. On the cut surface, the mammary tissue was partially autolyzed and half-liquefied. Dilation of lactiferous sinuses and ducts can be seen with mild autolysis, and the sinuses and ducts were filled with milk-yellow exudate. The other organs were not collected due to severe autolysis.

**Laboratory Results:** BHV-4 was isolated from the mammary tissue. The viral DNA was detected by nested PCR from the same tissue.

**Contributor’s Morphologic Diagnosis:** Mamma: Galactophoritis, necrosuppurative, severe, with eosinophilic inclusion bodies in ductal epithelium and many bacilli, with squamous metaplasia, Holstein, bovine.

**Contributor’s Comment:** Histologically, autolytic changes were not too severe to recognize microscopic lesions in some areas of the mammary tissues, though the autopsy was carried out 3 days after the cow’s death. In such areas, most of the lactiferous ducts and sinuses were filled with debris containing degenerated epithelium, neutrophils, and clumps of bacilli. The epithelial cells were degenerating and desquamating. Some of them had large swollen nuclei with eosinophilic inclusion bodies surrounded by a clear halo. There was focal squamous metaplasia in the sinus and ductal epithelium. Intranuclear inclusion bodies were sometimes seen in these metaplastic cells. The tunica propria, and interlobular connective tissue was severely dilated with congestion, edema, and infiltrates of neutrophils and mononuclear cells. There was mild to moderate neutrophilic infiltration in mammary acini. No inclusion bodies were seen in the acinar cells.

Although a few investigators described isolation of BHV-4 or detection of the viral DNA from milk of cows with clinical mastitis, no one has reported either histopathological changes of mammary tissue associated with BHV-4 or in situ detection of BHV-4. In the present study, we detected intranuclear inclusion bodies in the mammary tissues of a cow with clinical mastitis. Immunohistochemistry could be successfully used to detect BHV-4 antigen, and electron microscopy revealed herpesvirus particles in the cells with inclusions. Infection of BHV-4 was also demonstrated by virus isolation and nested PCR technique.

It could not be definitively determined whether BHV-4 was a primary infection or was secondary to bacterial mastitis. The fact that inclusion bodies appear for only a transient period 2-3 days after experimental respiratory infection of BHV-1 may support the latter scenario. The possibility remains, however, that BHV-4 is a primary and persistent infection, as occurs in field cases of BHV-1 infection, in
which inclusion bodies occasionally persist long enough to be found in bronchial or alveolar epithelium. The primary BHV-4 infection may facilitate secondary bacterial infection.

BHV-4 was associated with degeneration and desquamation of epithelial cells. These lesions were principally similar to those seen in endometria of cows naturally infected with BHV-4. It was not clear whether BHV-4 infection caused squamous metaplasia in the sinus and ductal epithelium. Although no bacteria were isolated, probably due to the treatment with antibiotics, suppurative inflammation in the present case was most likely caused by bacterial infection.

AFIP Diagnosis: Mammary gland: Galactophoritis, necrotizing and suppurative, diffuse, severe, with numerous bacterial colonies and epithelial eosinophilic intranuclear inclusion bodies, Holstein, bovine.

Conference Comment: Bovine herpesvirus-4 is a gammaherpesvirus and has been isolated from cows with mastitis, abortion, metritis, vaginitis, enteritis, and pneumonia, as well as from healthy cattle. It is reported to be an emerging cause of endometritis in cattle. It has been isolated from a variety of animals, including lions, domestic cats, and pigs, although the pathogenic role in these animals is unknown.

Other important bovine herpesviruses are alphaherpesviruses. Bovine herpesvirus-1 causes infectious bovine rhinotracheitis, infectious pustular vulvovaginitis and balanoposthitis. Bovine herpesvirus-2 causes bovine mammillitis, an economically important disease that causes lesions on the teat and udder, and on the muzzle of suckling calves. Bovine herpesvirus-5 causes encephalitis and is believed to result from direct spread from the nasal cavity, pharynx, and tonsils through migration along the trigeminal nerve.

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References:

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