CASE I – 02-534 (AFIP 2838765)

Signalment: 13-year-old, male, Moluccan cockatoo, *Cacatua moluccensis*, avian

History: Bird presented to referring veterinarian for three-months long progressive swelling in the region of the right radiohumeral joint, which began after it fell ill from its perch and developed a right wing droop. A biopsy taken 18 days prior to presentation here was read as mucinous carcinoma (Antech). The swelling doubled in size in approximately one month. Two days before referral, the bird picked at the biopsy site, which initiated marked hemorrhage. The bird was presented for wing amputation.

Gross Pathology: The proximal humerus was embedded in a soft mass up to 6 cm in greatest dimension. Cut surface of the mass was very soft and friable with gray to finely granular yellow foci; the outline of the humerus was obscured. Several cutaneous ulcers were also present (due to self-trauma).

Laboratory Results: None.

Contributor’s Morphologic Diagnosis: Humerus: Mucinous carcinoma of air sac origin.

Contributor’s Comment: The referral diagnosis of "mucinous papillary carcinoma" was originally perplexing because birds do not have cutaneous adnexal glands other than the uropygial gland. The humerus of psittacines is a pneumatic bone as it contains air sacs. Your sections (decalcified and from the proximal most humerus) contain a well-differentiated mucinous carcinoma seen as large papillae containing acini with a mucinous columnar epithelium within air sacs lined by squamous epithelium. Transformation from squamous epithelium to a mucinous epithelium can be seen. The tumor was designated a carcinoma because of very occasional epithelial anaplasia and extension through the humeral cortex. (Wing amputation was performed because metastases were not detectable by CT examination of the lung). The primitive stroma
often has foci of osseous metaplasia; occasionally, there is osteoid infiltration of mucin, which has escaped from disrupted acini.

Peripheral to the humerus (not present in your section) was plaque-like Splendore-Hoeppli bodies covering ulcerated segments of neoplastic glandular epithelium containing Gram-positive cocci (\emph{Streptococcus} sp. had been cultured by the referring veterinarian).

Neoplasms of the Moluccan cockatoo are infrequent; nephroblastoma, lymphosarcoma, papilloma of the feet and synovial sarcoma have been reported (Pye et al.). While adenocarcinomas metastatic to the lung have been reported (Griner; Leach; Stewart), there are few reports of either primary pulmonary carcinoma or air sac carcinoma (Schmidt and Quesenberry; Powers et al.).

**AFIP Diagnosis:** Humerus: Adenocarcinoma, cystic and mucinous, well-differentiated, with stromal osseous metaplasia, Moluccan cockatoo, \emph{Cacatua moluccensis}, avian.

**Conference Comment:** The air sacs are extrapulmonary extensions of the parabronchi that assist in air movement but not in gaseous exchange, and are lined by a single layer of epithelium, supported by mesothelial serosa. Involvement of the air sacs or the lungs in primary neoplasia is uncommon. Histologically, this neoplasm is expansile, non-encapsulated, and composed of cysts lined by well-differentiated low cuboidal to columnar epithelium with goblet cells (which is compatible with air sac epithelium), in a tubular, cystic and papillary pattern. The mesenchymal stroma is moderately cellular yet cytologically bland. The mitotic rate is low. There is rare prominent atypia where the cells have very large nuclei with coarse chromatin and single to multiple, prominent nucleoli, with foci of micropapillary growth by these cells. Although these features may not be present in every slide, the contributor did provide a photomicrograph to the AFIP that demonstrates this atypia in support of a well-differentiated adenocarcinoma.

Conference participants generated considerable discussion on whether this is a well-differentiated malignancy or a benign neoplasm that is locally destructive because of its location, and reflected on the histologic appearance of the stroma. This eventually led us to consultation with Dr. H.L. Shivaprasad, Professor, University of California, Davis, and Drs. F.Y. Schulman and T.P. Lipscomb, Surgical Pathology Consultants to the Armed Forces Institute of Pathology. All three consultants essentially agreed with the contributor that the most likely origin is the air sac based on the reported location and histologic appearance.

We are grateful to Drs. Shivaprasad, Schulman, and Lipscomb for their assistance in this case.

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**References:**

CASE II - 42412 (AFIP 2787174)

Signalment: Adult, female, Caiman Lizard (Dracaena guianensis)

History: The lizard developed skin lesions on its tail, possibly from aggression with enclosure mates. The lesions progressed and ultimately the distal 1/3 of her tail was amputated. Despite apparent healing at the amputation site, her condition declined over the next two months. She was euthanized after developing a large oronasal fistula.

Gross Pathology: A large (1.1 x 20.0 x 0.8 cm) defect was present in the rostral right hard palate connecting the oral cavity to the nasal cavity. Thick dark brown exudate covered the exposed surfaces of the nasal cavity. The tail tip was blunt and covered by smooth black skin (healed amputation site). Coalescing firm, tan nodules distorted approximately 80% of the liver. One nodule was confluent with a similar mass in the caudal left lung. A 5 mm in diameter red ulcer was present in the stomach.

Laboratory Results: Not applicable.

Contributor’s Morphologic Diagnoses: 1. Liver: Severe multifocal to coalescing subacute to chronic necrotizing and granulomatous hepatitis with intralesional protozoa (Etiology: Entamoeba invadens)
2. Liver: Moderate multifocal portal fibrosis and edema
3. Liver: Parasitism (trematode eggs)

Contributor’s Comment: In addition to the liver, amoebic infection was present in the lung, stomach and spleen. Entamoebiasis in reptiles occurs worldwide and is a common cause of morbidity and mortality, mostly in lizards and snakes. Although E. invadens is occasionally pathogenic in turtles, it is likely that turtles (and possibly...
crocodilians) more commonly serve as reservoir hosts. The organism is transmitted by ingestion of cysts that have been shed in the feces of another reptile. The cysts develop into trophozoites in the intestine and either invade the mucosa of the gastrointestinal tract or are transformed into cysts to be excreted and continue the cycle. Diagnosis of the infection can be made antemortem by identifying cysts or trophozoites in feces or a colonic wash. Trophozoites are 10 to 15 μm (up to 30 μm) in diameter and have a single nucleus with a single central endosome and a ring of peripheral granules beneath the nuclear membrane. Cysts are 11 to 20 μm in diameter and have four nuclei. *Entamoeba invadens* is a member of the *Entamoeba histolytica* group of amoebae, some of which are listed below.

*Entamoeba histolytica* group
- *E. anatis* (ducks)
- *E. dispar* (primates; nonpathogenic)
- *E. equi* (horses)
- *E. hartmanni* (primates; nonpathogenic)
- *E. histolytica* (primates; canids; swine)
- *E. invadens* (reptiles)
- *E. moshkovskii* (primates; nonpathogenic)
- *E. ranarum* (amphibians)

The fibrosis and edema seen in many portal regions are not typical of amoebiasis and suggest biliary obstruction. A likely possible etiology is biliary trematodiasis (as indicated by scattered trematode eggs present in most liver sections) although no adult flukes were detected in the bile ducts or gallbladder.

**AFIP Diagnoses:** 1. Liver: Hepatitis, necrotizing, acute, multifocal to coalescing, moderate, with numerous amoebic trophozoites, etiology consistent with *Entamoeba invadens*, Caiman lizard (*Dracaena guianensis*), reptile.
2. Liver: Hepatitis, granulomatous, multifocal to coalescing, mild, with few trematode eggs.

**Conference Comment:** The contributor has provided a concise summary of the obligate protozoan parasite, *Entamoeba invadens*. Conference participants discussed which morphologic changes should be attributed to amoebiasis and which were induced by trematodiasis. Trematodes that are important in reptiles are usually of the order *Digenea*. These parasites typically penetrate the intestinal wall, cross the peritoneal space and subsequently invade the liver. They migrate through the hepatic parenchyma and ultimately enter the bile ducts to mature and lay eggs. Adult trematodes incite an inflammatory response in the bile ducts, which can result in fibrosis in chronic cases. In this case, the severity of periportal fibrosis varies significantly between slides; all agreed trematodiasis is the likely cause.

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**References:**
CASE III – 37722 (AFIP 2593757)

Signalment: 10-month-old, female, avian, White-Throated Laughing Thrush (*Garrulax albogularis eous*)

History: Captive born at the Zoological Society of San Diego. Housed in a multispecies aviary with other passerines. Found dead with one leg caught in a rodent trap.

Gross Pathology: There were multiple fractures of the frontal bone surrounding the right orbit with associated hemorrhage in the subcutis, frontal bone and right cerebral hemisphere. The liver was dark red, enlarged, and extended 1.5 cm caudal to the keel. Throughout the liver were multifocal, up to 0.2 cm in diameter, tan foci which replaced 30% of the parenchyma. The spleen was markedly enlarged (4.2 x 1.0 x 0.8 cm), white-tan, multilobulated and soft. The bird was in good body condition and there were no lesions on either leg.

Laboratory Results: Cytology of impression smears - In all slides of the lung, liver and spleen stained with Wright Giemsa, there were mononuclear cell infiltrates with cytoplasmic 2 micrometer in diameter, spherical to oval, lightly basophilic organisms with a 1 micrometer clear halo. No acid-fast bacteria were seen with Ziehl-Neelsen stains.  
Parasitology - Samples of colonic contents were negative for protozoa and metazoa by direct mount, sedimentation and Sheathers flotation techniques.

2. Liver - intravascular monocytic cytoplasmic protozoa (*Atoxoplasma* sp.), white-throated laughing thrush (*Garrulax albogularis eous*), avian.  
3. Liver - hepatocellular fatty change, minimal, diffuse, white-throated laughing thrush (*Garrulax albogularis eous*), avian.

Contributor's Comment: In the section of liver submitted, there are nodular, multifocal to coalescing, perivascular cellular infiltrates which replace one third to one half of the hepatic parenchyma and slightly compress the adjacent parenchyma. The infiltrates are composed of sheets of round mononuclear cells (macrophages and/or lymphocytes) with a scant to small amount of cytoplasm. In some areas (in which the cells are not
autolysed) many of the cells contain a single cytoplasmic 1 to 2 micrometer diameter, spherical to oval, lightly basophilic organism. Nuclei are normochromatic to hyperchromatic, round to bean-shaped and eccentric. Monocytes in blood vessels in the section also contain cytoplasmic organisms. There were similar mononuclear infiltrates in the spleen, lungs, intestinal tract, pancreas, coelomic adipose tissue, kidneys, skeletal muscle, heart, and bursa. A single apicomplexan protozoal parasite with a parasitophorous vacuole was seen, with electron microscopy, in the cytoplasm of the mononuclear cells in the sections of liver. The bird was probably weak from the protozoal infection, caught it’s leg in the rodent trap and then fell. The head trauma secondary to the fall, combined with the protozoal infection caused the bird's death.

Several other white-throated laughing thrushes from the same exhibit had cytoplasmic protozoa in monocytes or blood samples. Cellular infiltrates, similar to this case, were seen in hepatic biopsy samples from these birds. Fecal samples from these birds were positive for coccidia with Sheather's flotation technique. Fecal samples were submitted to Dr. Ellis Greiner at the University of Florida for oocyst sporulation. Sporulated oocysts that have two sporocysts, each with four sporozoites (Isospora morphology) have been found in similar cases submitted to Dr. Greiner.

The diagnosis of atoxoplasmosis is presumptive, based on the finding of merozoites in mononuclear cells and oocysts with Isospora morphology in feces. Inflammatory reactions to these coccidia have been described as mononuclear, lymphocytic or lymphohistiocytic. In some reports, as in this case, the cells containing the protozoa are thought to be neoplastic. It is not clear whether these "neoplastic" proliferations are polyclonal or monoclonal. Whether the protozoal infection is the cause of the neoplasia or is secondary to immunosuppression has not been proven.

Atoxoplasma sp. (previously known as Toxoplasma, Lankesterella sp. and Isospora serini) have been found in many species of passerine birds and have been previously described in sparrows, canaries, grosbeaks, warblers, goldfinch, siskins and mynahs. Atoxoplasma sp. are coccidian parasites, probably species-specific, which are transmitted by ingestion of sporulated oocysts which have two sporocysts, each with four sporozoites (Isospora morphology). Merogony occurs in intestinal epithelial cells, lymphocytes, blood monocytes and tissue macrophages. Gametogony occurs in intestinal epithelial cells of the same individual host and oocysts are shed in the bird's feces.

AFIP Diagnosis: Liver: Mononuclear cell proliferation, multinodular, with intracytoplasmic protozoa, White-throated Laughing Thrush (Garrulax albogularis eous), avian.

Conference Comment: Atoxoplasma sp. is a coccidian of the phylum Apicomplexa. Apicomplexans are characterized on electron microscopy by an apical complex that is composed of a conoid, rhoptries, polar rings, micronemes, and subpellicular microtubules. The majority of atoxoplasmosis cases are self-limiting, except in fledglings, which are most susceptible and mortality can be high. Adult birds are asymptomatic, low-level shedders of the protozoa, which results in maintenance of the infection in the flock. Grossly, atoxoplasmosis causes hepatosplenomegaly.

Conference participants debated the most likely etiopathogenesis of this interesting case, discussing a lymphoid neoplasm or an unusual inflammatory lesion,
and the possible contributory role of the protozoa. The mononuclear cells expand, efface, and infiltrate the adjacent hepatic tissue, in a space-occupying manner, which is behavior similar to a neoplasm. Alternatively, in support of an inflammatory process, this lesion may be a mononuclear cell reaction to the small numbers of intracytoplasmic protozoa present.

We consulted with Drs. Lipscomb and Schulman, Surgical Pathologist Consultants to the AFIP, and Dr. Shivaprasad, Professor, University of California, Davis, on this difficult and intriguing case. The three consultants agreed that this lesion is a mononuclear cell proliferation with a strong association to the protozoa. Dr. R.J. Montali and Dr. Shivaprasad both suggested that we contact the Zoological Society of San Diego, for further information, and they have seen similar histologic presentations of atoxoplasmosis in this species, and suggest that a comprehensive species review is needed. Again, we thank all consultants and the moderator for their contributions to this conference.

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References:

**CASE IV - 44477 (AFIP 2840173)**

**Signalment:** 5-year-old intact female African Hedgehog (Alerix albiventris), breeding history unknown.

**History:** This 5-year-old African hedgehog was submitted for necropsy after a 7-month period of progressive weight loss. The hedgehog weighed 0.361 kg in January 2001, and in August 2001, weighed 0.296 kg. The animal was euthanized due to a poor prognosis.

**Gross Pathology:** Lungs, mottled pale tan, red, and pink; Teeth, abscesses, multifocal; Mammary gland, cystic, multifocal; Thyroid gland, cystic, focal; Liver, proliferative nodule, focal.

**Laboratory Results:** Serum chemistry and hematological exams were performed and there were no notable abnormalities.

**Contributor's Morphologic Diagnoses:** 1. Lung, Bronchopneumonia, multifocal, granulomatous, diffuse, chronic, severe with extensive fibrosis, mineralization, and acid-fast positive beaded bacteria consistent with *Mycobacterium* spp.

   Additional Histopathology (slides not submitted):
   3. Thyroid, C-cell hyperplasia.
   4. Skin (abdomen), dermatitis, superficial with crusting, chronic, mild.
   5. Liver, nodular hyperplasia.

**Contributor's Comment:** Mycobacterial disease has not previously been reported in African Hedgehogs, although it has been extensively reported in European hedgehogs. It has been hypothesized that European hedgehogs may serve as a reservoir for *Mycobacterium bovis* in New Zealand. This case suggests that African hedgehogs may harbor *Mycobacterium* spp., and even if mycobacteria are not a species that commonly affects humans, it could be important in immunosuppressed / immunocompromised individuals as the African Hedgehog gains popularity as a pet.

   The host response differs between species due to cell mediated and humoral responses. If both of these responses are effective, the host mounts a granulomatous or tuberculous reaction to the mycobacterial pathogen. If there is minimal cell-mediated immunity, as in the European hedgehog and rat, the humoral response takes over and no tubercles are formed, but persistent infection develops with a poorly defined focus.
with few necrotic cells. These mycobacterial infections then become progressive and infiltrative.

**AFIP Diagnoses:** 1. Lung: Pneumonia, granulomatous, multifocal to coalescing, severe, with suppurative bronchopneumonia, bronchiectasis, interstitial fibrosis, and type II pneumocyte hyperplasia, African Hedgehog (*Arelerix albiventris*), insectivore.

**Conference Comment:** Conference participants discussed the difficulty in formulating a morphologic diagnosis in this case because there are three overlapping patterns of pneumonia present. The granulomatous pattern typical of mycobacterial pneumonia was compounded by interstitial involvement and suppurative bronchopneumonia. Gram stains did not reveal an additional infectious etiology to explain the bronchopneumonia. There are four morphologically distinct patterns of pneumonia: 1) bronchopneumonia, 2) interstitial, 3) granulomatous, and 4) embolic pneumonia. Bronchopneumonia is the most common type in domestic animals, characterized by an aerogenous portal of entry, inflammatory exudate within airway lumina, a bacterial etiology, and typically a cranioventral distribution. Interstitial pneumonia involves an aerogenous or hematogenous portal of entry, diffuse pulmonary involvement, and results from an inflammatory process that occurs at the alveolar walls and bronchial interstitium. Typical etiologies include viruses, toxins, allergens and sepsis. Granulomatous pneumonia is caused by pathogens that are resistant to intracellular killing, such as mycobacteria, fungi, parasites and foreign bodies. Granulomatous pneumonia is characterized by an aerogenous or hematogenous portal of entry, and multifocal randomly distributed granulomas. Embolic pneumonia is defined by randomly distributed foci of septic emboli. The portal of entry is hematogenous.

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**References:**

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