THE DIFFERENTIAL DIAGNOSIS

Drury Reavill
Zoo/Exotic Pathology Service
2825 KOVR Drive
West Sacramento, CA 95605

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INTRODUCTION

The class will review six common clinical disease presentations; air sac thickening, crop stasis, dilation of the proventriculus and ventriculus, dyspnoea, joint enlargements, and neurologic clinical signs. We will generate a differential diagnosis (DDx) list for each of the conditions. The purpose is to practice developing a DDx list of disease conditions and to determine further testing procedures that will help reach a working diagnosis. In practice, clinical judgement, experience, and rules of thumb tend to be used for most medical decisions. Periodically reviewing the potential causes of a given clinical sign or presentation will help prevent missed disease conditions.

AIR SAC THICKENING

Thickening of the air sacs may be recognized radiographically as well as on endoscopic or necropsy examination. In many cases, the thickening is due to nonspecific edema with variable inflammation and occasionally microorganisms. Diagnostic techniques include biopsy or cytologic examination by direct imprints or lavage.

The common microorganisms that have been associated with airsacculitis include *Chlamydophila*; fungal infections caused by *Aspergillus*, *Mucor*, *Rhizopus*, and *Penicillium* species; and bacterial infections including *E. coli, Klebsiella pneumoniae*, *Streptococcus pyogenes*, *Staphylococcus aureus*, and *Mycobacterium* spp. (Hernandez-Divers, 2000). Rare cases of systemic adenovirus-like infections (Desmidt et al., 1991) have resulted in air sac thickening, as have sarcocystis infections in susceptible avian species (primarily Australian, Asian, and African origin psittacine birds).

Other causes of inflammation include egg-yolk coelomitis, foreign material aspiration, and toxic exposures. Egg yolk coelomitis, which is release of the proteins and lipids from ovarian follicles into the coelomic cavity, can elicit an inflammatory reaction involving the associated air sacs. Birds that have a lipid pneumonia either from aspiration of lipid material or from an endogenous lipid pneumonia, may also present with plaques thickening air sacs. One toxic exposure that has been associated with a generalized air sac thickening is exposure to sodium hypochlorite (Wilson et al., 2001).

Neoplastic lesions, including lymphoma and air sac carcinomas, will thicken the air sacs, generally as a multifocal lesion (Schmidt et al., 2003).

CROP STASIS

A number of infectious disease agents can result in crop stasis, leading to dilation of the crop. In young birds, ingluvial candidiasis will result in a variable thickening of the mucosa and stasis with dilation. A bacterial and protozoal ingluvitis may also result in crop stasis and dilation. The protozoa most commonly incriminated have been trichomonads.

Circovirus and polyomavirus are common systemic viral infections that can result in gastrointestinal stasis, most readily identified by stasis of the crop (Ritchie et al., 1991; Schoemaker et al., 2000).

Proventricular dilatation disease can result in crop stasis and subsequent dilation depending on the severity of the disease. A crop biopsy when there are functional changes involving the crop, has a higher diagnostic potential for identifying proventricular dilatation disease.

Masses in the tissues of the thoracic inlet, will result in a variable obstruction of the crop. The masses include goiter and other dysplastic lesions of the thyroid, thyroid carcinomas, and thymomas. Crop burns producing tissue edema and cellulitis frequently present as crop stasis. Foreign material and impacted food material in the crop will also result in dilation as well as stasis.

Crop stasis is reported as a sign of toxic exposure particularly to organophosphates and lead (Ochiai et al., 1993; Tully et al., 1993; Platt et al., 1999). Both of these toxins have direct effects on nerve function. Organophosphates inhibit the enzyme acetylcholinesterase that breaks down neurotransmitter acetylcholine, resulting in continued nerve stimulation. The diagnosis is by a history of exposure and measurement of serum cholinesterase concentration. The pathogenesis of lead-induced neuropathy is initiated by schwann cell damage resulting in the breakdown of myelin sheath and lead induced vascular endothelial damage and endoneuronial edema. Diagnosis again relies on a history of exposure and blood level measurement.

Some unexpected associated lesions presenting with crop stasis include pancreatic atrophy and small intestinal cryptosporidiosis (Quesenberry and Liu , 1986; Goodwin and Krabill, 1989). Both of these conditions most likely result in secondary and generalized gastrointestinal dysfunction. Some cases of severe renal failure and soft tissue mineralization will result in generalized gastrointestinal dysfunction that is most readily recognized as crop stasis and dilation (Schoemaker et al., 1997).

Crop stasis and/or dilation should be easily identified as a mass that is present at the thoracic inlet on the ventral side of the neck of the bird. Careful handling is suggested, as with any degree of compression, the crop contents can be retropulsed into the oral cavity and subsequently aspirated.

DILATED PROVENTRICULUS/VENTRICULUS

Dilation of the proventriculus and/or ventriculus can be identified either radiographically with or without contrast material or may be palpated on physical examination. Enlargement of the proventriculus/ventriculus is frequently described as a necropsy finding. The most common cause for this dilation is from post mortem autolysis.

The differentials for gastric dilation can include any number of infectious disease agents including clostridial infections, gastric mycobacteriosis, fungal gastritis, peritonitis and/or serositis and ulcerative or erosive gastritis. Infections involving the proventriculus/ventriculus can be difficult to identify antemortem. Radiographically, there may be gas within the lumen, a variable thickening of

the walls, or possibly, filling defects may be evident.

Proventricular dilatation disease is a common cause of dilation of the proventriculus and ventriculus in some species. The lesions of gastric ganglioneuritis ± leiomyositis are most frequently identified in cockatoos, conures, macaws, African grey parrots, and Eclectus parrots. Diagnosis in the live bird generally requires fluoroscopy to identify abnormal function as well as the dilation of the gastric sections. Confirmation is made by identifying the inflammation of the myenteric plexi or nerve bundles from the crop and/or gastrointestinal tract biopsies.

Neoplastic lesions of the gastric sections may produce a variable dilation although gastric tumors are more commonly associated with thickening of the sections due to the neoplastic proliferation.

Impaction of foreign material within the lumen will dilate the proventriculus and ventriculus. This material can be identified by contrast studies of the gastrointestinal tract and some cases will have intraluminal gas accumulation. From the few cases of foreign material impactions that have been examined, the gastric sections demonstrate normal fluoroscopic movements. Mineralization of the proventricular mucosa or of the koilin and muscular tunics has resulted in gastric dilation. From a review of cases (Reavill unpublished 2007) the soft tissue mineralization is common secondary to severe renal disease. Radiographically, there may be a mineral density of the gastric sections.

Although poorly described for psittacine birds in the literature, lead toxicity can present with dilation of the gastrointestinal tract. This is due to the lead-induced neuropathy resulting in breakdown of myelin sheaths and lead induced vascular endothelial damage and with endoneuronial edema (Platt et al., 1999).

An unexpected lesion that has been linked with dilated gastric sections is pancreatic disease due to atrophy, inflammation, or degenerative processes (Quesenberry and Liu , 1986). The association of the pancreatic lesions with the variable dilation of the gastric sections is unknown.

DYSPNOEA

In psittacine birds, it can be difficult to determine upper respiratory versus lower respiratory causes of dyspnoea. Careful auscultation may help localize the lesions. The common clinical signs of lower respiratory tract disease include tail bob, open-beak breathing, tachypnoea, pronounced sternal movement especially at rest, voice change, coughing and audible breath sounds. Upper respiratory clinical signs may also include wheezes, sneezing, nasal discharge, and swollen sinuses. Radiographs can be helpful in some cases if the bird is stable enough to survive radiographic examination. Many birds presenting with dyspnoea are generally suffering extensive damage to the pulmonary tissues before the clinical signs are evident, particularly at rest.

Lesions involving the syrinx are typically associated with changes in or loss of voice. Fungal infection is one of the most common diseases involving the trachea and the lungs. It is important to realize that Aspergillus is not the only fungus that will result in a fungal pneumonia and this may complicate interpretation of the current serology tests. Rarely, mycobacterium granulomas have been identified within the trachea, usually at the syrinx.

Aspirated foreign material will result in secondary inflammatory lesions and presentation with dyspnoea. Millet seeds are not uncommonly aspirated into the trachea of cockatiels. If identified early, it is possible to place an air sac tube in these birds and attempt to aspirate the seed from the

trachea before it has resulted in significant tissue edema and/or has produced any inflammatory exudates that may lodge the seed firmly within the lumen. Tracheal trauma including that from endotracheal tube placement, can result in an occlusive lesion or stenosis. Some cases may respond to repeated breakdown of the proliferative tissue in the lumen or by surgical resection and anastomosis.

Fungus, bacteria, and one virus, polyomavirus, have been identified as causes of pneumonia. Most fungal pneumonias and granulomas suggest immunosuppression as well as support exposure to an overwhelming number of fungal spores. The environment should be evaluated to identify a potential source of fungal spore formation (eg. wood shavings, corncob bedding, seed hulls). Review of the recent medical history may identify use of immunosuppressive drugs, chronic antibacterial therapy, neoplastic conditions, severe malnutrition (hypovitaminosis A), or underlying disease agents (parasites, virus, bacteria, chlamydophila). Fungal pneumonia is a common finding in young African grey parrots infected with circovirus. These types of infections are difficult to diagnose antemortem and frequently do not respond even to aggressive therapy. A rare fungal pneumonia is caused by several varieties of *Cryptococcus neoformans*, a saprophytic yeast-like fungus. *C. neoformans* rarely causes disease in birds, possibly due to the protection by their normal bacterial microflora and high body temperature. The clinical signs of infection include depression, weakness, anorexia, weight loss, acute diarrhea, incoordination, blindness, dyspnoea, nasal exudate, soft tissue swellings, oral masses, and death. The respiratory tract appears to be the portal of entry. Dissemination to the central nervous system is not unusual with this fungus. The lesions contain a myxomatous gelatinous material. A narrow-based budding yeast with a thick capsule can be identified by cytology of this material. There is one report of an unsuccessful therapeutic attempt with fluconazole (Parrott, 1991).

Bacterial pneumonia occurs either as part of a systemic infection or from inhalation of the bacteria into the respiratory system. Polyomaviral pneumonia is part of the systemic infection.

Neoplasm is uncommon in the respiratory system, but has been reported. The primary tumors in the trachea are osteosarcoma and leiomyoma (Schmidt et al. 2003). In the lung, there are bronchial carcinomas, fibrosrcomas, adenomas, and the undifferentiated tumor of cockatiels (Andre and Delverdier, 1999; Ellis, 2001). Many of these birds will not demonstrate any respiratory compromise until these masses are extremely large and compressing the majority of the pulmonary tissue.

Masses outside the respiratory tract can result in the primary clinical sign of dyspnoea. These include lesions in the thyroid gland, including hyperplasia, which has been associated with clicking respiratory sounds. Adenocarcinoma of the ventriculus, metastatic renal carcinoma, extrahepatic biliary cysts, lymphomas, and seminomas all have been associated with respiratory clinical signs. This is due to compression of the air sac system or space occupying lesions from the neoplasia. Another mass lesion that can result in dyspnoea is from hepatic disease, particularly vacuolar hepatopathy and/or hepatopathies that result in significant fluid accumulation. Egg-yolk coelomitis with release of yolk protein into the coelomic cavity is also associated with respiratory clinical signs. This again is due to compression or collapse of the abdominal air sacs as well as proteinaceous fluid accumulation within the respiratory system.

Exposure to airborne toxins is also commonly associated with the presentation of dyspnoea. These toxins include the fumes of sodium hydrochloride, the products of overheated Teflon®, the burn products from the operation of the self-cleaning cycle of an oven, and some carpet fresheners. A review of the recent environmental history may help identify a potential toxic exposure.

Chronic obstructive pulmonary disease (macaw pulmonary hypersensitivity) is generally associated with polycythaemia and appears to be most common in the blue and gold macaw. Early diagnosis is difficult due to the reserve capacity of avian lungs and relative inactivity of captive macaws. The lung lesions are generally advanced when polycythaemia occurs. The prominent lesion is the atrial smooth muscle hypertrophy and some atrial loss due to fusion and epithelial bridging. Uncommonly, there may be a proliferation of parabronchial lymphoid tissue and lymphoid nodule formations. Many of these macaws have been kept in aviaries with poor ventilation or exposed to the feather dander of cockatoos, cockatiels, or African grey parrots. Therapy is generally symptomatic.

JOINT ENLARGEMENTS

Enlargement of one or multiple joints is generally readily identified by physical exam. In cases, radiographs are recommended to evaluate the structure of the underlying skeleton. Soft tissue swelling can be aspirated for cytologic examination. Systemic infections can result in variable joint enlargement, and generally involve multiple joints. Systemic candidiasis has been reported, although bacterial infections are more likely to result in this lesion (Goodman and Widenmeyer, 1986).

Villonodular synovitis is a rarely described lesion of older cockatiels (Reavill, AAV Avian Pathology session 2000). It is an inflammatory and proliferative process of the joint synovium. One possible etiology of this proliferative lesion is of an underlying chlamydophila infection. In mammals, these proliferative lesions are commonly idiopathic and may be immune mediated.

Several tumors can affect the joints. These will generally involve a single joint, and the primary tumors are synovial cell sarcoma and pulmonary carcinoma. In both of these tumors, changes in underlying bony structure may be recognized radiographically. The pulmonary carcinoma cases are lesions of the respiratory system, including the air sacs. The humerus is most frequently involved and generally at the scapulohumeral joint with extension to the radiohumeral joint, from the air sac reflection into the humerus.

Trauma will readily result in enlargement of the joint, particularly if there is dislocation. In psittacine birds, femorotibial and coxofemoral joint luxations seem to be the most common.

Gout tophi accumulations within the joints are a common reason for birds to present with enlarged joints. Articular or synovial gout will present as white swellings over joints, most typically of the feet. It is common in cockatiels and budgerigars and appears painful. The cause is not completely understood but many birds have underlying renal disease. The clinical signs include a shifting leg lameness, inability to bend the toes, and nonspecific feather picking in some species. Aspiration and exfoliative cytology is used to differentiate gout from granulomas. Therapy is only palliative.

NEUROLOGIC CLINICAL SIGNS

Neurologic diseases can be recognized by a number of characteristic signs including seizures, paresis, paralysis, head tremors, and possibly head tilt. Neurologic examination of the bird can be very difficult, particularly for localizing the lesion. There are many cases that will present with neurologic clinical signs due to systemic illness and not from a lesion within the central nervous system.

The infectious disease etiologies include viruses (paramyxovirus, polyomavirus, herpesvirus, and Eastern equine encephalitis virus), bacteria, fungus, protozoa, and nematodes. Sarcocystis encephalitis is a protozoal infection more commonly identified in non-New World psittacine birds and

will generally result in concurrent significant respiratory dysfunction, leading to death.

Proventricular dilatation disease, particularly of African grey parrots, commonly presents with nonspecific neurologic signs including variable proprioceptic defect of the legs, weakness, or ataxia.

A number of intra-cranial tumors have been reported, most commonly in budgerigars. These include tumors of the ependyma, choroid plexus, adenohypophysis (the pituitary), pineoblastoma and unclassified tumors (Suchy et al., 1999).

Toxins that will result in neurologic clinical signs include the organophosphates and heavy metal toxicity, particularly lead.

Several diseases within organ systems outside the central nervous system may also present with neurologic clinical signs. Liver lesions, including severe hepatic lipidosis and chronic degenerative lesions, will occasionally be presented as birds with neurologic signs. Definitive identification of hepatic encephalopathy due to liver lesions has not been documented in birds. This type of lesion in mammals is generally associated with elevations in blood ammonia, which, again, has not been definitively identified in birds. The other organ system disease is of severe atherosclerosis. The neurologic clinical signs may be related to alterations in blood flow and possible tissue hypoxia. Occasionally, female birds have been described as having "yolk stroke". In these birds, which will present with either head tilts or tremors, yolk proteins can occasionally be identified within the vascular spaces in the central nervous system.

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