Mycobacteriosis in Pet Psittacines

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Mycobacteriosis is a common disease of captive birds. Post-mortem surveys in psittacine suggest an infection rate of 0.5-14%, with brotogerid parakeets (*Brotogeris spp.*), Amazon parrots (*Amazona spp.*), budgerigars (*Melopsittacus undulates*), and pionus parrots (*Pionus spp.*) most frequently infected. Mycobacteriosis in psittacines had been thought to be due primarily to *Mycobacterium avium subsp. avium* (MA). However, wider availability of polymerase chain reaction tests indicates the majority of avian infections may be due to *Mycobacterium genevense* (MGE).[1-4] Other species of mycobacteria have been identified infrequently in birds as well, including *Mycobacterium tuberculosis*, the primary cause of tuberculosis in non-immunocompromised humans.[1,5]

MA and MGE are typically shed in the feces of infected birds, although birds with primary pulmonary infections may shed the organism in respiratory secretions. Therefore birds primarily acquire mycobacteriosis through ingestion of the organism, with infections via the respiratory route occurring with less frequency.[1,5] Mycobacterial organisms have been demonstrated in the skin and presumably enter through a wound.[1] In collections of birds, transmission likely occurs from bird to bird via exposure to feces containing large numbers of organisms. However, infections may also be acquired though contaminated water and soil, as organisms are common and persist for long periods of time.[1]

After ingestion, MA and MGE infect the liver and small intestine. Hematogenous spread of the organism leads to infection of bone marrow lungs and air sacs, spleen, gonads and rarely kidney and pancreas, in order of frequency.[1] MA and MGE tend to produce diffuse enlargement of the target organs due to accumulations of macrophages in organ parenchyma. The liver may appear enlarged and tan without visible granulomas. In contrast, *M. tuberculosis* infections tend to produce visible nodules containing epitheliod cells, giant cells, and heterophils. The cytoplasm of affected cells is filled with acid-fast organisms.[1,6]

Symptoms of mycobacteriosis vary widely depending on length and severity of infection, and organ system affected. Birds can die acutely without recognized signs of illness. Birds can also present with weight loss, poor feathering, polyurea, diarrhea and abdominal distention. Less usual physical examination findings may include lameness, respiratory compromise, and cutaneous masses. Weight loss appears to be the most consistent finding in birds affected with mycobacteriosis. These birds typically fail to respond to routine antibiotic therapy. [,5,6]
Ante mortem diagnosis of mycobacteriosis can be difficult. Ancillary blood work abnormalities may be few and are generally non-specific. While hemogram abnormalities are variable, typical disseminated mycobacteriosis in psittacines tends to produce moderate to marked elevations in white blood cell numbers characterized by heterophilia and monocytosis. Reactive lymphocytosis can be present. The packed cell volume is often decreased, except in the case of primary respiratory mycobacteriosis, where the packed cell volume can be greatly elevated. These hemogram abnormalities, however, can be present in a number of inflammatory and chronic disease conditions other than mycobacteriosis.[8]

Hepatic mycobacteriosis can produce elevations in enzymes such as alanine aminotransferase (ALT), aspartate aminotransferase, (AST), and lactate dehydrogenase (LDH). However, in birds these enzymes are also present in varying amounts in a variety of other tissues such as muscle, kidney and heart. Therefore, elevations may not truly reflect hepatocellular damage. Conversely, enzymes can be normal in the face of severe hepatic disease.[9] If liver function has been compromised, hepatic mycobacteriosis may produce elevations of serum bile acids.[10] In some infections, plasma protein electrophoresis produces a persistent polyclonal gammopathy that may drop in later stages of the disease. Protein electrophoresis may also reveal hypoalbuminemia secondary to reduced hepatic synthesis.[11]

Radiographs may reveal an enlarged liver or thickened intestinal loops. Pulmonary granulomas may be present. In cases of invasion into bone marrow, endosteal bone densities may be present in the humerus, tibia, ulna and rarely the femur.[6]

The documentation of acid-fast organisms in histopathologic samples of target organs provides presumptive diagnosis. Acid-fast organisms may also be detected in feces, but must be distinguished from non-pathogenic saprophytes. Culture of avian tissue and feces for mycobacterial organisms is difficult. MA may require one to six months to grow, and MGE has not been documented to grow on conventional mycobacterial media.[3,12] Intradermal tuberculosis testing as used in humans correlates poorly with the presence of disease in psittacine species.[6,13] Recently, polymerase chain reaction tests (PCR) have become readily available to detect mycobacterial genetic material in fresh tissues, feces, and paraffin-block tissues. PCR can detect very low numbers of organisms, distinguish between species of mycobacterium, and be completed in one to three days.[3,12]

In humans, disseminated mycobacteriosis due to MA is common in patients with AIDS and occurs late in the course of the disease. Prior to the AIDS epidemic (pre-1981), infections with MA were considered a "novelty", with an estimated 3000 cases occurring worldwide per year. The majority of cases involved immunocompromised patients, in particular those having undergone organ transplant or suffering from hairy cell leukemia. Approximately 40% of AIDS patients will eventually develop MA without preventative treatment, and incidence is directly linked to decreasing CD4-T lymphocyte counts.[14-16] In the early 1990's MGE began to be recognized as a cause of mycobacteriosis in AIDS patients as well, although with much less frequency than MA. Both organisms produce similar clinical pictures in humans, with fever, weight loss, and anemia common features of the disease.[16-18]

Treatment of avian mycobacteriosis has been attempted with reports of positive outcomes.[19,20] However, debate exists as to the advisability of treating pet birds with a potentially zoonotic disease. The source of infections in humans in most likely environmental, as organisms are common in food, water and soil. Humans with disseminated MA and MGE disease have heavy GI tract infections, suggesting ingestion of the organisms as the primary route of infections. Epidemiology studies utilizing DNA fingerprinting have attempted to shed light on the exact source of MA organisms, but correlation between MA in humans infected with HIV and their surroundings have been inconclusive.[14,15] The fact that humans are regularly exposed to MA and MGE is supported by a study that demonstrated the DNA of MGE in 25% of intestinal biopsy samples collected from non-HIV patients.[17] It is unlikely, therefore, that birds with disseminated MA or MGE are significant health risks to humans with normal immune systems. However, persons with HIV or other diseases impacting the immune system are at increased risk, especially when CD4-T lymphocyte counts drop below normal.[14-16]

It must be noted that birds with mycobacteriosis due to *M. tuberculosis* are a health risk to persons with normal and abnormal immune systems, particularly children and the elderly. In addition, AIDS patients have a 50 times increased risk of disease due to *M. tuberculosis* than non-immunocompromised persons.[15] Most authorities are in agreement against recommending treatment of birds with *M. tuberculosis* for these reasons.

Treatment of tuberculosis in avian patients is modeled after treatment protocols for tuberculosis in humans.[20] Treatment in humans almost always involves the use of a combination of antituberculous drugs, as resistance to a single drug can develop rapidly. Treatment often lasts nine months or longer, as organisms can only be killed during replication, which occurs only once every 16 to 20 hours. Organisms can also persist for months in caseous lesions and macrophages where replication seldom occurs. Therapy is also aimed at achieving the highest possible blood levels of drug rather that maintaining constant blood levels. Therefore, the highest tolerable levels of drugs are given once daily, not in divided dosages.[14-16]

MA infections in humans are highly resistant to all currently available *single* antituberculous drugs, again emphasizing the necessity of multiple drug therapy. No drug studies exist on the use of antimycobacterial drugs in psittacines, therefore information on efficacy and toxicity is anecdotal only.. Dosages for a number of selected antimycobacterial drugs have been suggested by VanDerHeyden and others based on human pediatric dosages, metabolic scaling, and anecdotal reports.[20] (Table 1). Several recent drug studies in humans indicate clarithromycin, ethambutol and rifabutin as the drugs of choice for the treatment of AIDS-associated MA.[16]

Case reports

Three birds with confirmed mycobacteriosis based on demonstration of acid-fast organisms in biopsies of the liver were treated with a combination of clarithromycin (Biaxin, Abbott Laboratories, North Chicago, IL, USA), ethambutol (Myambutol, Lederle Laboratories, Wayne, NJ, USA), and rifabutin (Mycobutin, Pharmacia Laboratories, CA, USA) with or without enrofloxacin. After twelve months of therapy, two birds were negative for acid-fast organisms on liver biopsy. The third is currently in the fourth month of treatment. A fourth bird diagnosed with mycobacteriosis was euthanized. Table two summarizes the physical exam findings, methods of diagnosis, treatment and outcomes.

Table 1. Published Antituberculosis Drug Dosages

Drug	Human Pediatric Dosage	Psittacine Dosage
Isoniazid	10-20 mg/kg	30 mg/kg
Rifampin	10 mg/kg	10-45 mg/kg
Rifabutin		15-45 mg/kg
Ethambutol	10-15 mg/kg	15-30 mg/kg
Streptomycin	20-40 mg/kg	20-40 mg/kg
Clarithromycin	7.5-15 mg/kg	60 mg/kg
Ciprofloxacin	10-15 mg/kg	80 mg/kg
Clofazamine	1-2 mg/kg	6 mg/kg

Table Two. Summary of Four Confirmed Cases of Mycobacteriosis

Signalment	Physical exam findings	Diagnosis	Treatment	Outcome
Budgerigar Female 2 years	Weight loss Enlarged liver	Liver biopsy *Mycobacterium sp.*	Rifabutin Ethambutol Clarithromycin Enrofloxacin	Apparent cure
Grey-Cheek Parakeet Female 11 years	Weight loss Feather plucking Enlarged liver	Liver biopsy PCR: *Mycobacterium avium*	Rifabutin Ethambutol Clarithromycin Enrofloxacin	Apparent cure
Pionus Parrot Female 6 years	Weight loss Depression Swelling at tattoo site	Liver biopsy Acid-fast organism in feces PCR: *Mycobacterium Avium*	Rifabutin Ethambutol Clarithromycin	Pending
Blue & Gold Macaw Male 12 years	Weight loss Feather plucking Swelling at tattoo site	Liver biopsy Acid-fast organisms in feces PCR: *Mycobacterium avium*	None	Euthanized

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