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Hepatic Fibrosis and Bile Duct Hyperplasia in a Young Orange Winged Amazon Parrot (*Amazona amazonica*)

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Abstract : A 6-month-old orange winged Amazon parrot (*Amazona amazonica*) was presented for evaluation of weight loss, anorexia, and abdominal distension for two months. Clinical and laboratory examinations revealed evidence of hepatic failure, including transudative ascites, increased serum serum aspartate aminotransferase and bile acids, and decreased albumin-to-globulin ratio. Hepatic fibrosis with bile duct hyperplasia and chronic hepatitis was diagnosed by liver biopsy. The cause of this condition remained unclear, but exposure to hepatotoxins was suggested.

Key words **:** Amazon parrot, bile duct hyperplasia, bird, hepatic fibrosis.

Introduction

Hepatic fibrosis is a nonspecific, chronic debilitating liver disease that results commonly from chronic active hepatitis in psittacine birds (4,15). The etiology is usually undetermined; however, chronic malnutrition, various viral or chlamydial infections, subclinical or chronic toxin exposure, and immune-mediated disorders have been proposed (4,15). The initial causative insults may precede any severe clinical signs and quickly disappear prior to chronic hepatitis, which makes it very difficult to identify the exact cause of chronic active hepatitis (4). Chronic active hepatitis is relatively common in psittacine birds, particularly in Amazon parrots, cockatiels, macaws, and budgerigars (7,15).

Bile duct hyperlaisa is frequently observed in psittacine birds with liver diseases including chronic active hepatitis, hepatic fibrosis, and hepatocellular lipidosis (14,15). The cause of bile duct hyperplasia is also often undetermined but mycotoxin exposure has been suggested (14). Because diagnosis and confirmation of the causative factors of both diseases is very limited, liver biopsy for histopathologic and microbiologic examinations is essential (6,13).

Case

A 6-month-old orange winged Amazon parrot (*Amazona amazonica*) was presented with a two-month history of weight loss, anorexia, and abdominal distension. The pet bird was kept indoors with separately caged other parrots in a same room. The bird lived in stainless steel cage with ornaments made of wood. The bird's diet consisted of commercial weaning diet (Vetafarm Neocare, Vetafarm. Ltd.) and sunflower seeds. No previous medical problems were reported and no bird in the house had any clinical signs of illness.

On physical examination, the bird was depressed and stood widely when perching. The feces were loose with green urates. The abdomen was distended and the liver margin was firm at the caudal sternum on palpation. The pectoral muscles were mildly atrophic. The lung and air sac auscultations and visual examination of the oral cavity were unremarkable.

A blood sample was obtained for complete blood count and plasma biochemistry. The abnormal results were moderate leukocytosis (34×10^3; reference, $6\text{-}17 \times 10^3$), heterophilia (89%; reference, 30-75%) with toxic changes, markedly elevated serum aspartate aminotransferase (AST, 1000 U/L; reference, 150-344 U/L), and markedly increased bile acid concentration (1180 μmol/L; reference, 33-154 μmol/L) (9). Plasma protein electrophoresis revealed decreased albumin (0.8 g/dL; reference, 1.85-3.24 g/dL), increased alpha-1 globulin (0.4 g/dL; reference, 0.05-0.32 g/dL), increased gamma globulin (1.6 g/dL; reference, 0.17-0.6 g/dL), and decreased albunin-to-globulin ratio (0.23; reference, 1.1-2.1), which were consistent with chronic active inflammation (2). Whole body radiographs revealed severe hepatomegaly, compromised air sacs, and decreased serosal details (suggestive of ascites) (Fig 1A and 1B). On ultrasonographic examination, hepatomegaly with diffusely homogenous echotexture, dilated enterohepatic duct, and perihepatic ascites were observed. Abdominocentesis was performed for ascites analysis. The ascites was a transudate with lightly yellow and clear in gross appearance, low specificity gravity (1.018), low total protein concentration (1.5 g/dL), and low cellularity (165 cells/μL).

Liver disease was suspected based on the clinical examina-

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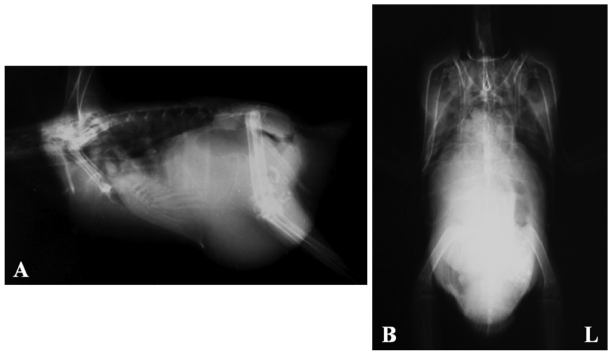

Fig 1. Radiographs of an Amazon parrot with hepatic fibrosis and hepatitis. A: Right lateral view. This radiograph shows marked hepatomegaly with cranial displacement of the heart, dorsal displacement of the proventriculus, and caudodorsal displacement of ventriculus. B: Ventro-dorsal view. This radiograph shows a widening of the hepatic silhouette and a loss of the cardio-hepatic waist.

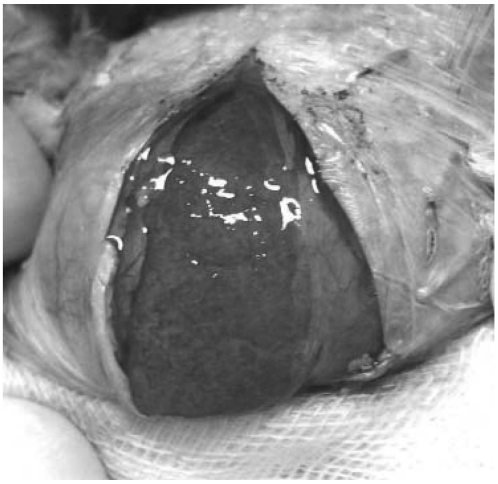

Fig 2. The liver of an Amazon parrot with hepatic fibrosis and hepatitis during ceilotomy for liver biopsy. The liver is enlarged and the capsular surface is irregular and reticular.

tion, blood profiles, protein electrophoresis, imaging tests, and ascite analysis. Differential diagnoses included infectious hepatitis (bacterial, viral, mycobacterial, chalmydial, or parasitic), hepatic lipidosis, hepatic neoplasia, and toxicosis. Because the owner declined liver biopsy, liver fine needle aspiration was performed under general anesthesia with isoflurane. No infectious organisms, abnormal pigments, or cells were observed in liver cytology. The results of bacterial and fungal cultures were unremarkable.

Doxycycline (25 mg/kg, oral, once a day; Sinil Pharm., Seoul, Korea) and silymarine (10 mg/bird, oral, once a day; Sinil Pharm., Seoul, Korea) were administered for 6 weeks to estimate medical response. The owner was advised to remove all seeds and peanuts from the bird's diet and to avoid any possible exposure to chemicals or toxins. After 6 weeks of medical treatment and diet change, clinical signs improved (increased appetite and activity and defecating normal yellow-

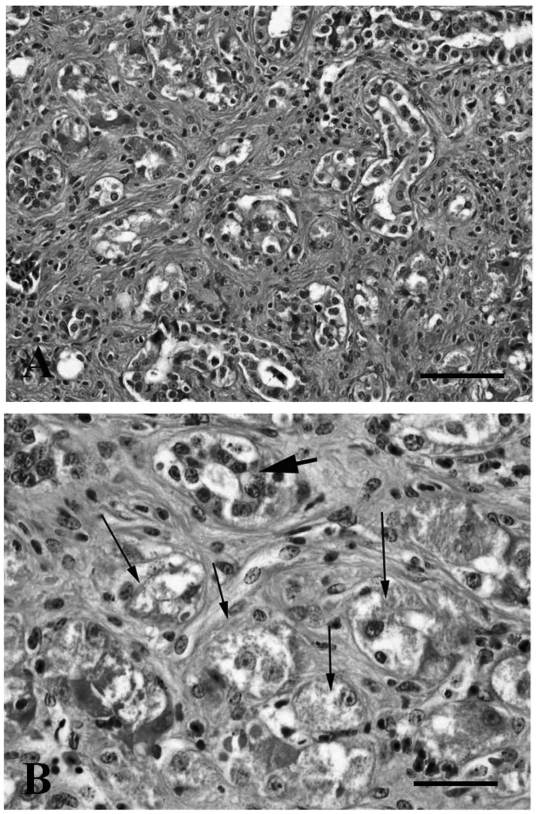

Fig 3. Microphotograph of the liver from an Amazon parrot with hepatic fibrosis and hepatitis. A: The normal architecture of liver is disrupted by severe fibrosis, hepatocellular loss, and bile duct hyperplasia. Scale bar = 100μm (hematoxylin and eosin. × 100). B: At higher magnification, the remaining hepatocytes are swollen and degenerate with cytoplasmic vacuolation (thin arrows). The bile ducts (thick arrow) are hyperplastic. Scale bar = 100 μm (hematoxylin and eosin. × 400).

ish urates). Nonetheless, there was no improvement in abnormal blood profile. Liver biopsy was therefore performed under the owner's permission. The bird was anesthetized with isoflurane, and a wedge biopsy of the liver was obtained by a celiotomy through a midline approach (6). The liver was enlarged and firm on palpation with reticular hepatic surface and thickened capsule and small amounts of ascites was observed during the biopsy procedure (Fig 2). The bird recovered from the anesthesia uneventfully. The biopsy sample was submitted for histopathologic examination. Microscopically, normal hepatic structures were altered by severe loss of hepatocytes, marked fibrosis, bile duct proliferation, and multifocal mild to moderate lymphocytic and heterophilic inflammation. The remaining hepatocytes were degenerate with cytoplasmic vacuolation. No infectious etiology was evident. (Fig 3A and 3B). A diagnosis of hepatic fibrosis with bile duct hyperplasia and hepatitis was made. The underlying cause of this condition remained unclear, but exposure to a hepatotoxin was proposed.

Discussion

The diagnosis of liver disease is challenging because most liver tissue is compromised before hepatic dysfunction becomes clinically evident (11). Hepatic dysfunction can result from various causes and the clinical history and clinical signs are highly variable. Multiple laboratory tests are performed to measure hepatic function, but these tests often give no indication as to the viability of the remaining hepatic tissue or the cause of damage (10). Among the numerous laboratory tests, the plasma bile acid assay serves as a more accurate and specific prognostic indicator in the case of acute hepatitis that may show only nonspecific enzyme elevation (7). A recent study demonstrated that, in psittacine birds, bile acid test exhibited the highest correlation with histopathologically confirmed hepatic disease, compared with protein electrophoresis and serum hepatic enzyme levels (3). Fasting bile acid elevation with hepatobiliary disease is typically much greater than postprandial elevations in birds, including orange-winged Amazon parrot. Therefore, clinically a single non-fasting sample is recommended in birds (5,7). Two common conditions that cause marked elevation in fasting bile acid are bile duct hyperplasia and severe hepatic fibrosis (7). The parrot in the present case also had markedly increased serum bile acid level, although routine laboratory tests failed to determine the cause of hepatic damage.

Hepatic biopsy is often required to definitively diagnose and appropriately characterize hepatic disease (12). A hepatic biopsy specimen can be obtained by either blind or ultrasound-guided percutaneous liver biopsy (Tru-cut biopsy), endoscopic biopsy, or liver wedge biopsy during celiotomy. Among these techniques, surgical approaches allow for more precise targeting of focal lesions and more immediate control of complications (12). Hepatic samples are submitted for bacterial and fungal culture, cytologic evaluation, and histopathologic examination (12). Because the diagnosis of specific causes may not be determined, diagnostic sampling through hepatic biopsy is beneficial for the accurate diagnosis of the cause and for the evaluation of the severity of hepatic disease (15).

Liver disease due to toxin exposure has been infrequently diagnosed because the history provided by the owners is minimal, acute clinical signs may have disappeared, and the lesion worsened chronically (4,15,17). When minimal history is provided, chemical analysis of animal tissues and consistent histological change are necessary for diagnosis (17). The histopathological findings of hepatic fibrosis with hepatocellular loss, bile duct hyperplasia, and multifocal chronic inflammation in the present case were suggestive of a toxic hepatopathy. Common hepatotoxins for pet birds are mycotoxins such as aflatoxins and citrinin (1,15). The diet for this bird consisted of commercial weaning food and sunflower seeds. Mycotoxins derived from sunflower seeds were suspected as a possible primary etiology. One previous report suggested that young Amazon parrots have a high susceptibility to hepatotoxins in comparison with other parrot species (1).

The early targeted therapeutic plan in this bird was focused on infectious disease at initial presentation. Appropriate nutritional changes and hepatic protectants (silymarin) were also recommended. Clinical signs progressively improved with medication and hepatic protectants might have prevented further hepatic damage. Silymarin is often prescribed in birds with hepatic disease and there is anecdotal evidence of clinical improvement. Recently, two studies showed that silymarin has hepatoprotective effects in experimentally induced aflatoxicosis in chickens and pigeons (8,16).

In conclusion, an Amazon parrot in this case was diagnosed as chronic hepatic fibrosis with bile duct hyperplasia and hepatitis based on serial diagnostic tests. The diagnosis of avian hepatic disease should be made based on the results of multiple diagnostic tests, including physical examination, laboratory tests, imaging studies, and hepatic biopsy. The diagnostic plan should be designed to investigate the underlying causes for an appropriative treatment plan.

Acknowledgements

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담관비대를 동반한 간섬유화에 이환된 어린 아마존 앵무새 (orange winged Amazon parrot, *Amazona amazonica*)

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요 약 : 6개월령 아마존 앵무새(orange winged Amazon parrot, *Amazona amazonica*)가 2달 간 지속된 체중저하, 식욕감퇴, 복부팽만을 검사 받기 위하여 내원하였다. 신체 검사와 실험실 검사에서 유출성 복수, 아스파라진산 아미노전이효소와 담즙산의 증가 및 알부민-글로불린 비율의 감소와 같은 간부전이 의심되는 소견을 보여주었다. 간 생검을 통하여 담관 비대를 동반한 간섬유화가 진단되었다. 이 증상의 원인은 확실하지 않지만, 간독소에 의한 것으로 여겨진다.

주요어 : 간섬유화, 담관비대, 새, 아마존 앵무새