Ale Aguirre, DVM, Diplomate ACVIM, Red Bank Animal Hospital, Tinton Falls, New Jersey

Chronic Liver Disease

Liver disease is a frequently encountered chronic disease process in companion animals. Chronic liver disease is defined as any hepatopathy that has been present for more than 6 to 8 weeks. Common causes include chronic active hepatitis, copper storage hepatopathy, and drug-induced hepatopathy. A larger but more complex group of hepatopathies are those related to infectious, inflammatory, and immune-mediated disease processes. Anorexia, vomiting, weight loss, polyuria/polydipsia, distended abdomen, behavioral changes, and stranguria are common presenting signs. Pertinent physical examination findings include hepatomegaly, jaundice, ascites, abdominal pain, pyrexia, and coagulopathies.

Patient Management

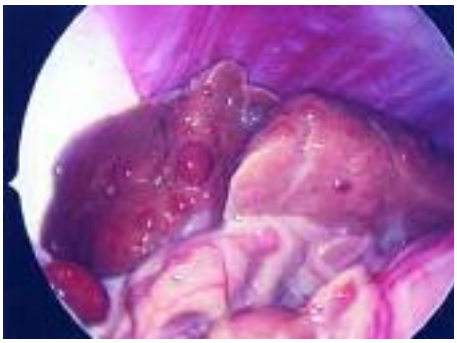
Primary Testing

The initial step in evaluating patients suspected of having chronic hepatopathy includes a complete blood count, chemistry panel, and urinalysis. Changes on the complete blood count are often nonspecific and may include mild normocytic normochromic nonregenerative anemia, leukocytosis, and alteration in platelet count.

Valuable information can be gathered from the degree of enzyme elevations and evaluation of synthetic liver products, such as albumin, cholesterol, and blood urea nitrogen. Biliary diseases tend to manifest with elevations in alkaline phosphatase, α-glutamyltransferase, and cholesterol, whereas chronic hepatopathies generally have greater elevations in alanine aminotransferase and aspartate aminotransferase.

Urinalyses often reveal isosthenuria, bilirubinuria, and ammonium biurate crystals. Bilirubinuria may be detected before the development of jaundice. Bilirubinuria can be normal in dogs but is always pathologic in the cat.

Laparoscopic biopsy from a Labrador retriever dog with copper storage hepatopathy



Laparoscopic liver image of a dog with chronic fibrosing lymphoplasmacytic hepatitis (chronic active hepatitis)

Second-Tier Diagnostics

Second-tier diagnostics include bile acids, infectious disease testing (*Leptospira*, feline leukemia virus, and feline immunodeficiency virus), endocrine profiles (thyroid level, adrenocorticotropic hormone stimulation test, or low-dose dexamethasone suppression test), coagulation studies, and abdominal imaging. Bile acids provide important information on hepatic function and may suggest portosystemic shunting of blood. If the total bilirubin level is elevated because of cholestasis, the bile acid level is often high. As a result, bile acids are often not warranted in icteric patients.

Coagulation studies are important in patients that are hypoalbuminemic or have significant liver enzyme elevations. Abdominal radiography and abdominal ultrasonography provide information on the appearance of the liver, presence of congenital or acquired shunts, and presence of cystic calculi.

The limitations of hepatic aspirates in the evaluation of chronic liver disease have been recognized in a recent article.[1] Agreement between aspirates and histopathologic findings was found to be shockingly low in dogs (30%) and cats (51%). Therefore, liver aspirates must be interpreted with caution.

Third-Tier Diagnostics

Laparoscopic liver biopsies are currently preferred by many internists and surgeons and are considered third-tier diagnostics. Scintigraphy and portograms are other diagnostic modalities that are typically performed at referral centers or teaching hospitals to help diagnose portosystemic vascular abnormalities.

When to Consider Referring

Referral to a specialty practice or teaching hospital should be considered under a variety of circumstances. Any dog or cat that has multiple, persistently elevated liver values and is younger than 18 months of age should have a complete evaluation. Many of the suspected inherited chronic hepatopathies and portosystemic shunts typically manifest at a young age. Breeds with presumed hereditary hepatopathies include West Highland white terrier, Bedlington terrier, Skye terrier, Doberman pinscher, cocker spaniel, and Labrador retriever dogs.

continues

Patients that have jaundice or ascites should be referred for further evaluation. In addition, prolonged anorexia warrants a referral because nutrition is an essential part of the management of many chronic hepatopathies. Coagulopathic patients should be administered vitamin K (0.5 to 1.5 mg/kg SC Q 12 H) and referred for further supportive care and diagnostics.

When Referring is Not an Option

Diagnosis

Treatment of chronic liver disease is most successful when a histopathologic diagnosis is rendered and interpreted. Surgical biopsies can be performed in many clinical settings when a referral hospital is not readily available. Care should be taken to investigate the patient's coagulability before surgery. Various liver biopsy techniques have been reported, but the guillotine method is used most commonly.

Chronic liver diseases often affect multiple parts of the liver to differing degrees; therefore, sampling both relatively normal liver tissue and a nodule or lesion is essential. When submitting tissues for histopathology, comment on the appearance of the liver, the degree of involvement, and the number and size of the nodules. A small piece of liver should be submitted for aerobic and anaerobic bacterial cultures as well as fungal cultures in endemic areas. Another small piece of liver should be frozen and saved for quantitative metal analysis (copper and zinc) or polymerase chain reaction pending the histopathology results.

Therapy

Medical therapy should be tailored to the underlying disease process. S-adenosylmethionine has been shown to be beneficial for many liver diseases, primarily because of its antioxidant effect. It should be given at a dose of 17 to 20 mg/kg PO Q 24 H for 3 weeks and then decreased to every other day. The dose in cats is 200 mg per day. Enteric-coated formulations are preferred and should be given on an empty stomach to increase bioavailability. Silibinin (milk thistle) has become widely available in recent years, but it may not provide a consistent benefit in cases other than *Amanita* mushroom toxicity. The dosage ranges from 7 to 15 mg/kg per day. Ursodeoxycholic acid (ursodiol) is beneficial in patients with inflammatory hepatopathies or in conditions with elevated bile acid concentrations. The dose is 5 to 15 mg/kg orally Q 12 H.

Immunomodulatory therapy should be restricted to patients demonstrating histologic evidence of moderate to severe nonsuppurative inflammation (lymphocytes, plasma cells, and macrophages). Prednisone is commonly used at a dosage of 1 mg/kg orally Q 12 H (dogs) and 2 mg/kg orally Q 12 H (cats). The dose should be tapered approximately 25% to 50% every 2 to 3 weeks until a once-daily or an every-other-day dose is achieved.

Hepatic encephalopathy is a common sequela to chronic liver disease and is characterized by blindness, aggression, stupor, staring into space, and ataxia. More severe manifestations include seizures, dementia, and coma. Management of hepatic encephalopathy is vital for the patient's long-term survival and entails a protein-restricted diet (Hill's l/d [www.hillspet.com] or Royal Canin Hepatic Support [www.royalcanin.com]), small frequent meals, lactulose (0.5 to 1.0 ml/kg PO Q 12 H), and metronidazole (7 to 10 mg/kg PO Q 12 H). The dose of lactulose should be adjusted to achieve soft stools, but care should be taken not to induce diarrhea. Metronidazole can be compounded into 30- to 60-mg capsules for small patients.

Despite severe hepatic injury, a patient can survive for months to years if given proper supportive care. Special attention should be paid to blood glucose concentrations, coagulation profiles, nutritional support, and management of hepatic encephalopathy.

The Referral Process

When referring a patient, clinical history, physical examination findings, response to medical therapies, drug history, and exposure to toxins are vital pieces of information in addition to blood analysis results and radiographs.

See Aids & Resources, back page, for references, contacts, and appendices.