Diagnosis and Treatment of Liver Disease

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There are many aspects of equine hepatic disease which the equine practitioner must be familiar. These include: (1) the causes of equine liver disease, (2) clinical signs associated with liver failure, (3) interpretation of biochemical test of liver disease and failure, (4) ancillary tests used in evaluation and management of equine liver failure, and (5) treatment and prognosis of liver failure.

Causes of Equine Liver Disease

Liver disease is common in horses and foals suffering from septic, hypoxic, neoplastic, or metabolic conditions, but fortunately progression to liver failure is rare. Causes of liver failure include:

Toxic causes:
- pyrrolizidine alkaloid toxicosis (e.g., *Senecio spp., Amsinckia spp*.)
- alsike clover
- Panicum grasses (Kleingrass; fall panicum)
- Although iron has frequently been blamed as a toxic cause of liver failure in horses, it is not well documented.[1]
- mycotoxins – rarely cause liver failure

Infectious causes: Cholangiohepatitis,[2] Tyzzer's disease

Inflammatory, non-infectious causes:
- chronic active hepatitis
- neoplasia
- granulomatous (disease)

Metabolic causes:
- hepatic lipidosis
- hyperammoninemia in horses with gastrointestinal disease[3]
- hyperammoninemia in Morgan foals

Obstructive causes:
- biliary stones
- right dorsal colon displacements
- papillary stricture – foals with duodenal ulcers[4]
- neoplasia
- hepatic torsion
- portal vein thrombosis

Unknown causes:

- Theiler's disease – both plasma/serum associated[5,6] and outbreaks not associated with blood products
- following neonatal isoerthrolysis

The clinical signs of liver failure can vary, depending mostly upon:

1. duration – acute or chronic
2. predominant biliary vs. hepatocellular injury
3. specific causes

Horses with acute liver failure are more likely to have central nervous system signs as their initial and predominant sign. Horses with chronic liver disease leading to failure commonly (but not always) have weight loss and/or photosensitivity as a clinical finding. Gastric impaction and bilateral laryngeal paralysis are two of many complications that may be seen with equine hepatic failure.[7]

Horses with liver disease that is most pronounced in the biliary system are often more jaundiced, more likely to be colicy (due to biliary obstruction and possibly an enlarged liver), have photosensitivity and less likely to have CNS signs.

Specific causes of liver failure can also result in more specific findings. These include fever with cholangiohepatitis, ventral edema with hepatic lipidosis, mild abdominal distention and abnormally tight colonic bands with right displacement of the colon causing biliary obstruction.

Biochemical testing is imperative in the diagnosis of both liver disease and liver failure.[8] Biochemical results can be helpful in narrowing the differential diagnosis for the liver failure and, when evaluated over time, can help predict prognosis. Liver specific enzymes include sorbital dehydrogenase (SDH) and gamma glutamyltransferase (GGT) which respectively reflect hepatocellular and biliary injury. Aspartate aminotransferase (AST) and alkaline phosphatase (AP) also respectively reflect hepatocellular and biliary injury, but are not liver specific. Sorbital dehydrogenase would be expected to increase in the serum with any mild hepatocyte injury (endotoxemia, etc.). It has a short half life (T½) which can be very helpful in determining resolution or progression of the hepatic insult. GGT is released mostly from biliary epithelium and, in the horse, often continues to elevate for a few days (presumably due to biliary hyperplasia) after the hepatic insult is no longer present. HCT and serum iron are frequently high in horses with severe liver disease. Race horses may rarely have mild increases (50-140 IU/L) in GGT without any other evidence of liver disease. This may be due to focal lesions in the biliary system (e.g., parasitic cysts) or drug-induced increases in GGT.

Liver function tests only become abnormal when approximately 60-70% of liver function is lost and these tests include elevations in direct bilirubin, blood ammonia, prothrombin and partial thromboplastin time, serum iron and gamma globulins (with chronic disease).

An increase in direct bilirubin is a highly sensitive and specific marker of liver failure. When the increase in direct bilirubin is 25% or more of the total bilirubin, this is suggestive of a predominant biliary disease. Septic foals with intestinal ileus sometimes have elevations in direct bilirubin with minimal evidence of hepatocellular dysfunction. This may be due to biliary stasis or resorption of the bilirubin from the intestinal tract. Regardless, treatment should focus on the sepsis and intestinal ileus. There may be a decrease in BUN and albumin (with chronic diseases). Serum or plasma bile acids can be an early predictor of liver failure when values rise above 30 umol/L. Serum triglycerides are increased in equines with hepatic lipidosis. In foals with hepatic failure, hypoglycemia is often present, while in adult horses, blood glucose is generally normal or increased.

Ultrasound examination and liver biopsy are the two most commonly used ancillary tests for detecting liver disease. Ultrasound exam may reveal dilated bile ducts, biliary sludge, biliary stones, hepatic fibrosis, hepatomegaly, smaller than normal liver (very subjective), hepatic lipidosis and hepatic masses. Liver biopsy is best performed after the liver has been visualized on ultrasound exam on either the right or left side. Liver biopsies are best used to determine amount of fibrosis, inflammation, predominant location of disease and for culture purposes.[9]

Treatments will vary depending on cause. Supportive treatments for most cases of equine liver failure include crystalloid therapy with supplemental dextrose and potassium. If hepatoencephalopathy is a concern, a low protein (high branch chain-low aromatic amino acid ratio) diet should be fed and neomycin[a] or lactulose[b] should be given per os (via syringe) to decrease enteric ammonia production. Feeds with small amounts of carbohydrates and branch chain amino acid should be given every 2-4 hours. Horses with maniacal behavior due to hepatoencephalopathy can be sedated with small amounts of alpha-2 agonist such that the horse's abnormal behavior is controlled yet maintaining the head in a normal position to prevent worsening of cerebral edema. Mannitol[c] can be used for suspected brain edema in fulminant hepatoencephalopathy.[10] Horses with hepatic disease should be protected from sunlight. Pentoxyfilline[d] should be administered for inflammatory and/or fibrosing liver diseases.[11] S-adenosylmethionine (SAMe)[e] (5 g P.O. S.I.D.) can be administered if oxidative injury is suspected. Intravenously administered acetylcystein[f] has been used with acute fulminant disease, but its value in treating equine hepatic diseases is unknown.

Antibiotics should be administered if septic cholangiohepatitis is a differential diagnosis. Intravenous penicillin[g] (or ampicillin), gentamicin[h] and metronidazole[i] are reasonable choices as is enrofloxacin and metronidazole. Depending upon culture and sensitivity, trimethoprim sulfa may be appropriate. If there is a physical obstruction of the biliary duct, e.g., cholelith or obstruction caused by right colon displacement, surgery is indicated. For chronic acute hepatitis, pentoxyfilline (7.5 mg/kg P.O. q 12 h), SAMe, colchicine[j] (0.03 mg/kg P.O. q 24 h) and possibly steroids (Prednisolone 0.5-1.0 mg/kg P.O. q 24 h)) are used. Ursodeoxycholic acid[k] has been used in the equine, but its safety is not proven. Hepatic lipidosis is best treated with fluids and nutritional support.[12]

Take Home Message

In many cases, a causative reason for liver disease and failure in horses cannot be determined. Some liver diseases, e.g., cholangiohepatitis, Theiler's disease, pyrollizidine alkaloid, alsike clover, panicum grasses, hepatic lipidosis can be easily diagnosed after considering history, biochemical findings, ultrasound examination and liver biopsy if needed. Treatment is often successful for many of the above as long as fibrosis is not prominent.[13]

References and Footnotes

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a. Biosol®, Upjohn, Kalamazoo, MI 49001.
b. Cephulac®, Hoechst-Marion Roussel, Kansas City, MO 64134
c. Mannitol®, Abbott Labs, Chicago, IL 60064.

d. Trental®, Hoechst-Marion Roussel, Kansas City, MO 64134.
e. Zenfonil, Vetoquinol, Tampa, FL 33610.
f. Mucomyst®, Abbott Lab, North Chicago, IL 60064.
g. Pfizerpen®, Rolrig, New York, NY 10017.
h. Gentocin®, Schering-Plough, 07083.
i. Generic Metronidazole, Teva Pharmaceuticals, Sellersville, PA 18960.
j. Colchicine®, Abbott Lab, Chicago, IL 60064.
k. Actigall®, Ciba, Summit, NJ 07901.