Case File: Cholangiohepatitis

Signalment and History
- 10-year-old Thoroughbred gelding
- Weight: 1,221 lb.
- Presenting complaints: Fever, icterus, mild colic

History
Three days prior to presentation at the Veterinary Teaching Hospital, the patient was lethargic, anorectic, febrile (104°F), and had mild, intermittent colic. The referring veterinarian began treatment with flunixin meglumine (1.1 mg/kg IV) and trimethoprim sulfamethoxazole (30 mg/kg PO q 12h). The fever was responsive to flunixin meglumine, but the horse remained lethargic and anorectic. On day of presentation, the horse began to pass dark brown urine. The horse was examined by the referring veterinarian and was found to be icteric and mildly dehydrated. It was treated with 10 mL B-vitamin complex IV and 1 gallon of electrolyte water via nasogastric tube and was referred to the hospital.

The horse had been diagnosed six months prior with duodenitis-proximal jejunitis and appeared to have made a full clinical recovery. Annual vaccination for Eastern, Western, and West Nile encephalitis; tetanus; rhinopneumonitis; and influenza was performed. He was dewormed one month prior to onset of signs, and had been rotationally dewormed every 60 days. He was housed in a stall and run, and fed a mixture of grass and alfalfa hay supplemented with 1 kg pelleted feed twice daily. The horse had not travelled outside of Colorado for the previous two years. No other horses on the premises were affected.

Physical Examination
On presentation, the horse had signs of mild colic (pawing, occasional kicking at its abdomen, bruxism), but was alert and responsive. Rectal temperature was 99.9°F, heart rate was 40 beats per minute, and respiratory rate was 16 breaths per minute with normal thoracic auscultation. Sclerae and oral mucous membranes were icteric (see Figs. 1 and 2). Dehydration was assessed at 5% based on slightly tacky mucous membranes and mildly prolonged skin tent. Normal gastrointestinal borborygmi were present. Rectal and neurologic exams revealed no abnormalities. There were no other significant findings.
Initial Problem List
Problems identified from the history and physical exam included icterus, fever, mild intermittent colic, dehydration, pigmenturia, lethargy, and anorexia.

Case Assessment
In general, differentials for the presence of both icterus and fever include acute hepatitis, chronic active hepatitis, cholelithiasis, hepatic abscesses, immune-mediated hemolytic anemia, and equine piroplasmosis and anaplasmosis. Icterus and fever in combination with mild intermittent colic increase the likelihood of cholangiohepatitis and/or cholelithiasis. Enteroliths or gastric ulceration could also cause similar signs, but fever is typically not present with either condition and icterus is usually mild (anorexia associated).

Initial Diagnostic Testing
1. A complete blood count revealed the presence of neutropenia, lymphopenia, and few echinocytes. Neutropenia with a regenerative left shift and slight toxic changes is most likely consistent with increased margination of, and tissue demand for, neutrophils in response to a septic process. The lymphopenia was mild and most likely represents a stress response. Echinocytes are most often seen as an artifact, but can also be a result of potassium depletion or envenomation.

2. A blood biochemical profile demonstrated moderate elevated activities of SDH and AST, a marked increase in GGT, and severe hyperbilirubinemia. Elevations in SDH and AST indicated mild hepatocellular damage. As the CK level was within normal limits, a hepatic origin of AST elevation was suspected. The marked increase in GGT is consistent with biliary disease. The icteric plasma correlated with the substantially elevated total bilirubin well beyond levels typically associated with fasting hyperbilirubinemia (bilirubin was not fractionated, which is standard practice for the clinical pathology lab at CSU).

3. Bile acid measurement revealed elevated bile acids (BA). While an elevated BA level is highly specific for the presence of liver disease, it is not specific for the type of liver disease. Increased concentration of BA in the blood may occur as a result of shunting or decreased blood flow to the liver, failure of the liver to remove BA from the enterohepatic circulation, failure of the hepatocytes to conjugate BA for excretion, or failure of excretion with subsequent regurgitation of BA into the blood (biliary obstruction).
4. Urinalysis demonstrated the presence of bilirubin in the urine. Bilirubinuria indirectly supported an elevation in conjugated bilirubin.

Based on history, physical examination, and laboratory findings, a presumptive diagnosis of cholangiohepatitis and possibly cholelithiasis was made.

**Additional Diagnostic Testing**

Coagulation times were measured to assess the potential risk of hemorrhage during liver biopsy. Coagulation times may also serve as an assessment of liver function and clotting times may be prolonged in horses with liver failure due to decreased production of soluble coagulation factors (II, V, VII, IX, X).

Abdominal ultrasound examination was performed (see Fig. 3) to examine the liver and biliary morphology and in an attempt to detect choleliths. Furthermore, liver biopsy is best performed after the liver has been visualized on ultrasound exam. The ultrasonographic examination findings were consistent with cholestasis (suggestive of cholangiohepatitis), but could not identify the source of the obstruction. A cholelith could not be ruled out as the biliary tree could not be visualized entirely.

Liver biopsy was performed in the left 8<sup>th</sup> intercostal space and the biopsy site was selected on the basis of ultrasonography. The horse was monitored closely following the biopsy for clinical signs consistent with hemorrhage. Liver biopsy samples were placed in formalin for histopathological examination. Histological assessment of liver biopsy samples are extremely valuable to characterize the disease process (amount of fibrosis, presence and severity of inflammation, localization of disease [i.e., hepatocellular versus biliary]) and to assess prognosis. If indicated, additional samples should be taken for aerobic and anaerobic culture. In this horse’s case, histopathological examination of the liver biopsy samples demonstrated marked bridging fibrosis of portal areas with marked portal biliary hyperplasia with moderated to marked accumulations of neutrophils, lymphocytes, and plasma cells in and around the bile ducts. The marked portal fibrosis that was often centered around bile ducts was suggestive of a cholangiohepatitis.

![Fig. 3: Color flow Doppler examination of the liver; left abdomen. Note the distended bile duct (arrow), immediately dorsal to the blood vessel.](csuvth.colostate.edu)
Case Assessment

Based on history, physical examination, laboratory findings, ultrasound examination and histopathology, a diagnosis of cholangiohepatitis (portal hepatitis) was made.

Pathogenesis: Cholangiohepatitis is associated with biliary stasis and ascending infection of the biliary tree from the small intestine. Infection subsequently spreads to the periportal region. If choleliths are formed, they typically follow infection and biliary stasis. Portal hepatitis may also be due to hematogenous spread of bacteria through portal circulation subsequent to a compromised mucosal barrier. Either scenario is a possible explanation for this horse, as the history indicates a previous duodenitis-proximal jejunitis potentially resulting in small intestinal ileus and compromise of the mucosal barrier.

Etiology: Enteric bacteria such as *E. coli*, *Salmonella sp*, *Aeromonas sp*, and *Citrobacter sp*, are the most common isolates in cases of equine cholangiohepatitis. An *E. coli* was cultured from this horse’s liver.

Case Management

- Fluid therapy: Normosol-R (60 mL/kg/day) supplemented with 2.5% dextrose and 2 mL of B-vitamin complex
- Analgesia, anti-inflammatory therapy: Flunixin meglumine (0.5 mg/kg IV q 12h)
- Antimicrobial therapy: Initially the horse received TMS (30 mg/kg PO q 12h). After liver biopsy culture results became available, TMS was discontinued and enrofloxacin (5 mg/kg IV q 24h) therapy was initiated. Enrofloxacin therapy was continued through normalization of GGT
- Diet: Grass hay (low protein) and water (free choice)
- Monitoring: Blood glucose, PCV, and TP (while on fluid therapy); CBC, biochemistry profile, and bile acids to monitor disease progression/resolution

Case Outcome

On day 3 of treatment, the horse had decreasing icterus and bilirubinemia, improved appetite, and only occasional bruxism. By the end of day 5, the horse was weaned off fluid therapy and flunixin therapy was discontinued. With continued clinical and biochemical improvement, the horse was discharged on day 9. Treatment with enrofloxacin was continued at home.

A CBC and chemistry panel were repeated by the referring veterinarian five days after discharge from the hospital. The CBC revealed no abnormalities. AST had returned to within reference range, although the total bilirubin was still mildly elevated. GGT remained mildly elevated, indicating continued bile duct disease.

Ultrasonography matched clinical improvement with complete resolution of biliary dilation. Clinical pathology showed continued improvement with decreasing GGT and total bilirubin and normal bile acid concentration.

Acknowledgements

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Equine News & Events

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Basic Arthroscopy, August 22

Advanced Arthroscopy, August 23-24

Combined Basic and Advanced Arthroscopy, August 22-24

Standing Arthroscopy of the Equine Stifle Joint, August 25