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Original Research

Hepatic Disease of Horses in the Western United States

Eileen S. Hackett [a,*], David C. Twedt [a], Daniel L. Gustafson [a], Patricia C. Schultheiss [b]

[a] Department of Clinical Sciences, Colorado State University, Fort Collins, CO
[b] Department of Microbiology, Immunology, and Pathology, Colorado State University, Fort Collins, CO

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ABSTRACT

Comprehensive clinical and standardized histologic descriptions of horses with naturally occurring hepatic disease in the western United States have not been performed. The purpose of this study was to describe clinical and histologic features of horses with hepatic disease admitted to a referral hospital in the western United States. A retrospective case review of 92 horses of various breeds residing in the western United States older than 1 year of age admitted between 2000 and 2010 with liver disease confirmed by histopathology was performed. Clinical data were retrieved from the medical record. Slides were reviewed, with a standardized hepatic histologic evaluation by a single board certified veterinary pathologist. Case follow-up information was obtained through phone interview. Sex was evenly distributed, and median age was 10 years (range, 1–31 years). Portal inflammation, portal fibrosis, necrosis, and lipidosis were commonly observed, and the majority of horses had moderate to severe grades of histologic injury. Sixty-eight horses were euthanized, and 24 were discharged from the hospital, with follow-up available for 19 obtained through phone interview. Six horses (32%) were euthanized within 1 year of hospital discharge, three from progression of primary liver disease, and three from colic. Hepatic disease in horses in the western United States often has serious consequences, with severe illness and often death of as a clinical outcome.

1. Introduction

Hepatic disease in horses can have serious consequences. Because signs of liver disease in horses are often nonspecific, hepatic biopsy and histologic evaluation is most often necessary to determine the type of injury and possible etiology of disease [1]. There are multiple reported causes of liver disease in horses [2–8]. The liver is the primary site of detoxification of ingested substances, and ingestion of toxic plants while grazing is a common cause of liver injury [9]. Furthermore, plant-associated hepatic diseases observed in horses may be regionally specific. Much of what is currently known about horses with liver disease is based on five retrospective reports of naturally occurring disease. These studies included groups of 40, 50, 81, and 116 horses in the United Kingdom [4,9–11] and 84 horses evaluated in California [12]. For most clinical reports, histologic descriptions either were not available for all cases, lacked detail, or were not standardized. In those retrospective reports, the mortality rate of liver disease in horses was reported to be 60% [9], 72% [4], 68% [12], and 21% [10]. A recent study from the United Kingdom, that did include standardized histology, reported 67 of 81 horses (83%) survived greater than 6 months from hospital discharge [11].

The objectives of this study were to describe both the clinical and standardized histologic description of horses with hepatic disease admitted to the Colorado State University Veterinary Teaching Hospital and to determine prognostic factors, clinical outcomes, and survival time.

2. Materials and Methods

A computerized search of Colorado State University Veterinary Teaching Hospital records was performed.

* Corresponding author at: Eileen S. Hackett, Department of Clinical Sciences, Colorado State University, Fort Collins, CO 80523.
E-mail address: Eileen.Hackett@colostate.edu (E.S. Hackett).

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Criteria for selection included horses older than 1 year of age admitted between January 1, 2000, and December 31, 2010, with a clinical diagnosis of liver disease determined by the attending clinician (board certified in a veterinary specialty) and confirmed by histopathologic examination. Tissues for histologic examination had been obtained either by surgical biopsy or necropsy examination, which was performed following euthanasia for progression of primary clinical disorder or presumed poor prognosis. Slides were then retrieved from the Colorado State University Veterinary Diagnostic Laboratory repository. Slides of hepatic tissue were reviewed in conjunction with a single board-certified veterinary pathologist (P.C.S.). A standardized data collection sheet was used to record histologic evaluations.

2.1. Clinical and Clinicopathologic Details

Clinical data retrieved from the medical record included signalment, presenting complaint, state of residence, length of illness before admission, and admission clinicopathologic values. The clinicopathologic values recorded included serum bile acids, bilirubin, gamma-glutamyltransferase (GGT), aspartate aminotransferase (AST), sorbitol dehydrogenase (SDH), total white blood cell count, segmented neutrophil count, band neutrophil count, albumin, globulin, packed cell volume, and plasma total protein.

2.2. Histology

Hepatic histologic specimens were observed for the presence or absence of neoplasia, bile stasis (bile lakes variably located in canaliculi, hepatocytes, and sinusoids), and congestion (dilation of sinusoids with erythrocytes). Portal fibrosis, biliary hyperplasia, necrosis, lipidosis, hydropic degeneration, and inflammation were graded within each specimen based on severity as: absent (0), mild (1), moderate (2), or severe (3). Severity scales were generated to promote consistency in observation among specimens similar to previously published reports [11,13]. Periportal fibrosis was graded on amount of fibrous connective tissue present. Mild fibrous expansion of the portal tracts was characteristic of mild portal fibrosis. In moderate portal fibrosis, an increase in fibrous expansion was seen with rare portal-portal septa. Severe portal fibrosis was accompanied by septal fibrosis with multiple connective tissue bridges linking portal tracts. Specimens with portal fibrosis were further classified for the presence or absence of cirrhosis. Cirrhosis was defined as severe bridging portal fibrosis and architectural distortion. Biliary hyperplasia was graded based on the relative quantity of biliary ducts present within portal areas. Cellular necrosis was graded based on quantity of cellular necrosis, independent of location. Lipidosis was graded based on quantity and location of lipid infiltrate within hepatocytes. In specimens with mild lipidosis, microvesicular lipid infiltrate was restricted to the area surrounding the central vein. Moderate lipidosis was characterized by macro- and microvesicular lipid infiltrate extending from the central vein to portal tracts. Severe lipidosis was characterized by prominent hepatocellular ballooning throughout the lobule. Regarding hydropic degeneration, specimens were graded based on quantity of hydropic change, independent of location. Hydropic degeneration was characterized by cell swelling and a cloudy cytoplasmic appearance secondary to intracellular water accumulation. Inflammation was graded based on quantity of inflammatory cells, independent of pattern. Three patterns of inflammation were observed: periportal, random multifocal, and central. A primary histologic diagnosis was assigned to each specimen based on relative severity of concurrent lesions. The histologic severity score for each specimen was defined as the maximum severity of lesion between 0 and 3, recorded among all lesion categories evaluated.

2.3. Follow-up

For horses that survived to hospital discharge, follow-up information was obtained through phone interview. Time and cause of death were recorded for each horse, if available. Follow-up time was reported as number of days from hospital discharge until death or time of owner contact.

2.4. Statistical Analysis

All continuous variables underwent Shapiro–Wilk analysis for normality, and as most variables were not normally distributed, results were presented as median and range. Wilcoxon matched pairs signed rank was used to test relationships among severity of portal fibrosis and biliary hyperplasia and severity of lipidosis and inflammation. A Mann–Whitney test was used to investigate effects of duration of illness on presence of lipidosis and to compare continuous variables between horses that underwent necropsy versus surgical biopsy. Continuous data were analyzed with logistic regression to associate impact of these variables on long-term survival defined as survival >1 year following hospital discharge. Statistical software was used to perform analysis (Graphpad Prism version 5.0a, Graphpad Software, Inc, La Jolla, CA, and Stata, v12.1. College Station, TX, and Stata, v12.1. College Station, TX). Level of significance for all comparisons was $P < .05$.

3. Results

The computerized records search for the period described identified 92 horses with liver disease and concurrent liver histologic examination with slides available for retrieval from the Colorado State University Veterinary Diagnostic Laboratory repository. Of these, histologic specimens were collected from necropsy examination in 68 horses and surgical biopsy specimens in 24 horses.

3.1. Clinical and Clinicopathologic Details

Within the group of 92 horses, sex distribution included 50 males (4 stallions and 46 geldings) and 42 females. Median age was 10 years (range, 1–31 years). Multiple breeds were represented including 42 Quarter Horses, 12 American Paint Horses, 8 Arabians, 8 Thoroughbreds, and 4 Morgans. There were two horses of each of the following breeds: Appaloosa, Warmblood, American Miniature, Percheron, and Pony. There was one horse of each of the following breeds: Icelandic Pony, Spanish Mustang, Clydesdale,