PAPER

Chronic hepatitis in the English springer spaniel: clinical presentation, histological description and outcome

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Context
Canine chronic hepatitis (CH) is a well-recognised disease in the UK. Several breeds of dog have been shown to be predisposed, and CH occurs more commonly in middle-aged and older animals. Known causes include certain viruses and bacteria, toxins and drugs, and breed-associated defects in copper metabolism, although the aetiology of most cases is unknown. There is an increased prevalence of CH in the English springer spaniel (ESS), but a description of the disease and its potential aetiology have not been reported. This study describes the history, clinical signs, clinicopathological abnormalities, diagnostic imaging findings, histological appearance and outcome of ESSs with CH. The study also investigated the role of aetiological factors, including copper and the infectious agents canine adenovirus type 1 (CAV-1), parvovirus, herpesvirus and pathogenic Leptospira species.

Main conclusion
CH occurs in young to middle-aged ESSs, the majority of which present with non-specific clinical signs. All dogs have increased serum liver enzymes. Hepatic histopathology shows prominent hepatocyte necrosis and apoptosis with a diffuse, primarily lymphocytic inflammatory infiltrate and varying degrees of fibrosis. Investigations showed no evidence of currently known canine hepatotropic viruses, pathogenic Leptospira species or copper accumulation. The disease carries a relatively poor prognosis.

Approach
Details of ESSs with a histological diagnosis of CH were obtained from cases presenting to the Department of Veterinary Medicine, University of Cambridge and additional practices. Data included signalment, clinical signs, physical examination findings, results of laboratory tests and imaging. Laboratory data examined included serum biochemistry, complete blood count and coagulation times. Paraffin-embedded tissue was obtained for review and sections were stained with a panel of stains; copper accumulation was scored on rhodamine-stained sections. PCR for CAV-1, parvovirus, herpesvirus and pathogenic Leptospira species was performed on liver tissue.

Results
Sixty-eight cases were identified. The median age at presentation was three years and seven months (range seven months to eight years and five months). There were 48 female and 20 male dogs. Clinical signs at presentation included lethargy (n=63), decreased appetite (n=58), vomiting (n=34), weight loss (n=31), diarrhoea (n=21) and polydipsia (n=21). Five dogs were asymptomatic at presentation and were investigated only for increases in serum liver enzymes.

Alanine aminotransferase and alkaline phosphatase were elevated in all dogs, and bilirubin was increased in 69 per cent of cases. Resting bile acids were increased in 76 per cent of cases, and hypoalbuminaemia and decreased urea were apparent in 38 per cent and 22 per cent of cases, respectively. On ultrasonographic examination, the liver appeared small in 49 dogs and normal in size in 19 dogs. Changes in hepatic parenchymal echogenicity were present in 62 dogs.

Histopathology demonstrated prominent hepatocyte necrosis and apoptosis and an inflammatory cell infiltrate, primarily of lymphocytes; all dogs showed a lesser number of plasma cells. All dogs had evidence of increased fibrous connective tissue on reticulin staining. Thirty-eight dogs had bridging fibrosis, of which 22 had cirrhosis. Positive staining for copper was present in 21 dogs, although this was mild, multifocal and located primarily in the periportal region.

PCR for the identification of CAV-1, parvovirus, herpesvirus and pathogenic Leptospira species was negative in all cases. The dogs were treated with a range of medications and the median survival time of all dogs was 189 days (range one to 1211 days). The median survival time of symptomatic dogs was 171 days (range one to 1211 days) and that of asymptomatic dogs was 203 days (range 66 to 413 days).

Interpretation
This study demonstrates that CH in the ESS occurs in young to middle-aged dogs and that females are predisposed. However, as the age and sex distribution of ESSs in the UK was not known, it is possible that similar predispositions may exist in the population as a whole. Clinical signs at presentation were non-specific, although the majority of dogs were lethargic and had a decreased appetite. Icterus was a common finding on physical examination, and the number of cases with hyperbilirubinaemia is higher than reported in other breeds of dog with CH. Despite the lack of clinical signs in some dogs, all dogs had evidence of fibrosis on histological examination of liver tissue, suggesting that their disease was chronic. This study used a candidate PCR approach to identify potential aetiological infectious agents, and although the results were negative, this does not rule out the involvement of pathogens with divergent sequences from those tested or the presence of a previously undocumented infectious agent. The disease carries a relatively poor prognosis. No standardised treatment regimen was used so it was not possible to assess the effects of treatment on survival.

Significance of findings
Clinicians should be aware that CH occurs in young to middle-aged ESSs in the UK. The majority of dogs have non-specific clinical signs, although some dogs may be asymptomatic. The presence of elevated liver enzymes appears to be the best initial screening test; in addition, two-thirds of dogs in this study had hyperbilirubinaemia. The disease does not appear to be associated with the presence of selected infectious agents or copper accumulation, suggesting that screening for these agents is not necessary. Treatment is symptomatic and supportive but the disease carries a relatively poor prognosis. Further studies are warranted to better understand the possible genetic basis for CH in this breed and to enable breeders to implement schemes to reduce the disease in future generations.
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