Hepatitis in dogs

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Abstract

Liver diseases are a major focus of research in the Faculty of Veterinary Medicine. In a clinical population 1% of the dogs has a form of hepatitis. There are several aspects of canine hepatitis which make comparison with human hepatitis very useful. As a whole, liver diseases and especially different forms of hepatitis in dogs develop highly similar to human hepatitis (fulminant, acute, chronic). This makes dog diseases interesting to study important aspects in the pathogenesis of the disease. We have shown that in humans and dogs identical processes with respect to formation of fibrosis, regeneration, stem cell activation, and oxidative damage occur. In most aspects identical pathogenesis and pathophysiology of canine and human hepatitis make these spontaneous dog diseases ideal models to study the effect of new modes of intervention to stimulate regeneration and reduce or prevent cirrhosis.

Introduction

Hepatitis is a frequent liver disease in dogs. The primary inflammatory disease in dogs affects the parenchyme (hepatitis) which is different from the situation in cats where it is primarily of biliary origin (cholangitis) [1].

Following destruction of hepatic parenchyma (apoptosis or necrosis), an inflammatory reaction, regeneration of parenchyma, fibrosis, and ductular proliferation may occur. When hepatocytic destruction is limited and the reticulin network remains intact, regeneration with complete restitution of the liver structure can occur. Severe parenchymal destruction with extensive loss of hepatocytes often is followed by ductular proliferation. Many of these structures contain both liver-cell and bile-duct elements and may reflect regenerative proliferation of an hepatic stem cell population analogous to oval cells in the rat, or transformation of regenerating hepatocytes into ductular-like structures. These structures generally are most prominent in the periportal areas. Like in man, these are CK7-positive liver progenitor cells. With chronic parenchymal damage or extensive loss of hepatocytes fibrosis and postnecrotic scarring may occur with the formation of intrahe-
patic portovenous shunts; in these cases prolonged regenerative effort will result in regenerative parenchymal nodules.

The diagnosis of hepatitis and its classification (acute, chronic, etc.) is only possible with histology of the liver. The histopathologic diagnosis includes the type, pattern and extent of the necrosis and inflammation, and the possible cause, and in more chronic cases the presence, pattern and extent of fibrosis and regeneration. The activity of the inflammation is defined by the amount of hepatocellular necrosis and inflammation, and the chronicity is determined by the amount of fibrosis.

For veterinary medicine there is a liver consensus group of the World Small Animal Veterinary Association (WSAVA). This group has recently published a consensus for the nomenclature and the clinical and histological diagnostic criteria in the diagnosis of liver diseases [1]. These world standards and the accepted nomenclature has been used in this chapter.

Acute hepatitis in dogs

Etiology

Acute hepatitis can be caused by chemicals (the most familiar are organic solvents such as CCl₄ and phosphorous), viral infection [2] (infectious canine hepatitis due to the Canine Adenovirus 1 [CAV-1]), and mycotoxins (especially aflatoxin B1). Acute hepatitis may also be caused by various toxins, such as mushroom toxins (Amanita) or blue-green algae toxins (Cyanophyceae). Drugs also may cause acute hepatitis in dogs. Drug-induced hepatitis has been reported after treatment with nalidixic acid [3, 4]. Additional forms of drug-induced hepatitis in dogs have been reported in dogs like idiosyncratic drug toxicity (sulfonamides, carprofen, and amiodarone), or dose-dependent drug toxicity (acetaminophen) [5, 6]. CAV-1 is, so far, the only known hepatitis virus in dogs, but the similarity of forms of acute and chronic hepatitis between dogs and man indicates that, like in man, there may be more hepatitis viruses in idiopathic cases of canine hepatitis. There are three forms of CAV-1-caused hepatitis, peracute, acute and chronic.

Hepatitis resulting from sepsis (non-specific reactive hepatitis), and hypoxia (haemolysis, shock) are not discussed here.

Pathogenesis and pathology

Depending on the extent of the liver cell necrosis, intracellular enzymes will be released and bile will leak back into the circulation. In acute hepatitis all of the enzymes (ALT, AST) and bile acids are usually highly elevated. Fever can, but does not always, occur as a result of pyrogens from necrotic tissue and from reduced removal of endotoxins and bacteria from the portal