

INFECTIOUS CANINE HEPATITIS

(*Rubarth disease*; canine adenovirus infection; *hepatitis contagiosa canis*)

ICH has also been referred to as **Rubarth's disease**, after Dr. Carl Sven Rubarth, a veterinarian who first described the disease in the late 1940s.

Infectious Canine Hepatitis (ICH) is an acute, contagious disease of dogs caused by canine **Adenovirus Type-1** (of genus Mast-Adenovirus) and mostly occurs in **dogs that are less than 1 year of age**.

Incubation period is 4-9 days. CAV-1 is shed in saliva, feces, and urine, and transmission occurs through direct dog-to-dog contact or contact with contaminated fomites such as hands, utensils, and clothing. The disease is spread mainly by **excretion of virus in the urine**, and is acquired as a **naso-oral infection**, after causing pharyngitis and tonsillitis as initial signs. Virus may be excreted in the urine for as long as 30 days.

PATHOGENESIS

Initial infection occurs through the **nasopharyngeal, conjunctival, or oropharyngeal route**, and the virus replicates within the **tonsils / tonsillar crypts**, after which it spreads to regional lymph nodes and the bloodstream via lymphatics. Subsequently, infection of hepatocytes and **endothelial cells within a variety of tissues** occurs, such as the lungs, liver, kidneys, spleen, and eye with resultant hemorrhage, necrosis, and inflammation. The virus replicates in the nucleus of host cells, where crystalline arrays of virions form. There is severe condensation and margination of nuclear chromatin, with inclusion body formation. Within the liver, the virus initially infects Kupffer's cells and subsequently spreads to hepatocytes. Chronic kidney lesions and **corneal clouding ("blue eye")** result from immune-complex reactions following recovery from acute disease.

SIGNS

The disease affects mainly young dogs of around 1 yr age. Clinical signs generally occur after an incubation period of 4 to 9 days, although many dogs probably show no signs of illness. **Three overlapping disease syndromes** have been described.

The first is **Peracute Disease** with circulatory collapse, coma, and death within 24 to 48 hours.

The second, most commonly described syndrome is **Acute Disease**, where dogs either recover or die within a 2-week period.

The third is a more **Chronic Form** that occurs in dogs with partial immunity, and **death is due to hepatic failure**, weeks (subacute disease) or months (chronic infection) after initial infection.

The **ACUTE DISEASE** is variably characterized by the presence of fever, tonsillitis, conjunctivitis, inappetence, lethargy, weakness, polydipsia, vomiting, diarrhea, hematemesis, abdominal pain expressed by moaning sounds, tachypnea, and icterus.

The disease begins with high fever, apathy (lack of interest, listlessness), followed by anorexia (loss of appetite), lethargy, and polydipsia, intense thirst. Fever (104° F) at

onset, but may fall suddenly to subnormal levels as death approaches. Vomiting & bloody diarrhoea containing frank blood or melena is commonly seen with abdominal pain. Widespread petechial and ecchymotic hemorrhages and hematuria can be seen. The mucous membranes appear **anaemic**, and slight **icteric**. Tonsils are reddened and swollen, and **Tonsillitis** is observed as initial diagnosis.

Conjunctivitis and / or Corneal oedema with diffuse, **opaque cloudiness of the cornea** ("blue eye") occurs in the 1-3 week of illness and results from replication of virus within corneal endothelial cells.

Rarely, neurologic signs such as hysterical seizures, clonic spasms of the extremities and neck, paralysis of the hindquarters and extreme agitation, ataxia, circling, apparent blindness, head pressing, and nystagmus have been reported in association with CAV-1 encephalitis.

Infection of the glomerular endothelium is followed by tubular infection, development of interstitial nephritis, and viruria. Viral shedding in the urine can occur for up **to 6 to 9 months** after infection. In the urine, albumin may be present in significant amounts.

Other clinico-pathological findings include **neutropaenia** and **lymphopaenia** during the course, with Lymphocytosis during recovery; prolonged bleeding and coagulation times; and elevation of SGOT and SGPT.

LESIONS

The virus has an **affinity for parenchymal, Kupffer cells & Endothelial cells of the liver**. Affected cells develop **specific large basophilic INTRANUCLEAR inclusion bodies**, and become necrotic. **Reticulo-endothelial cells** and sometimes other cells, such as **renal tubular epithelium**, may also be affected.

Gross pathologic findings in dogs with ICH include **blood-tinged ascites** or hemoabdomen; a slightly enlarged, **congested or mottled liver**; mild splenomegaly; enlarged, congested, and **swollen lymph nodes**; and **fibrin deposition on the surface of abdominal viscera** resulting from endothelial damage and loss of coagulation factors of hepatic origin. **Wall of Gall bladder** is oedematous and thickened.

The most characteristic microscopic lesion is **focal hepatocellular necrosis**, particularly in the **periportal region** and intranuclear inclusion bodies within **Endothelial Cells, Kupffer's cells and hepatocytes**.

Hepatocytes become acidophilic, lose their outline, nuclei is not visible, and ultimately disappear, to be replaced by **dilated sinusoids**. **INTRANUCLEAR Inclusion Bodies** are prominent, usually in cells peripheral/ adjacent to areas of necrosis. The inclusion body, **almost fills the nucleus**, having a rather indistinct outline, and takes basophilic colour in sections with H & E. Recovery is followed by complete regeneration of the liver.

Intranuclear inclusion bodies also occur in the **reticulo-endothelial cells** and **endothelial cells of the spleen**. In the kidney, intranuclear inclusions may be found in endothelial cells of the glomerular tufts.

The lesions in the brain are directly related to the changes in the capillary endothelium. The endothelial cells may contain intranuclear inclusions. Many of the capillaries are surrounded by a small collar of haemorrhage.

DIAGNOSIS

Diagnosis in the living animal is difficult because of the non-specific nature of the symptoms. However.

- Microscopic demonstration of intranuclear inclusion bodies in surgically removed tonsils, or liver biopsy specimens, confirms the presumptive clinical diagnosis.
- The diagnosis can also be confirmed by virus isolation and immunofluorescence.
- Differential Diagnosis: from Canine Distemper, Leptospirosis