Infectious canine hepatitis – it's still out there

Michael Hardcastle, Veterinary Anatomic Pathologist at Gribbles Veterinary, Auckland, discusses the prevalence and diagnosis of ICH, and its persistence despite the availability of vaccination.

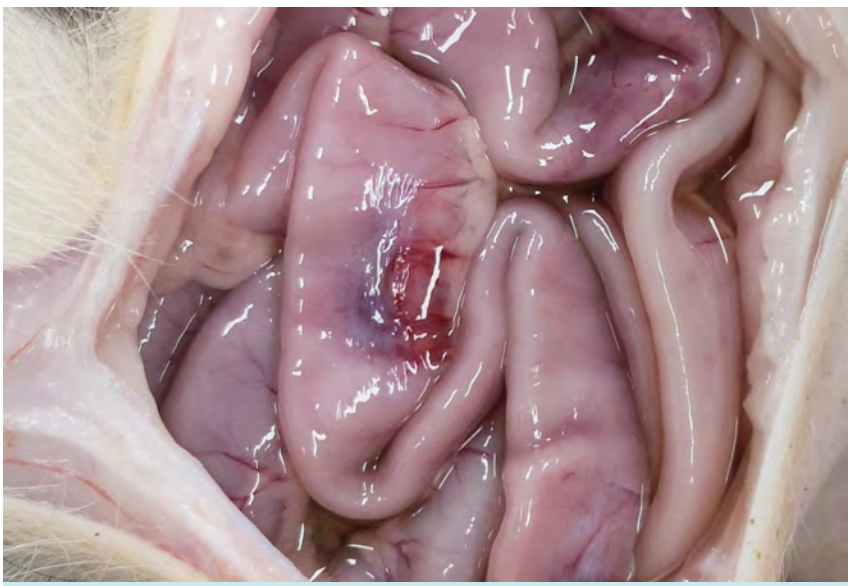

FIGURE 1: Intestinal serosal haemorrhage and a peritoneal effusion.

DOGS AND CATS in New Zealand are fortunate to be relatively free of contagious diseases, with many viral diseases preventable or minimised by vaccination. Disease due to canine parvovirus-2 is probably the most significant of these. However, our laboratories occasionally diagnose other viral diseases, and it is worth highlighting that these organisms are still in circulation despite the availability of vaccination.

A one-month-old, cross-bred puppy from north Auckland presented collapsed, with cold extremities and a temperature of 35.6°C. They had reportedly been clinically normal the previous evening. An in-house haemogram showed anaemia with a haematocrit of 21.1% (reference interval 37.3–61.7) and possible thrombocytopenia (26K/µL, reference interval 148–484 with a caution to check the blood film). Biochemistry showed increased alanine transaminase (357U/L, reference interval 8–75). The puppy died despite supportive care. At postmortem examination, there were areas of intestinal serosal haemorrhage and a serous peritoneal effusion (Figure 1), a few strands of fibrin adherent to the liver and pancreatic oedema.

Two other puppies from the same litter died suddenly. In-house laboratory testing of the three surviving litter mates showed variable haematocrits (28.6%, 30.8% and 22.8%) but no thrombocytopenia. Their mother was a rescue dog with neonatal puppies when adopted; she had no known vaccination history.

A range of fixed tissues submitted from the postmortem of the first puppy was processed for histopathology. It showed a range of lesions; the most significant were prominent intranuclear inclusion bodies in most hepatocytes and some endothelial cells, often filling the nucleus (Figure 2, white arrow), along with multifocal necrosis of hepatocytes (Figure 2, blue arrow). Intranuclear inclusion bodies were also seen in macrophages or endothelial cells of the bone marrow, spleen, lymph node, lung, kidney, heart and small intestine, where they were associated with mesenteric vasculitis and haemorrhage. Other findings included lymphoid necrosis/apoptosis in the spleen and lymph nodes consistent with a viral infection.

The first puppy was diagnosed as a case of infectious canine hepatitis (ICH), caused by canine adenovirus-1 (CAV-1). In a puppy with haemorrhagic lesions, canine herpesvirus-1 could also have been considered; however, it tends to affect younger puppies than this one, mainly presents with renal haemorrhages, has fewer and smaller inclusions and does not target hepatocytes.

Clinically, diagnostic options for ICH in New Zealand are limited as serology, polymerase chain reaction or other tests are not readily available through commercial diagnostic laboratories or the Ministry for Primary Industries' Animal Health Laboratory, according to Laboratory Technical Officer for Diagnostic and Surveillance Services Danni Thornton. Therefore the diagnosis is typically based on a consistent history, clinical signs, antemortem clinical

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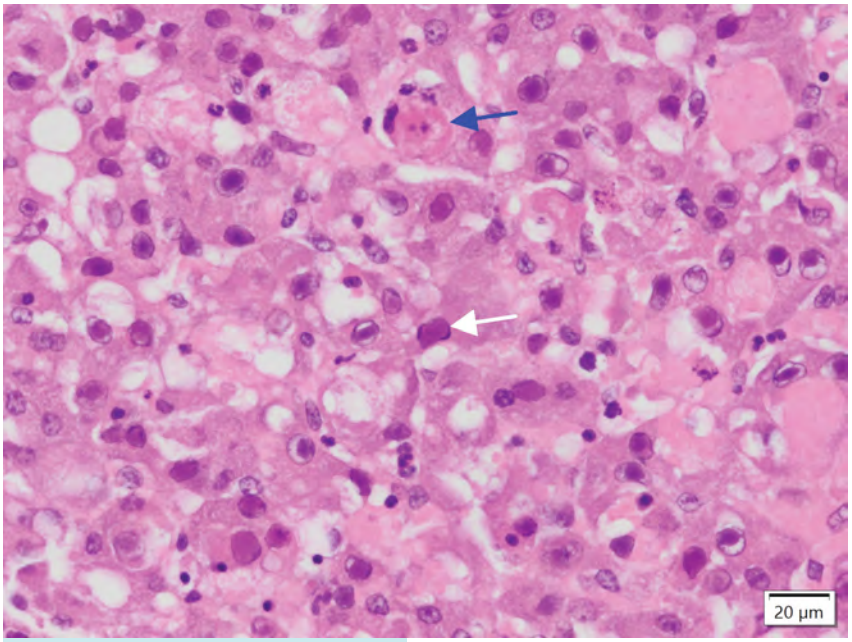

FIGURE 2: Histopathology showing prominent intranuclear inclusion bodies in most hepatocytes and in some some endothelial cells (white arrow); multifocal necrosis of hepatocytes (blue arrow).

pathology and postmortem examination with histopathology.

ICH is spread by direct or indirect contact with infected urine, faeces, saliva and respiratory secretions (Hornsey et al., 2019). It causes viraemia after oronasal exposure and initial localisation in the tonsils. It mainly affects young dogs and tends to be seen sporadically or as small outbreaks in kennels. The severity of disease seems to be dependent on neutralising antibody titre (Greene, 2012). It can present as sudden death in peracute infections. In less acute diseases, clinical signs may range from vomiting, melaena, fever, tachypnoea, tachycardia, abdominal pain, hepatomegaly, non-specific nervous signs, mucosal petechiae, pallor and mild icterus to mild pharyngitis, tonsillitis, coughing (pneumonia), cervical lymphadenomegaly and dependent oedema, or inapparent infection. Convalescing dogs may develop corneal oedema ('blue eye'), considered a hypersensitivity reaction to immune-complex deposition. In animals who survive, it seems that the liver can regenerate rapidly (Cullen and Stalker, 2016), although some sources suggest that partially immune dogs may develop chronic hepatitis (Greene, 2012).

Clinicopathologic findings include leukopaenia with lymphopaenia and neutropaenia, progressing to neutrophilia and lymphocytosis during recovery. Thrombocytopenia is common and clotting times are variably prolonged. Liver enzymes (alanine transaminase, alkaline phosphatase and aspartate transaminase) increase proportionate to the degree of hepatic necrosis, but hyperbilirubinaemia is uncommon. Proteinuria and hypoglycaemia may be identified. Hepatocellular intranuclear inclusions might be found antemortem on cytology or in liver biopsies (Greene, 2012).

At postmortem there may be lymph node oedema or haemorrhage and blotchy/'paint brush' haemorrhages on the gastrointestinal tract or serosa, or haemorrhage in other organs such as the kidney, lung, bone and brain. There may be slight icterus. The liver may be large and friable; there may be ascites with fibrin strands; and the gall bladder may also be enlarged and oedematous. Haemorrhages are considered to be largely due to a consumptive coagulopathy, since endothelial damage initiates the clotting cascade (Cullen and Stalker, 2016).

Treatment options are supportive and include fluid therapy (crystalloids, plasma or whole blood), glucose infusions and strategies to reduce ammonia production (eg, enemas) (Greene, 2012).

ICH is seen sporadically in New Zealand, with cases reported anecdotally every few years and occasionally mentioned in *Surveillance* magazine (Anonymous, 2010). It is interesting that it persists in New Zealand despite our lack of wild carnivores (overseas, reservoirs for ICH and other infectious diseases such as canine distemper). According to Massey University Associate Professor Nick Cave, possible reservoir species in New Zealand include mustelids (Nick Cave, personal communication, July 2020). However, ICH frequently causes subclinical infections, is shed for months in urine and is robust in the environment, resisting disinfectants (Greene, 2012). This makes its persistence in the New Zealand canine population, despite the availability of vaccination, probably not surprising – especially since the prevalence of vaccination is unknown but certainly less than 100%. VS

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