APPROACHES TO DIAGNOSIS AND TREATMENT OF HEPATIC DISEASE

Author : Rachel Sant

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Rachel Sant examines the signs of liver disease in cats and considers some of the diagnostic tools available before suggesting treatment options

Summary

Feline liver disease is not uncommon and several clinical syndromes are recognised. Clinical signs are often non-specific, although ascites, jaundice, hepatic encephalopathy and coagulopathies may be seen, which are more localisable to the liver. Blood sampling may reveal elevated liver enzymes, anaemia of chronic disease and changes such as low urea, albumin and glucose can be seen in cases of liver dysfunction. Ultrasound is a helpful tool, but liver biopsy is generally required for definitive diagnosis. Treatment involves managing the specific disease process if one is discovered, as well as supportive treatment such as nutrition, anti-oxidants and ursodeoxycholic acid.

Key words

liver, biopsy, cholangitis complex, hepatic lipidosis

THE liver has a large functional reserve, so often clinical signs of liver disease are not seen until late in the disease process. It also has a large regenerative capacity, meaning the prognosis for full recovery is often good if diseases are treated early, even in severe disease.

The liver has a large range of functions, including carbohydrate, fat and protein metabolism and storage, synthesis of coagulation factors, hormone metabolism, detoxification of drugs and toxins, and bile acid synthesis and storage.

Cats have different anatomy and biochemical make-up to dogs, particularly with regard to their liver.

In cats, the bile duct joins the (generally) single pancreatic duct, thereby allowing reflux and mixing of gastrointestinal (GI) contents with bile and pancreatic secretions, in comparison to the dog, which has two separate ducts. Cats have a relative deficiency of the enzyme glucuronyl transferase, which means they have a reduced capacity to metabolise certain toxins and drugs. Cats also have a high activity of protein-catabolising enzymes and, therefore, a high protein requirement, which cannot be down-regulated quickly, even in conditions of starvation or illness.

When considering liver enzyme activities, it must be remembered cats do not have a steroid-induced isoenzyme of alkaline phosphatase (AlkP), so an increased level is more significant than in the dog. AlkP and alanine aminotransferase (ALT) also have a short half-life in the cat so elevations can indicate more severe damage. However, cats are much less likely than dogs to develop cirrhosis of the liver.

Presentation

Feline liver disease is not uncommon and can present in a variety of ways. The cholangitis complex (previously called cholangiohepatitis) is the most common, but cats can also have neoplasia (primary or secondary), hepatic lipidosis, portosystemic shunt or toxic hepatopathies. The liver may also be damaged secondarily to other diseases, for example, metastatic neoplasia, feline infectious peritonitis or toxoplasmosis (Table 1).

Often, cats with liver disease have a vague, non-specific history, with signs such as anorexia, weight loss, poor weight gain in young animals (Figure 1), fever, polyuria/polydipsia (PUPD) and vomiting or diarrhoea, but may sometimes have more specific signs that help localise the problem to the liver, such as jaundice, ascites or hepatic encephalopathy. Many animals will only have their liver disease diagnosed after blood sampling. The severity of clinical signs does not always reflect the degree of liver damage and the resultant prognosis.

Jaundice (or icterus) is the yellow discolouration of serum or tissues caused by an increase in bile pigments. The normal liver can take up and excrete a large amount of bilirubin, so to cause jaundice there must be either an increase in production (from the breakdown of red blood cells or myoglobin) or impairment in bile handling or excretion. Not all cats with liver damage will be jaundiced (fewer than 50 per cent).

Jaundice may be prehepatic, hepatic or posthepatic. Prehepatic jaundice is caused by massive red

cell breakdown, for example immune-mediated haemolytic anaemia. Hepatic jaundice is caused by any liver disease that reduces the uptake of bilirubin, and posthepatic jaundice is caused by blockage or rupture of the bile duct.

In any cat with possible liver disease it is important to take a full history, including any drug administration and access to toxins. Consistent clinical signs may prompt further testing, starting with blood sampling and urinalysis.

Biochemical changes may include elevated liver enzymes or changes relating to liver failure, such as low glucose, albumin, urea and cholesterol. Bile acid stimulation testing can be used to challenge the liver's ability to take up bile acids, which is reduced when liver function wanes and this is particularly useful for the diagnosis of portosystemic shunts.

Complete blood count may reveal a low PCV in cases of prehepatic jaundice, but more commonly will reveal anaemia of chronic disease (mild normocytic, normochromic anaemia) or sometimes a microcytic (iron deficiency) anaemia. Platelet count should be evaluated as this is relevant if you are considering biopsying the liver. Clotting times can be prolonged in liver disease so may also be measured, and certainly should be performed prior to most forms of liver biopsy.

Urinalysis can be unremarkable, but a low urine specific gravity is often associated with liver disease. Bilirubinuria may also be seen. Cats have a higher renal tubular absorptive capacity for bilirubin than dogs, so bilirubinuria is always pathologic.

Once liver disease is suspected, further testing may be carried out. If there is ascites then analysis of the effusion (protein level, cell count, cytology, culture) can be helpful to categorise the effusion into transudate, modified transudate, exudate and so on. Radiography is rarely helpful in liver disease although radio-opaque choleliths can be seen on occasion, and the liver size can be ascertained. Radiography is unhelpful in cats with ascites. In these cases, ultrasound is a more helpful tool, which can be used to reveal nodules, changes in liver echogenicity and structure, bile duct and gall bladder changes and can also be used to direct needles for bile aspiration and/or fine needle aspiration biopsies if desired. Small volume effusions that may not be clinically recognised can also be diagnosed and sampled in this way.

Liver biopsy may be indicated in some situations – for example, cats with persistent elevation of liver enzymes, multifocal hepatic lesions on ultrasound or systemic disease with liver involvement. It is often unhelpful if the liver is only involved in a secondary capacity, or if surgery will be required anyway, for example, portosystemic shunt (when a biopsy is likely to be taken at the time of definitive surgery). Biopsies may be taken by fineneedle aspirate (FNA), Tru-Cut, laparoscopy or laparotomy. Before biopsying the liver it is sensible to check the platelet count and to carry out clotting times – prothrombin time (PT) and activated partial thromboplastin time (aPTT).

FNA is only suitable for obtaining cytology samples (which do not always correlate with

histopathological results). It is a relatively safe biopsy technique, especially when carried out under ultrasound guidance, although moderate to severe bleeding is still possible. It is helpful for diagnosis of hepatic lipidosis or lymphoma, but less helpful in other conditions where the small size of the sample can limit the information obtained.

Tru-Cut biopsies should be carried out under sedation or anaesthesia and under ultrasound guidance. These can be more helpful for assessing liver architecture as they are larger samples, but as the samples are still relatively small, multi ple samples must be obtained from all representative areas of the liver.

Laparoscopic biopsies, or those taken at laparotomy, are generally larger samples so are more invasive, but are more representative of the pathologic changes present. Samples should also be taken from other abdominal organs – for example, small intestine or lymph node – during this procedure. There is a risk of haemorrhage with any liver biopsy, although direct visualisation during laparotomy means this can be addressed at the time.

Biopsies should be sent for histological review, but it may also be helpful to take impression smears at the time of sampling and also to perform bacterial culture of a biopsy. If possible, bile should also be aspirated when biopsying the liver and this should be sent for bacterial culture.

Cholangitis complex

Cholangitis has been divided in two main forms – acute neutrophilic or chronic lymphocytic – but this may be artificial and the diseases may be more of a continuum.

Neutrophilic cholangitis can affect cats of any age, producing an acute disease causing fever, anorexia, vomiting and jaundice. Blood sampling may show elevated liver enzymes, increased bilirubin, neutrophilia and a left shift. Abdominal ultrasound often reveals a thickened gall bladder wall and distended bile duct. Bile “sludge” or choleliths may be visualised in some cases. Liver biopsy shows a neutrophilic infiltration in the lumen and/or epithelium of bile ducts which can extend into the liver parenchyma. A more mixed inflammatory infiltrate can be seen in more chronic cases.

This variety of cholangitis is usually caused by ascending infection from the GI tract, such as *Escherichia coli* or *Enterococcus*. Bile culture is recommended. Cats need a long course (four to six weeks) of suitable antibiotics plus supportive treatment and the prognosis is good if treated early.

Concurrent bowel and pancreatic disease is common and needs to be addressed in addition.

Lymphocytic cholangitis is more often seen in younger cats (commonly Persians) than those with neutrophilic cholangitis. Polyphagia may be seen and cats commonly have a long history of mild

disease, in comparison to acute cholangitis, where cats present acutely and often quite unwell. A proportion of these cases have high globulins and a high protein abdominal effusion, which may be difficult to distinguish from feline infectious peritonitis.

Ultrasound of the liver may reveal patchy echogenicity of the liver parenchyma and the liver may be enlarged on radiography or on palpation.

Liver biopsy shows lymphocytes in portal areas, with portal fibrosis and sometimes loss of bile ducts. The aetiology is unknown, but postulated to either be a chronic bacterial infection (progression of acute neutrophilic cholangitis) or of immune-mediated origin. Treatment is with antibiotics and immunosuppressive doses of prednisolone, with chlorambucil or other immunosuppressives being used in some cases.

Other supportive treatments – such as ursodeoxycholic acid or S-adenosylmethionine (see later) – may be used in addition. Cats often need lifelong therapy, although therapy can be tapered and stopped in some cases.

Hepatic lipidosis

Hepatic lipidosis (HL) may be primary (idiopathic disease, common in the US) or secondary to underlying diseases such as pancreatitis, neoplasia or diabetes.

HL is a catabolic state leading to mobilisation of peripheral fat, causing fat deposition in hepatocytes, hepatocyte swelling and acute loss of hepatic function. Cats may be markedly jaundiced and depressed. Liver enzymes are elevated, although GGT often remains normal or near normal, which is often a helpful diagnostic clue. Clotting times are prolonged.

Ultrasound shows hepatomegaly and hyperechoic liver parenchyma. FNAs show hepatocytes swollen with lipid. Nutrition is the mainstay of treatment – cats often need feeding tubes, possibly a nasogastric tube to start with as they may not be well enough to have an anaesthetic to place an oesophagostomy tube (Figure 2) at first, high protein diet, intravenous fluids and supportive treatment.

Treatment of liver disease

If a specific disease process is found then the cause should be eliminated and any drugs that may harm the liver further should be avoided.

Neutrophilic cholangitis should be treated with a long course of antibiotics, preferably chosen according to bile or tissue culture or with fourquadrant cover.

Suitable antibiotics include amoxicillin plus a fluoroquinolone and clindamycin or low dose metronidazole. Immunosuppression, such as prednisolone or chlorambucil, may be used in cases

of lymphocytic cholangitis.

Ursodeoxycholic acid is often used in liver disease as it improves bile flow and displaces toxic bile acids so is protective to hepatocytes. S-adenosylmethionine (SAMe) is an anti-oxidant, anti-inflammatory and membrane stabiliser, which also helps to support the liver.

Other drugs may be required in certain situations, for example, metoclopramide/ maropitant in cases of vomiting or nausea; pain relief in cases during/after surgery; vitamin K in cases with prolonged clotting times; and vitamin B_{12} in cats with concurrent intestinal disease who are inappetent. Nutritional support should also be addressed, including consideration of suitable feeding tubes.

References

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