Liver diseases in cats - still the big 4?

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Introduction

In liver diseases, the following 4 groups should be differentiated:

1. diseases of the vessels (vascular)
2. diseases of the bile ducts (biliary)
3. diseases of the parenchyma (parenchymatous)
4. neoplastic diseases (neoplastic)

In cats, congenital as well as acquired portosystemic shunts are much rarer than in dogs. There are 4 diseases that make up the majority of clinically relevant feline hepatopathies:

1. hepatic lipidosis
2. cholangitis (neutrophilic or lymphocytic)
3. lymphoma
4. FIP

Since both lymphoma and FIP are systemic diseases and in view of the time, this lecture will focus mainly on hepatic lipidosis and cholangitis.

Hepatic lipidosis

Hepatic lipidosis (HL) is the most common liver disease in cats (1). It is caused by a catabolic metabolism with excessive lipid accumulation in the liver and can lead to severe liver dysfunction and death. The distinction between primary (idiopathic) and secondary (to diabetes mellitus, hyperthyroidism, pancreatitis, IBD, alimentary lymphoma, cholangitis, CKD, FLUTD, neoplasia, etc.) is very important because possible additional diseases strongly influence the therapeutic plan and the prognosis. According to a recent study (2), gastrointestinal problems, pancreatitis, cholangitis and stress are the most important triggers of a secondary HL. Early detection and aggressive treatment are very important for the prognosis of this disease. Prognosis is good with timely diagnosis and aggressive therapy; otherwise mortality is very high (38% in (2)).

Most cats with HL are overweight, medium to old, and have a history of anorexia, although the trigger of anorexia is not always known. The most common anamnestic complaints are anorexia, depression, weakness, vomiting, salivation, diarrhoea or constipation, and weight loss. Some of these signs may also indicate hepatic encephalopathy. Dehydration, poor hair coat, jaundice, hepatomegaly, and ventroflexion of the neck are often observed during clinical examination.

The diagnosis has two purposes: to prove the lipidosis and to recognize and treat underlying problems. The chemistry panel may show signs of cholestasis, often with AP, ALAT and ASAT elevated. Bilirubin is often elevated, whereas urea is normal or even below reference range. Compared to other liver problems, GGT is rarely elevated. Decreased electrolytes and albumin as well as elevated cholesterol and glucose levels can also be observed. To rule out underlying problems, at least thyroid hormones, FeLV / FIV, fPLI, chest x-rays as well as an abdominal ultrasound should be performed. The liver is usually diffusely hyperechoic in relation to the falciform fat and may be slightly or moderately enlarged. Ultrasound guided fine needle aspiration followed by cytology is often sufficient to establish a strong suspicion of HL (at least 50 % of hepatocytes are vacuolated).

The therapy of HL has the following goals:

- early, adequate nutrition to end the catabolic metabolism (3)
- adapted fluid therapy including potassium substitution
- prevent / treat complications (vomiting, hepatic encephalopathy, bleeding, …)

For almost all cats, a feeding tube has to be placed (usually an oesophageal tube, possibly a naso-oesophageal tube (short-term) or a PEG tube (long-term)). The diet should contain high quality proteins and fats, with protein reduced diets when signs of hepatic encephalopathy are present. Depending on the preference of the clinician, various vitamins, antioxidants and other supplements are added. However, for most lack clinical studies demonstrating positive effects. Generally well accepted are supplementation with cobalamin (250-500 µg SC 1x per week), vitamin K1 (0.5-1.5 mg / kg SC q12h 3-5x initial) and S-adenosyl-methionine (SAMe) (35-60 mg / kg q12-24h initial, then 20 mg / kg q24h). Supplementation with taurine (250-500 mg / day) and arginine (250 mg / 100 kcal) is often recommended. Rarely needed are vitamin E (10-100 IU / kg q12h PO) and L-carnitine (250-500 mg / cat / day). Ursodeoxycholic acid with its choleretic and anti-inflammatory effects may be helpful and indicated if there is no obvious obstruction of the bile ducts (10-15 mg / kg q24h PO). In addition, the electrolytes must be controlled and possibly supplemented in the fluids (KCl, K-phosphate, Na-phosphate). Antibiotics and glucocorticoids are not recommended.

Cholangitis

Cholangitis (formerly cholangiohepatitis) is the second most common liver disease in cats after HL. Different classification systems exist based on the predominant inflammatory cells (neutrophils, lymphocytes), the proliferation of the bile ducts, as well as the occurrence of fibrosis. The WSAVA Liver Standardization Group defined the following major forms of cholangitis in the cat in 2006 (4; the first 2 forms prevail):

1. neutrophilic cholangitis
2. lymphocytic cholangitis
3. cholangitis associated with liver flukes
4. lymphocytic portal hepatitis

Table 1: Comparison between neutrophilic and lymphocytic cholangitis

There are experts who think that lymphocytic cholangitis is a chronic stage of neutrophilic cholangitis. There is no evidence, however, and the following facts speak against it:

- cats with lymphocytic cholangitis rarely have a history of liver disease before
- cats with neutrophilic cholangitis have no increased risk of lymphocytic cholangitis afterwards
- inflammatory infiltrates in the bile ducts present only in the neutrophilic form
- pancreatitis (+/- IBD, triaditis) often associated with neutrophilic cholangitis but rarely with lymphocytic form
- clear evidence of ascending infection only in neutrophilic cholangitis

A new study from the UK suggests that neutrophilic cholangitis is much more common than the lymphocytic form (5). This is good for the cats, because patients with neutrophilic cholangitis can be largely cured with adequate therapy, whereas the lymphocytic form focuses on successful long-term management (6). For this purpose, prednisolone appears to be more important and potent than ursodeoxycholic acid (7). In addition to the clinic, laboratory and cytology / biopsies, a bacterial culture of bile +/- parenchyma is often indicated to differentiate between the two forms. Ultrasound-guided percutaneous cholecystotomy usually seems to be without complications, whereby in neutrophilic cholangitis bacterial infestation can very often be detected (mostly E. coli, Enterococcus sp.; 8). Fluorescence in situ hybridization (FISH) in bile and parenchyma is even more sensitive than classical culture (8), but is not (yet?) available for routine diagnostics.

Literature

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Table 1: Comparison between neutrophilic and lymphocytic cholangitis

	lymphocytic cholangitis	**neutrophilic cholangitis**
predisposition	younger cats, Persians	acute: young-middle-aged, mostly ♂ chronic: middle-aged
clinic	often relatively unremarkable	mostly lethargic / ill
appetite	possibly polyphagia	mostly anorectic
jaundice	**+/-**	**+**
ascites	**+/-**	**-**
lymphadenopathy	**+/-**	**-**
hepatomegaly	**+/-**	**-**
laboratory changes		
neutrophilia	**+/-**	+ (with left shift)
lymphopenia	**+/-**	**-**
ALT ↑	**+**	**+**
ALP ↑	**+**	**+**
bilirubin ↑	**+**	**+**
bile acids ↑	**+/-**	**+**
globulins ↑	**+**	**-**
ultrasound	+/- hyperechogenic liver	+/- hyperechogenic liver biliary stasis
pathology		
cellular infiltrate	primarily lymphocytes	primarily neutrophils
distribution lesions	mainly portal	mainly bile ducts
fibrosis	variable, possibly extensive	-
other diseases	(pancreatitis?)	pancreatitis, IBD
therapy	immunosuppression (mainly glucocorticoids)	antibiotics choleretics