

PROBLEM #1 - ICTERUS:

SO: This animal is profoundly icteric. Icterus is yellow discoloration of tissue due to hyperbilirubinemia. The bilirubin is mixed, both conjugated (direct) and unconjugated, although mostly conjugated.

A: Icterus occurs due to 3 general mechanisms: (1) increased production of bilirubin due to hemolysis (RBC destruction due to intravascular & extravascular hemolysis), (2) primary liver disease causing decreased uptake, conjugation and/or excretion of bilirubin, and (3) post-hepatic (obstruction of the common bile duct due to an intraluminal or extraluminal lesion).

In this case, hemolysis seems unlikely as the anemia is very mild and not in proportion to the severe increase in bilirubin. A Coomb's test was also negative. The normochromic, normocytic, non-regenerative nature of the anemia in this case is more compatible with an anemia of chronic disease rather than hemolysis.

On the other hand, there is good evidence of liver disease. The marked increase in liver enzymes could result from either primary liver disease or biliary obstruction. At this stage I cannot differentiate which.

DfDx: Feline Hepatic Lipidosis is the most common cause of icterus in cats and should be ruled out in this case. FHL results from excessive mobilization of lipid from peripheral fat stores such that it exceeds the ability of the hepatocytes to process and excrete it. The marked swelling due to accumulation of lipid in hepatocytes results in intrahepatic cholestasis (compression of bile canaliculi) and hepatocellular damage. This cat's period of anorexia is compatible with FHL, although an underlying disease producing the anorexia should be ruled out. (FHL can be secondary to pancreatitis, cholangiohepatitis, IBD and possibly a host of other diseases.) The marked elevation in liver enzymes is also compatible with FHL.

Feline Cholangitis – Cholangiohepatitis Syndrome (CCHS) is the second most common cause of icterus in cats. This condition is most commonly characterized by non-suppurative inflammation and fibrosis in and around intrahepatic bile ducts. The gall bladder and common bile duct are sometimes affected as well. The result is cholestasis which can result in elevation in both AP and ALT/AST. In other cases, CCHS is suppurative in nature and thought to represent an ascending infection from the small intestine.

Pancreatitis is both an underlying cause of FHL and a potential cause of hepatitis and/or cholangitis. In cats, the pancreatic duct opens into the common bile duct so that processes affecting the pancreas also commonly affect the hepatobiliary system. Moreover, the liver is located in close proximity to the pancreas. The release and activation of digestive enzymes in and around the pancreas can also affect the liver, causing hepatocellular injury.

Although it is not as common in cats as in dogs, extrahepatic bile duct obstruction (EHBO) could produce the clinical problems in this animal. Possible obstructive lesions include choleliths, tumors arising in the bile duct, small intestine, liver or pancreas, inflammation, fibrosis or strictures, and (rarely) parasites. Extrahepatic cholestasis due to obstruction could produce an increased AP and secondarily result in hepatocyte damage (ALT/AST) as bile backs up in the liver.

Neoplasia, both primary in the liver and metastatic, is also a consideration in this case. Lymphoma, which can cause diffuse hepatomegaly, nodular hepatomegaly, or hepatic masses is most common in the cat. Primary hepatocellular or biliary carcinoma are other considerations as primary tumors. Neoplasia can produce bile duct obstruction and/or cause hepatocellular damage as the tumor invades the liver and distorts hepatic architecture. Metastasis to the liver from another site, such as the pancreas, is also a possibility.

Cirrhosis or end stage liver is a possibility, although it is uncommon in cats. In this condition, chronic, persistent injury results in ongoing loss of hepatocytes, fibrosis, and regenerative attempts that produce

abnormal lobular architecture. In most cases, the underlying cause is no longer apparent at the time of diagnosis. In the cat, chronic CCHS would be one known cause (see above).

P: (initial plan)

Possible considerations include:

Abdominal ultrasound: this is probably the most sensitive way to evaluate (image) the hepatobiliary system. Imaging would allow us to address several DfDx's including neoplasia and EHBO (which, in addition to the obstructive lesion, can produce characteristic changes in the common bile duct - thickening, dilation, and tortuosity). Since we are also considering a fine needle aspirate or biopsy, it might be important to rule out EHBO. Otherwise, the needle or biopsy instrument might puncture a dilated bile duct or gall bladder and produce bile peritonitis. A tumor which diffusely infiltrated the liver, like lymphoma, can be difficult to detect by U/S, whereas focal or multifocal lesions are easier to image. Ultrasound can also reveal density changes due to FHL (liver) and pancreatitis, although the sensitivity is limited. Ultrasound can also reveal changes compatible with cirrhosis (decreased size, nodular surface, & change in density due to fibrosis).

Fine Needle Aspirate (FNA) of liver: If the abdominal ultrasound does not reveal EHBO, a FNA and cytology would allow us to address FHL which should produce diffuse vacuolation of hepatocytes. Alternatively, if U/S reveals a mass in the liver, ultrasonography can be used further to guide the needle into the lesion.

GGT: Like AP, GGT synthesis is induced by cholestasis. For some reason, FHL is less likely to produce an increased GGT in contrast to EHBO. As I would not be comfortable making a diagnosis or ruling out FHL based on a single non-specific laboratory finding, I think the FNA would be better.

Feline Pancreatic Lipase Immunoreactivity (fPLI): This is a new test that specifically measures lipase produced by the feline pancreas. It shows great promise for improving our ability to diagnose pancreatitis in cats. Still, if I were going to ultrasound the abdomen, I'd also attempt to image the pancreas for changes in echogenicity (detectable changes in density) compatible with pancreatitis.

Depending on the results of these tests, it may eventually be necessary to obtain a liver biopsy. This is the only way to diagnose feline CCHS. If the cat remains anorexic, placement of a feeding tube may also become necessary. Before considering an invasive procedure or biopsy, we should measure clotting times to rule out a coagulopathy. Since most clotting factors are produced in the liver, a clotting abnormality is a definite concern. If it exists, we may need to transfuse with plasma and/or provide Vitamin K prior to any procedure likely to result in significant bleeding. A severe coagulopathy might preclude an invasive approach.

PROBLEM #2 - Markedly Increased Liver Enzymes (both ALT/AST and AP):

SO: The marked increase in enzymes is compatible with both hepatocellular injury and cholestasis as described above in Problem #1 (icterus).

A: ALT and AST are both intracellular enzymes which are released into the plasma with hepatocyte damage (leakage) and necrosis. ALT is liver specific, while AST is not. In contrast, AP is not a damage enzyme but its synthesis is increased (induced) by several stimuli, notably cholestasis. An elevated AP is always significant in cats because of the short half-life of the enzyme in this species.

Elevation of all the measured enzymes, especially at this level, is compatible with either primary hepatic disease or biliary obstruction (post-hepatic disease). It is impossible at this stage in this case to determine if either cholestasis (AP) or hepatocellular damage was primary, or if both occurred approximately simultaneously.

DfDx's: See Problem #1. All of these DfDx's could produce the marked elevations in enzymes noted in this case.

P: Initial Plan: Pursue primary liver disease and rule out bile duct obstruction as outlined in Problem #1 (icterus).

PROBLEM #3 - HEPATOMEGALY:

SO: Physical examination revealed hepatomegaly characterized by extension of the liver beyond the ribs and by rounded edges. The hepatomegaly appears to be diffuse, but further assessment (imaging) would be required to confirm.

A: The liver gets too big because of “too much” of something or “too many” of something. Important examples include:

Congestion (too much blood): e.g. due to congestive heart failure or occlusion of the hepatic vein. There is (as yet) no evidence of cardiac disease but further investigation may be warranted. Occlusion (e.g. thrombosis) of the hepatic vein might be assessed by ultrasound.

Biliary Obstruction (too much bile): If the common bile duct is obstructed (see Problem #1, icterus), the backup of bile into the liver could produce hepatomegaly.

Infiltration (too many cells): The liver could be enlarged due to infiltration with tumor cells, such as lymphoma, metastases from another primary site, or growth of a primary liver neoplasm. Likewise, the liver could be infiltrated with inflammatory cells as in hepatitis. In the cat, inflammatory cells would most likely be located in the portal and periportal area (feline CCHS – see Problem #2 above).

Infiltration with a substance: Hepatocytes could be diffusely swollen due to intracytoplasmic lipid accumulation (FHL – see above). Another uncommon possibility is infiltration with amyloid (hepatic amyloidosis).

Specific DfDx: See Problem #1 (icterus)

P: (Initial Plan)

See above Problem #1. Ultrasound can be used to evaluate the hepatobiliary system (EHBO, neoplasia, hepatic vein thrombosis, liver density (e.g lipidosis), etc. Since FHL is my first DfDx, I think a FNA is the best way to rule out lipid accumulation, so long as the ultrasound is compatible and does not include evidence of bile duct obstruction. See Problem #1 plan regarding FNA.

MASTER PLAN (Day 1)

- fPLI – draw blood & submit
- Abdominal ultrasound
- FNA & cytology – Liver, ultrasound guided