PATHOLOGY OF LIVER & BILIARY TRACT

Lecture 5
Idiopathic & proliferative conditions; diseases of the biliary tract

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IX. Diseases of uncertain origin

- Equine serum hepatitis
- Idiopathic chronic hepatitis of dogs
- Lymphocytic portal hepatitis in cats
9.1 Equine serum hepatitis

- Syn. - Theiler’s disease,
- Etio: *serum-transmissible virus*?
- 1-2 months after injection with a biological of equine serum
- Jaundice and encephalopathy
- Small, flabby and pale liver
- **Histo:**
  - Centrilobular to massive necrosis
  - Fatty degeneration
  - Cholestasis
  - Mononuclear infiltration
  - Slight fibrosis and regeneration

*Equine serum hepatitis*, liver, horse. Histo:
There is centrilobular to massive necrosis (n). The remaining periportal hepatocytes show lipid-containing vacuoles (arrows). P: Portal vein.
Equine serum hepatitis, liver, horse. Note the enhanced lobular pattern associated with centrilobular necrosis and periportal inflammation / steatosis.

Equine serum hepatitis, liver, horse. The liver is characteristically small and flabby.
9.2 Idiopathic chronic hepatitis in dogs

Chronic-active hepatitis:
- Descriptive term
- Pattern of inflammation (human liver)
- Predictive of progressive inflammation/fibrosis $\rightarrow$ cirrhosis
- Interpreted erroneously as a disease entity by vets

From Noah’s arive
9.2 Idiopathic chronic hepatitis in dogs

- **Etiology:**
  - Leptospirosis
  - ICH
  - Progression from AH
  - Therapeutic drugs
  - Copper toxicosis (36%)

- **Gross**
  - Small liver, coarsely nodular

- **Histo**
  - Portal & periportal mononuclear inflammatory cells
  - **Piecemeal necrosis** ("interface hepatitis")
  - Intrahepatic cholestasis
  - Bridging fibrosis
  - Regenerative nodules

Example of cirrhosis secondary to chronic hepatitis, dog.

Images from Noah’s arkive
Canine chronic hepatitis, microscopic lesions

Hepatocytes of the **limiting plate** (arrows) are usually affected (piecemeal necrosis)

**Chronic active hepatitis.** End-stage liver with chronic hepatitis. The liver lobular architecture is replaced by irregular nodules of regenerative parenchyma (n) separated by tracts of connective tissue (c) with an inflammatory infiltrate and pigment accumulation.

*Robbins and Cotran Pathologic Basis of Disease (2010), 8th ed., Elsevier, Inc. chapter 18*
9.3 Lymphocytic portal hepatitis

- Cats > 10 years
- Aging change or subclinical form of disease
- Slow progression to portal fibrosis/biliary hyperplasia
- Lymphoplasmacytic inflammation
- No cholangitis, no periportal inflammm/necrosis
- Immune mediated disorder?
- No assoc with IBD or pancreatitis

Lymphocytic portal hepatitis, cat. Large numbers of lymphocytes surrounding expanding a portal area and surrounding hyperplastic bile ducts (arrows). P = periportal parenchyma

http://www.askjpc.org/vspo/show_page.php?id=130
X. Proliferative lesions of liver

- Non-neoplastic
  - Hepatocellular nodular hyperplasia
  - Regenerative nodules
  - Bile duct hyperplasia

- Neoplastic
  - Benign
  - Malignant
    - Primary
    - Metastatic

Cholangiocellular carcinoma, dog
10.1 Non-neoplastic proliferations

10.1.1 Nodular hyperplasia
- Single or multiple, yellow to tan, < 3 cm
- Disorganized plates of hepatocytes with vacuolar changes
- Lobular pattern is preserved but a little distorted
- No fibrosis, necrosis or inflammation

10.1.2 Regenerative nodules
- Surrounded by fibrous tissue
- Necrosis and inflammation are common
- Involve the entire organ

10.1.3 Bile duct hyperplasia
- Non-specific response to biliary or hepatocellular damage
- Accompanied by fibrosis

Nodular hyperplasia (top, H) and regenerative nodules (bottom), microscopic appearance. P = Normal parenchyma
Hepatic nodular hyperplasia, dogs (left)

Regenerative nodules in hepatic cirrhosis (right)


From Noah’s arkive
10.2 Neoplastic diseases of the liver

Most malignant tumors in liver are **metastases** from other organs.

**Primary** liver tumors arise from:
- hepatocytes
- bile ducts
- gall bladder
- diffuse neuroendocrine system
- mesenchymal tissue

Metastatic mammary gland carcinoma, liver dog. Cut surface (right).
10.2.1 Hepatocellular adenoma

- Benign neoplasm
- Young ruminants
- Single, unencapsulated, red to brown, nodular, may be pedunculated.
- Well differentiated hepatocytes
- **No portal tracts or bile ducts**
- Not easy to differentiate from nodular hyperplasia in old dogs
10.2.2  Hepatocellular carcinoma

- Syn: Hepatocarcinoma
- Malignant
- Most often seen in dogs
- Must differentiate from adenoma
- Gross
  - Often solitary; involves an entire lobe
  - Multilobulated and grey-white to yellow-brown
- Histo
  - Cells arranged in a trabecular pattern (3 or more cells thick),
  - Individual hepatocytes exhibit atypical and bizarre forms

**Hepatocellular carcinoma**, liver, dog (top) and chimpanzee (bottom). Single, large, lobulated, pale mass involving more than one lobe. **Histo**: Irregular trabeculae of atypical hepatocytes showing marked anisokaryosis, karyomegaly (k) and mitotic figures (arrow).
10.2.3 Cholangiocellular adenoma
- Benign tumour; from the bile ducts
- Often cystic

10.2.4 Cholangiocellular carcinoma
- Relatively common (described in all species)
- Multilobulated, firm, central areas of depression/necrosis (umbilicated).

Cholangiocellular carcinoma, liver. dog. Multiple nodules of tumor, some of which are umbilicated (arrows). Histo: Tubular structures of neoplastic bile duct epithelial cells (N) are invading the adjacent normal hepatic parenchyma (H).
10.2.5 Other tumors

Lymphoblastic leukemia, liver and spleen, dog. Note marked hepatosplenomegaly due to diffuse infiltration by neoplastic cells.

Lymphoma, liver, pig (right, top) cat (right, bottom). Note that the liver from the pig has multiple nodules disseminated in the parenchyma while in the cat’s liver is enlarged with enhanced lobular pattern.

From Noah’s arkive
XI. Diseases of the biliary tract

11.1 Structure and function

- Gallbladder
  - stores, concentrates and releases bile
- Hepatic bile ducts
  - carry bile from different lobules of the liver
- Common bile duct
  - Carry bile to intestine
- Bile = water, cholesterol, bile acids, bilirubin, inorganic ions, etc.
- Secretion provides
  1. Bile acids - for digestion of dietary fats
  2. Excretory route for various metabolites and drugs
  3. Buffers - neutralize acid pH from the stomach

Bile drainage system of a sheep
11.2.1 Gallbladder stones (choleliths)

- Concretions of normally soluble components
- Mixture of cholesterol, bile pigments, bile salts, calcium and proteinaceous matrix
- Due to supersaturation and precipitation of bile (2ry to ascending bacterial infections?)
- Not significant until obstruction occurs

**Gallbladder stone**, elephant

**Cholelithiasis**, liver, gallbladder, pigs

11.2.2 Biliary obstruction

- Causes: cholangitis, parasites or fibrosis, cholelithiasis (gallstones)

- Result: post hepatic jaundice, hepatic atrophy and biliary fibrosis

**Biliary obstruction due cholelithiasis**, liver, bile duct and gallbladder, cat. Unopened bile duct and gallbladder showing distension and distortion (*top*). These structures contain several choleliths and fibrous septa, possibly secondary to inflammation (*bottom*).
11.2.3 Gallbladder distension

- Common result of fasting
- *Lantana camara* toxicosis
  - Toxic metabolite: Lantadene A
  - Cholestasis, icterus, photosensitization
- Secondary to biliary obstruction
11.2.4 Gallbladder murocele

- Gallbladder dilation
- Accumulation of mucoid secretion
- Small breeds of dogs
- Cause?
  - Decreased gall bladder motility
  - Abnormal bile composition
  - Bile stasis
  - Cystic mucinous hyperplasia of mucosa
- Sequelae
  - Extrahepatic biliary obstruction
  - Ischemic necrosis and rupture

*Mucocele*, gallbladder, dog. Accumulation of bile-tinged mucoid material
11.2.5 Rupture of the biliary tract or gallbladder

- Usually traumatic in origin
- Steady leakage of bile into the peritoneal cavity
- Chemical peritonitis
- May be sterile or infected with enteric bacteria → rapidly fatal

Bile peritonitis secondary to gallbladder rupture, cow. Note large amounts of fibrinous exudate stained with bile.
11.2.6 Gallbladder edema

- **Causes**
  - Right Heart Failure
  - Infectious canine hepatitis
  - Others

From Noah's arkive

**Gallbladder edema**, salmonellosis, bovine.

**Gallbladder edema**, aflatoxicosis, pig.

**Gallbladder edema**, Infectious canine hepatitis, dog.
11.2.7 Cholangitis

- Intra-and extrahepatic bile ducts
- Extends to the parenchyma (cholangiohepatitis)
- Usually bacterial (if infectious)
- Portal of entry:
  - Hematogenous
  - Ascending from the intestine (obstruction and bile stasis)
- Suppurative inflammation
- Two important entities in companion animals:
  - Suppurative cholangiohepatitis (older cats, and dogs)
  - Lymphocytic cholangitis

In cats, bile and pancreatic ducts have a common entry to the duodenum. Simultaneous infection of these structures is common.
Lymphocytic cholangitis (Feline progressive lymphocytic cholangitis / cholangiohepatitis)

- Important in UK
- Cats 4 years and under (Persian)
- **Ascites**, icterus, hypergammaglobulinemia
- Active stage:
  - Lymphocytic inflammation within and around bile ducts
  - Extension to periportal parenchyma
- Chronic stage:
  - ↓ of lymphocytes
  - Bridging fibrosis
- Etiology:
  - No concurrent pancreatitis
  - Immune-mediated disorder?

**Feline lymphocytic cholangitis**, liver, cat. 
*Histo*: Large numbers of lymphocytes surrounding and infiltrating bile ducts (b); biliary hyperplasia (arrows).
11.2.8 Cholecystitis

- Inflammation of gallbladder
- Acute or chronic
- **Fibrinous** cholecystitis
  - Calves with acute salmonellosis and yersiniosis
- **Hemorrhagic** cholecystitis
  - Salmonellosis in cattle
  - Arsenic toxicosis

*Fibrinous cast*, gall bladder from a cow with salmonellosis

11.2.9 Cystic mucinous hyperplasia

- Cystic proliferation of the mucus-producing glands
- Gallbladder and bile ducts
- **Old dogs** and sheep
- Associated with mucocele

Pathologic Basis of Veterinary Disease, 5th ed.

Cystic hyperplasia of the gall bladder mucosa, liver, gallbladder opened, dog. Multiple green and pale yellow cystic nodules in the mucosa

Cystic mucinous hyperplasia, gallbladder, dog. The mucosa contains a mucous cyst. *Inset,* The mucosa is hyperplastic with prominent goblet cells that produce the mucus that fills the cysts.
11.2.10 Neoplasms

- Very rare in animals
- Adenomas (in cattle)
- Carcinomas

Gallbladder carcinomas, humans (left, bottom) with cholelithiasis in one of them (right, bottom). 

Gallbladder carcinoma (top, left) with invasion of the hepatic parenchyma (top, right), dog.
BEST WISHES IN THE FINAL