Canine Hepatocellular Pathology Quick Reference Guide (PQRG)
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Introduction:

PQRGs for neoplasms are designed for diagnostic pathologists so they are aware of the gross or microscopic information needed by clinicians to assign prognoses and offer therapy options. They can also be used to summarize key features to diagnosis a neoplasm and differentiate it from similar tumors. This Quick Reference Guide focuses on the histologic characteristics of hepatocellular adenoma and hepatocellular carcinoma. Other tumors derived from the liver are not discussed.

Diagnostic methods:

Fine-needle aspiration alone is not sufficiently accurate to distinguish these neoplasms. Histopathology is necessary, and excisional biopsies are preferred. However, clinicians may elect ultrasound guided needle-biopsies, but these samples provide limited tissue architecture which is needed for an accurate diagnosis. If needle biopsies are warranted, multiple sections of tumor with adjacent 'normal' hepatic tissue are recommended. The main complication is hemorrhage due to trauma of the biopsy procedures. Too little of the hepatic parenchyma is affected to induce bleeding defects

Patient information to collect includes:

Signalment (species, age, sex, breed), method of obtaining the sample, specimen size, interaction with adjacent tissues, and tissue margins.

Diagnostic Algorithm:

There are no grading systems for hepatocellular tumors. Diagnostic criteria that are helpful in differentiating hepatocellular adenomas vs carcinoma are summarized in the table below, in order of most important. The caveat being that the outcome which strongly supports malignancy, metastasis, is uncommon to rare, even with hepatocellular carcinomas.[1,2,3] Mitotic counts are often not helpful diagnostic features as poorly differentiated hepatocellular carcinomas can have many while well-differentiated carcinomas and adenomas have few. If differentiation becomes ambiguous, the use of the general term 'hepatocellular tumor' may be an appropriate option and then in the comment indicate which diagnosis is "favored" or most likely.

Diagnostic criteria	Hepatocellular Adenoma	Hepatocellular Carcinoma
Metastasis (intrahepatic or extrahepatic)	Does not metastasize	Rare; if present, strongly supportive
Lymphovascular invasion*	Not invasive	Uncommon; if present, supportive
Invasion of surrounding hepatic parenchyma	No, adjacent parenchyma compressed/atrophied	Variable; if present, supports aggressive
Trabecular architecture	Loss; uniformly sized, 2-3 cells thick	Loss; irregularly and variably thickened, 5-20 cells thick
Cell and nuclear variability (also see Figure 1)	Well-differentiated, resemble normal hepatocytes	Can be well- or poorly-differentiated; often lacks normal hepatocyte features

*** - See Guideline and QRG- Moore FM et al. Lymphovascular Invasion Guideline, version 1.0. Veterinary Cancer Guidelines and Protocols.** http://vetcancerprotocols.org

Immunohistochemistry:

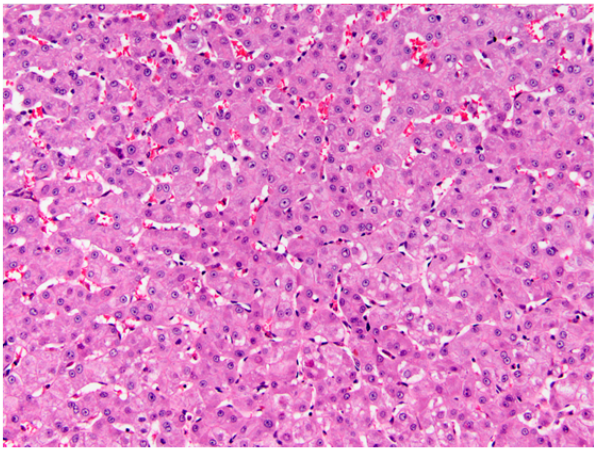
Morphology based on H&E sections is sufficient to diagnose *hepatocellular tumor* and usually distinguish indolent vs aggressive types. Immunolabeling with Keratin 19 (K19) can be used as a component to establish the diagnosis and to distinguish between adenoma and carcinoma but this needs validation.[4,5] Canine hepatocellular adenoma may have 0-5% immunolabeling with K19 while hepatocellular carcinomas often have more than 5% immunolabeling with K19.[4,5] This percentage is a subjective interpretation, morphometry to estimate percentage of labeling has not been reported; if <5% of tumor cells label = negative. If the tumor has pleomorphism, infiltrative growth pattern and >5% of neoplastic cells immunolabel for K19, then carcinoma is favored.

Clinical significance of diagnosis:

The histological distinction of hepatocellular adenoma vs carcinoma does not carry much significance clinically as the biologic behavior of both tumors is synonymous. Generally, both tumors have good long-term survival, and metastases are rare in dogs. The diagnosis of carcinoma does not portend metastases and/or incipient euthanasia. Morbidity or mortality arise from secondary complications, such as local compression of the liver from growth of the tumor, tumor necrosis and/or intraperitoneal hemorrhage, rather than metastases. A previous publication[6] subtyped hepatocellular carcinomas as multiple variants; however, at present there is insufficient data to support inclusion of subtyping in pathology reports. The diagnosis of hepatocellular carcinoma is sufficient for clinicians as there are no known differences in biologic behavior among the subtypes.

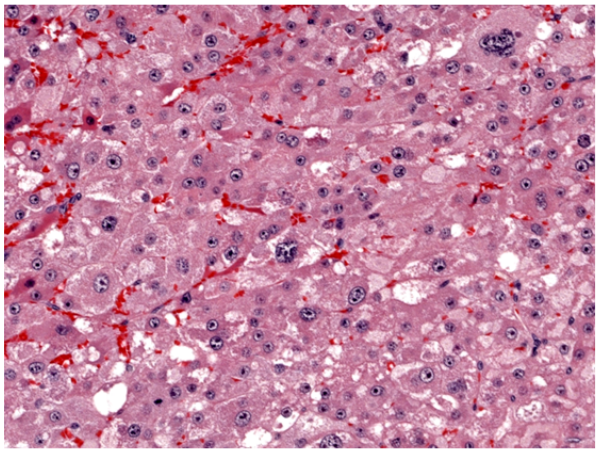
Figure 1:

Hepatocellular Adenoma



Uniform trabeculae of well-differentiated hepatocytes, well-demarcated from adjacent parenchyma by a circumferential zone of compression/atrophy, loss of normal lobular architecture within the tumor, no or limited cellular pleomorphism.

Hepatocellular Carcinoma



Irregularly thickened trabeculae of well- or poorly-differentiated hepatocytes, invasion into adjacent parenchyma may be evident, round or rarely spindle-shaped cytoplasm, one or more enlarged nucleoli.

Diagnostic features to include in pathology reports:

What is critical to be provided by the pathologist- Core	**What is not critical but highly recommended to be provided by the pathologist- Non-core**	**What is not needed to be provided by the pathologist- Non-core**
Histopathologic interpretation/ morphologic diagnosis Metastasis (intrahepatic or extrahepatic) Lymphovascular invasion Infiltrative grown pattern	Comment (especially for '*Hepatocellular tumor*' diagnosis) Mitotic count Surgical margin evaluation	Description Grading system - none Histopathologic subtype

Selected References:

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