Pathology of focal liver lesions

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Liver cancer is the 6th most common tumor worldwide, with increasing incidence. Several factors as hepatitisB, C virusa (HBV, HCV) infection, alcohol abuse, steatosis, toxic agents etc play improtant role in differential diagnosis. WHO classification differentiates benign epithelial and non-epithelial tumors and tumor-like lesions and malignant epithelial and non-epithelial liver tumors.

Benign epithelial tumors and tumor-like lesions:

Focal nodular hyperplasia (FNH): tumor-like lesion, a reaction to vascular malformation, 0,3-3% of general population, 10x more frequent than hepatocellular adenoma (HCA). It could be single or multiplex, often associated with other liver tumors. Female predominance. Classic and a „non classic" variants have been distinguised.
Gross: the lesion is non-capsulated, paler than the surrounding non-cirrhootic liver, central scarring and abnormal dilated vessels.
Histology: „hepatocytes" arranged in trabecules, ductal reaction (bile duct proliferation), inflammation (not always). No malignant transformation occurs.

Hepatocellular adenoma (HCA): rare benign tumor of hepatocytic origin with female predominance.. Normal afphafetoprotein level (AFP), increased vascular pattern. Etiopathogenesis: oral contraceptives, anabolic steroids, metabolic disorders etc.
Gross: Single or multiplex (adenomatosis, if the number of lesions is over 10 nodules), usually thin capsule.Yellow or pale, homogenous cut surface, highly vasculated (hemorrhages might occur).
Histology: „normal" hepatocytes, or larger. Cytoplasm: normal, or clear, fatty, dark eosinophilic, lipofuscin, Mallory bodies. Nuclear/cytoplasmic ratio: normal.
Immunohistochemistry: HepPar1, CK8, 18 pos., CK7, 19 neg, AFP neg, glypican3 neg
Molecular classification: „Classic", variants 1, 2, 3 (based on HNF1α and β-catenin mutation, Bioulac-Sage et al.2007).
Differential diagnosis: FNH, hepatocellular carcinoma (HCC), angiomyolipoma.

Premalignant and malignant epithelial tumors

Premalignant lesions in cirrhotic liver:
Large regenerative nodule (LRN, macroregerative nodule MRN)
Low-grade dysplastic nodule (LGDN)
High-grade dysplastic nodule (HGDN)

Dysplastic nodule-HCC-seuqqence not adenoma-HCC-sequence! (P.Schirmacher)

Hepatocellular carcinoma (HCC): the most common primary malignant liver tumor. Association with cirrhosis appr. 80%. Prognosis is correlated with staging, vascular invasion, number, size and location of lesions. Several staging classifications are known (TNM, Barcelona Clinic Liver Cancer (BCLC) staging system – Llovet et al. 2008). Etiopathogenesis: cirrhosis, HBV, HCV, hemochromatosis, aflatoxin, ethanol etc.

Gross: nodular, massive, diffuse, multifocal
Histology: trabecular, acinar, (pseudoglandular, adenoid), solid (compact), scirrhous.
Variants: clear cell, fibrolamellar, combined HCC (cholangiocellular(CCC), sclerosing
Grading: G1-4 (Edmondson and Steiner 1954, UICC 2002).
Immunohistochemistry: HepPar1 (+), AFP (+/-), CK7 (-), CK20 (-), CK8/18 (+), pCEA (canal+), vimentin (-), glypican3 (+/-), claudin 4(-), agrin (+). (Demonstration and value of the immunohistochemical markers will be presented).

Combined HCC and CCC
Intermediate carcinomas
Transitional type combined HCC-CCC
Small cell type HCC

Non-epithelial benign tumors and tumor-like lesions
Haemangioma
Angiomyolipoma
Infantile hemangioendothelioma
Mesenchymal hamartoma
Localized fibrous tumor
Solitary necrotic nodule
Inflammatory pseuotumor
Others

Non-epithelial malignant tumors
Epithelioid hemangioendothelioma
Angiosarcoma
Undifferentiated sarcoma (embryonal sarcoma)
Lymphoma and other hemopoetic tumors
Kaposi's sarcoma
Others

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