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Immunohistochemical diagnostic algorithms of neoplastic liver biopsies

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Abstract

Pathological analysis and evaluation of a liver biopsy is a crucial step within the diagnosis of single or multiple mass lesions within the liver. Accurate diagnosis is paramount in guiding appropriate treatment. This study conducted an enquiry for liver biopsies for the past 6 years with the diagnostic search codes of neoplasm, metastases, metastatic, adenocarcinoma, neuroendocrine carcinoma, sarcoma, and lymphoma. The aim was to review their pathological workup with a view to developing cost-efficient immunohistochemical diagnostic algorithms. a complete of 375 consecutive neoplastic liver biopsies were retrieved and subjected to pathological review. for sure the bulk up to 95% of the neoplastic lesions were metastatic lesions. some biopsies up to fifteen represented primary hepatocellular /cholangiocarcinoma, haemangioma, and cirrhosis. the most typical metastases [upto 61%] to the liver were colorectal in origin being Hepar-ve, CDX2+ve, and CK20+/CK7-ve. Other lesions included metastases from pancreas [12%], lung [8%] upper gastrointestinal [8%], neuroendocrine lesions [8%], ovarian [1%] and kidney/urothelial [2%]. Uncommon metastases encountered included hepatic metastatic meningioma, endometrial stromal sarcoma, and osteosarcoma. Immunohistochemical stains were the foremost useful test in identifying the first site of the tumor. Though diagnostic algorithms were developed especially within the case of the unknown primary, some biopsies received a medical diagnosis of over one organ because the primary site for clinicopathological correlation.

As liver metastases are usually easily accessible for core needle biopsy; accurate identification/specifics of the liver metastases are paramount for individualized precision medicine of treatment that will thus direct surgical resection, radiofrequency ablation/embolization or medical adjuvant therapy as indicated. Early HCC, small well-differentiated HCC of vaguely nodular type, shows increased cell density (>2 times than that of surrounding tissue), increased N/C ratio and irregular thin-trabecular pattern. The nodules carries with it varying numbers of portal tracts and unpaired arteries. Pseudoglandular pattern and diffuse fatty change are histological features. One distinguishing feature of HGDN from HCC is that the presence of tumor cell invasion into the intratumoral portal tracts in HCC. Given such detailed histological criteria, distinction of dysplastic from malignant lesions remains sometimes difficult. With the advances in immunohistochemical markers and molecular techniques, this diagnostic problem may be better addressed and attended. Besides, the immunohistochemical and molecular characteristics of hepatocellular nodules are more explicitly explored. during this review, a short summary of some recent works of those markers are going to be illustrated. HCA and FNH are benign hepatic nodules.

Diagnosis of those nodules has right along been supported morphological features, which cannot always be straightforward. Diagnostic problems include differenti- ating HCA and FNH (the latter is that the most typical benign hepatic nodule and carries a lowerrisk of tumor rupture leading to hemoperitoneum), additionally as differentiating these lesions from HCC. Besides, various histological features of HCA have aroused researchers' interest to explore further on this benign hepatocellular neoplasm. In recent years, a genotype classification on HCA has been proposed. According to Bioulac-Sage, et al., such classification of HCA is predicated on the explanations. to: 1) dissect the pathogenesis of HCA, 2) aid diagnosis by radiological means, 3) stratify the danger of progression to HCC, and 4) facilitate screening in familial cases.

The classification of HCA supported genotype consists mainly of three groups: 1) HCA with HNF-1α inactivating chromosomal mutation (H-HCA), 2) HCA with mutation of the β-catenin gene (b-HCA), and 3) inflammatory HCA (I-HCA). Each group of HCA is characterized by the expression of specific genes of interest by quantitative reverse transcription polymerase chain reaction (qRT-PCR) method[9]. FABP1 and UGT2B7, encoding liver carboxylic acid binding protein (L-FABP) and controlled by HNF-1α, are expressed in normal liver tissues. an occasional expression of those genes is found in H-HCA cases as compared with other non-mutated subtypes.

The expression of the transcripts of GLUL (encoding glutamine synthetase [GS]) and GPR49, two genes regulated by β-catenin, correlates with β-catenin mutation within the b-HCA subgroup. Up-regulation of SAA2 (encoding serum amyloid A2) and CRP (encoding C-reactive protein) characterizes the I-HCA. Besides, the transcript expression levels by qRT-PCR of the precise genes were found to correlate with the protein expression levels. Immunohistochemical stains thus are useful in classifying HCA supported the immunoprofile[9]. In summary, H-HCA is characterized by an absence of L-FABP staining; b-HCA shows GS (specificity 89%; sensitivity 100%) and β-catenin staining (specificity 100%; sensitivity 85%); while I-HCA expresses CRP and SAA (specificity 94%; sensitivity 94%), with or without β-catenin. Given the above, 5%-10% of HCAs are still unclassifiable. H-HCA constitutes about 35%-40% of

HCA. The mean age of presentation is 39 years and birth control device intake was noted in 92% of cases. It involves bi-allelic inactivating mutations of the HNF-1α gene. Histologically, H-HCA shows marked steatosis, no inflammatory infiltrates and no cytological abnormalities. Immunohistochemically, as mentioned above, there's lack of L-FABP expression among tumor cells in contrast with adjacent liver tissue. b-HCA constitutes around 10%-15%. anovulatory drug intake is noted in 100% of the cases. Morphologically, occasional cytological abnormalities and rosette formation are observed. Immunohisto- chemically, aberrant nuclear and cytoplasmic expression is characteristic. Besides, GS, encoded by GLUL, is additionally expressed during this group of HCA.

Recognition of b-HCA is very important because it is related to the next risk of HCC. I-HCA accounts for quite 50% of HCA. The mean age of presentation is 41 years, and contraceptive pill intake was observed in 90% cases. Clinically, association with high body mass index and alcohol consumption in patients is observed. Signs of inflammatory syndromes, e.g. raised CRP levels, are noted. Histologically, features of I-HCA include inflammatory infiltrates, sinusoidal dilatation or congestion, presence of thick-wall arteries (some being dystrophic), and ductular reaction. Steatosis could also be present but not as extensive. additionally, there's increased expression of SAA and CRP at mRNA and protein levels, and may be detected by immunohisto- chemical methods.

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