Liver Cell Adenoma: A New Perspective

Introduction:

Hepatocellular adenomas (HCAs) are rare, benign hepatic tumors that commonly occur in women taking oral contraceptives for more than 2 years. HCA is not a single disease but a heterogeneous group of tumors characterized by specific etio-pathogenic mechanisms and tumor biology. Based on genotype-phenotype classification, HCAs are currently categorized into three distinct subtypes that include inflammatory HCAs, hepatocyte nuclear factor - 1α [HNF-1α] mutated (Steatotic) HCAs and β-catenin mutated HCAs.

Different subtypes of HCAs have distinct genetic abnormalities which phenotypically reflect in their pathological features, clinical behavior, and prognoses. While the risk of bleeding is high with inflammatory HCAs, β-catenin mutated HCAs have significant risk of malignancy. Subsequently, treatment and surveillance options may vary. Although image-guided biopsy and/or surgical resection with pathological and immunohistochemical analysis is necessary for complete characterization of HCAs, imaging plays an important role in the diagnosis, characterization, detection of complications, and surveillance.

Role of Imaging & Histopathology:

After hepatic hemangiomas, Focal nodular hyperplasia (FNH) and Hepatocellular adenomas (HCA) are the most common benign hepatic lesions encountered in a non cirrhotic liver. They are often incidental imaging findings in asymptomatic patients. For several years, both radiologists and pathologists are actively engaged in differentiating these two benign lesions as management of these

two is different. Where as FNH does not need management, HCA is either followed with imaging or surgically resected because of risk of either hemorrhage or malignant transformation. Several studies have identified several risk factors hemorrhage and malignant transformation such as male gender, size of the lesion and HAC subtype. Knowledge of the subtype and size of the lesion are important determinants of surgical resection of HCA.

Inflammatory HCAs (IHCAs) are the most common type that accounts for about 40 %-50 % of all HCAs. Approximately 30% of all IHCAs show risk of bleeding and up to 10% of tumors show increased risk of malignancy.

HNF-1α mutated HCAs (HHCAs) constitute about 30-35 % of all HCAs and are the second most common type of HCAs according to genotype-phenotype classification Biallelic inactivating mutations of the HNF-1α gene are responsible for the development of HHCAs. HHCAs develop exclusively in female patients with more than 90% patients having a history of OCP use. They have an association with maturity onset diabetes of the young type 3, and familial hepatic adenomatosis. HHCAs are multiple in 50% of patients and they show very minimal risk of bleeding and almost no risk of malignancy.

β-catenin mutated HCAs (*β* HCAs) constitute about 10-15 % of all HCAs and are due to activating mutations of the *β*-catenin gen. *β* HCAs occur more frequently in men and are associated with male hormone administration, glycogen storage diseases, and familial adenomatosis polyposis (FAP). Of all HCAs, *β* HCAs carry the highest risk of malignancy and they are interpreted as borderline lesions between HCA and HCC.

The different sub types of HCA have distinct histological and Immunohistochemistry features useful in differentiating them from one another.

MR imaging is preferred to CT for cross sectional imaging of HCA due to better tissue characterization by MR imaging. Although biopsy and histopathology is necessary for differentiating the subtypes of HCA, MR imaging features reflecting the tissue composition of HCA are useful to identify the subtype of HCA.T1 chemical shift imaging is useful in identifying intra lesion lipid, T2 signal intensity and pattern of dynamic post contrast enhancement are also useful in differentiating the subtypes. Use of liver specific MR contrast agents are helpful in differentiating HCA from FNH.

HNF-1α mutated HCAs are characterized by intralesion lipid on T1 chemical shift imaging with mild T2 hyperintense signal intensity, mild enhancement in the arterial dominant phase with no persistent enhancement in the portal and delayed phases.

On the contrary Inflammatory HCAs demonstrate high T2 signal intensity, intense enhancement in the arterial dominant phase with persistent enhancement in the portal and delayed phase reflecting the intense vascularity with sinusoidal dilation and inflammatory tissue chracteristics of this subtype.

No unique imaging features are seen with β-catenin mutated and unclassified subtypes of HCA.

Summary:

Hepatocellular adenomas are diverse group of benign tumors characterized by specific genetic mutations, molecular abnormalities, pathological features, imaging findings, tumor biology, and natural history. MR imaging is not only useful in differentiating HCA from FNH, but also to some extent identifying the HCA sub type. Management of HCA depends not only on the established risk factors such as male gender, size (>5cm), association with Glycogen storage disease etc, but also on the subtype of HCA. Although histological and immunohistochemistry

analysis is more accurate in identifying the sub type, unique MR imaging features of the sub types are useful in differentiating them. Knowledge of the genotype-phenotype classification of HCA and imaging features of the subtypes helps the radiologist to go beyond mere differentiating the HCA from FNH.