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Anatomical pathology of hepatocellular carcinoma: A clinicopathologic review.

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Introduction

Hepatocellular Carcinoma (HCC) is the most common primary malignant tumor of the liver, accounting for over 80% of liver cancer cases globally. It typically arises in the background of chronic liver disease, especially cirrhosis caused by chronic Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), alcohol abuse, or Non-Alcoholic Fatty Liver Disease (NAFLD). Anatomical pathology provides critical insights into the diagnosis, staging, and prognosis of HCC through histopathologic evaluation and clinicopathologic correlation. [1].

Grossly, HCC may present as a single mass, multifocal nodules, or diffuse infiltrative growth. Tumor size can vary widely, and large tumors may exhibit areas of necrosis or hemorrhage. Microscopically, classic HCC is composed of malignant hepatocytes arranged in trabecular, pseudoglandular, or compact patterns. The degree of differentiation ranges from well to poorly differentiated, and histologic grading (such as the Edmondson-Steiner system) is a key prognostic factor.[2].

The cytologic features of HCC include increased nuclear-cytoplasmic ratio, nuclear pleomorphism, prominent nucleoli, and frequent mitotic figures. Immunohistochemistry (IHC) plays a crucial role in diagnosis, with markers such as HepPar-1, Glypican-3, Arginase-1, and heat shock protein 70 (HSP70) being commonly used. A panel of these markers enhances diagnostic accuracy, especially in poorly differentiated tumors. [3]

Vascular invasion, particularly into portal and hepatic veins, is a significant pathological finding and correlates with increased risk of recurrence and metastasis. Tumor encapsulation, satellite nodules, and bile duct involvement are additional important pathological features that influence staging and prognosis. Liver biopsy is reserved for atypical cases due to the risk of tumor seeding. When performed, histological confirmation provides definitive diagnosis and informs therapeutic decisions, including surgical resection, liver transplantation, or loco-regional therapies [4].

From a clinicopathologic perspective, HCC commonly presents with nonspecific symptoms such as abdominal pain, weight loss, and signs of liver dysfunction. Serum alpha-fetoprotein levels may be elevated in many patients, although this is not specific. Radiological imaging, especially contrast-enhanced CT or MRI, typically shows arterial enhancement and venous washout, which are characteristic features aiding diagnosis. Recent molecular studies have identified key genetic alterations in HCC, including mutations in TP53, CTNNB1 (β-catenin), and TERT promoter. These molecular markers are being increasingly integrated into pathological assessments and may help in stratifying patients for targeted therapies. [5].

Conclusion

Anatomical pathology remains the cornerstone of HCC diagnosis and management. Integration of histologic features, immunophenotype, molecular alterations, and clinical data offers a comprehensive approach for accurate classification and optimal treatment planning.

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