The Diagnostic Approach towards Combined Hepatocellular-Cholangiocarcinoma— State of the Art and Future Perspectives

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Abstract

Combined hepatocellular-cholangiocarcinoma (cHCC-CCA) is a rare primary liver cancer which displays clinicopathologic features of both hepatocellular (HCC) and cholangiocellular carcinoma (CCA). The similarity to HCC and CCA makes the diagnostic workup particularly challenging. Alpha-fetoprotein (AFP) and carbohydrate antigen 19-9 (CA 19-9) are blood tumour markers related with HCC and CCA, respectively. They can be used as diagnostic markers in cHCC-CCA as well, albeit with low sensitivity. The imaging features of cHCC-CCA overlap with those of HCC and CCA, dependent on the predominant histopathological component. Using the Liver Imaging and Reporting Data System (LI-RADS), as many as half of cHCC-CCAs may be falsely categorised as HCC. This is especially relevant since the diagnosis of HCC may be made without histopathological confirmation in certain cases. Thus, in instances of diagnostic uncertainty (e.g., simultaneous radiological HCC and CCA features, elevation of CA 19-9 and AFP, HCC imaging features and elevated CA 19-9, and vice versa) multiple image-guided core needle biopsies should be performed and analysed by an experienced pathologist. Recent advances in the molecular characterisation of cHCC-CCA, innovative diagnostic approaches (e.g., liquid biopsies) and methods to analyse multiple data points (e.g., clinical, radiological, laboratory, molecular, histopathological features) in an all-encompassing way (e.g., by using artificial intelligence) might help to address some of the existing diagnostic challenges.