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Combined Type HCC-CC: Change of Pathologic Diagnosis

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Over hundreds of years, primary liver cancers showing mixed hepatocellular and cholangiocellular differentiation was reported and many classifications and nomenclatures have been suggested. In WHO classification (4th edition, 2010), cHCC-CCA was defined as a tumor containing unequivocal, intimately mixed elements of both hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA). In this classification, cHCC-CCA was classified a classical type and three subtypes with stem-cell features, including typical subtype, intermediate subtype, and cholangiolocellular subtype. However, with increasing number of reported HCC-CCAs, we found that all kinds of primary liver cancers (HCC, CCA, intermediate carcinoma, and cholangiolocellular carcinoma [CLC]) could be exist alone or in combination with one another. To describe full arrange of cHCC-CCA appropriately, a new consensus terminology guideline for cHCC-CCA were proposed by the group of international group of hepatic pathologists, and accordingly, WHO classification of cHCC-CCA was updated in 2019 (5^{th} edition). The new classification for cHCC-CCA simply describes the forms and proportion of primary liver cancers in the tumor, instead of dividing types and subtypes of cHCC-CCA. Each histologic component of primary liver cancer is diagnosed by routine staining (histochemical staining including hematoxylin-eosin), and various protein expression assessed by immunohistochemical staining could be used as a supplementary tool for diagnosis. CLC is tumor resembling cholangioles (canals of Hering) where hepatic stem/progenitor cells are located. In updated classification, CLC is classified as cHCC-CCA when it is mixed with HCC or intermediate carcinoma. composed of tumor cells showing intermediate features between hepatocyte and cholangiocyte at the cellular level, and it displays both of hepatocytic and cholangiocytic IHC markers. Further study is needed to clarify whether intermediate cell carcinoma is a distinct clinicopathological entity rather than histopathological spectrum. There are limited data about the pathogenesis and molecular feature of cHCC-CCA.

Keywords: Primary liver cancer, Diagnosis, Stem cell, Cholangiolocellular carcinoma, intermediate carcinoma