Mini Review

Stem Cell Research and Regenerative Medicine

Study of Malignant Tumour Clinical Characteristics with Inflammatory Arthritis

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Abstract

Hematologic malignancy with cholangiocarcinoma (cHCC-CCA) is a rare primary liver cancer composed of differentiated cells of both hepatocytes and cholangiocytes. It is slightly more common in men and in Asian and Pacific islanders. Overall, the risk factors are similar to classical risk factors for hematologic malignancies. Taxonomies have evolved significantly over time. The latest WHO classification (2019) discards the previously accepted classification of cancers with stem cell characteristics and replaces the morphological diagnosis, primarily by routine staining, with the ability to distinguish between intermediate cancers. is emphasized. Assigned to subtypes and consider cholangiocarcinoma a subtype of cholangiocellular carcinoma. Immunohistochemical markers can be used for detailed identification but are of limited diagnostic value. Recent discoveries regarding the regulation of molecular signaling may provide new therapeutic approaches for this poor prognosis and difficult diagnosis.

Keywords: stem cells • Progenitor cells • Hippo signaling • Wnt signaling

Introduction

Primary liver cancer is the sixth most common malignancy worldwide (4.7% in men and women) and the third leading cause of cancer death (8.3%), especially after colorectal cancer and lung cancer. Incidence and age of onset vary greatly by region [1].Among primary malignant liver diseases; hematologic malignancies (HCC) are the most common form. In general, the mean age of diagnosis in North America and Europe is over 60 years, while the mean age of diagnosis in Asia and Africa is 30-60 years. Common risk factors include cirrhosis, viral hepatitis B and C infections, alcoholic fatty liver disease (NAFLD), and environmental exposure to aflatoxin, torotrast, anabolic steroids, oral contraceptives, alcohol, or tobacco. It is included. It contains. In addition, developmental disorders such as Abernethy malformation and other conditions resulting from genetic mutations or loss of function such as B. Alagille syndrome, ataxia telangiectasia, bile salt exporter protein deficiency, tyrosinemia, hepatocellular carcinoma. A small percentage of hepatocellular adenomas may progress to hepatocellular carcinoma [2].

They account for 15% of primary liver malignancies. Hepatolithiasis and recurrent suppurative cholangitis are strong risk factors for the development of cholangiocarcinoma. Hepatitis B and C virus infection, alcohol consumption, and smoking are known risk factors but are less associated with hepatocellular carcinoma. CCC is most common in East Asia due to parasitic infection. In addition, certain predispositions to cholangiocellular carcinoma, such as primary sclerosing autoimmune cholangitis (PSC), and congenital anomalies of the biliary system, such as Calorie syndrome, congenital liver fibrosis, and choledochocysts, have been reported in adulthood. I'm here. I am here. The risk of malignant transformation to CCC is approximately 15%. In addition to pure HCC and CCC, combined haematological malignancies and cholangiocellular carcinoma (cHCC-CCA) tend to occur in middle-aged men and are a rare but very common form of primary liver cancer reported in Asia. is a common form in is an interesting entity [3]. Slightly more than the Pacific people although

the importance of information on risk factors in the literature is generally limited due to their rarity, HCC-like factors such as male sex and hepatitis B virus infection were observed. Histomorphologically, the tumor shows a mixture of hematologic malignancies and cholangiocellular carcinoma features. Recent morphological and molecular pathological studies have pointed to a common cell of origin and opened new insights into underlying molecular signaling structures. However, there is still an obvious knowledge gap here. In this overview article, we summarize important foundations from decades of research, the development of perspectives on histological classification, the latest advances in molecular pathological analysis, and provide a brief overview of possible future approaches [4].

Results

Epidemiology

The combined incidence of hematologic malignancies and cholangiocellular carcinoma (cHCC-CCA) in primary liver cancer lesions is 0.4–14.2%. One of the largest series of primary liver lesions involved 465 patients diagnosed with cHCC-CCA, with an incidence of 0.77%. Another large study included 529 cHCC-CCA patients and reported an overall incidence of 0.05 per 100,000. These tumors were more common in Asian and Pacific Islanders (0.08 per 100,000) than in Caucasians and Blacks (0.05 per 100,000) and American/Alaskan Indians (0.04 per 100,000). Surprisingly, in his 10-year study, the incidence appeared to be increasing. The incidence of cHCC-CCA among different ethnic groups has been reported in the literature with conflicting results.A SEER database study was conducted over his 30 years of her 282 patients diagnosed with cHCC-CCA, which has a higher incidence of liver cancer than cHCC-CCA patients in the Asia-Pacific region. Men had fewer cholangiocarcinomas than women with cHCC-CCA. Men are more common than women, and patients in the Asia-Pacific region are more likely to develop liver cancer than those born elsewhere, and are more likely to develop liver cancer than cHCC-CCA. was higher, as described in previous studies in small cohorts. However, known incidence figures are subject to uncertainty, as most patients do not undergo surgical resection and may be misdiagnosed as HCC or CCC. Taken together, cHCC-CCA is rare, with a high incidence in men in Asia and the Pacific. However, due to its rarity, studies may show conflicting results [5].

Prognostic factors

In general, the description of risk factors for cHCC-CCA has been limited in recent years due to their rarity and inconsistent diagnostic classification. Risk factors for cHCC-CCA are comparable to those for hematologic malignancies (HCC), and clinicopathologic features indicate that cHCC-CCA is a variant of HCC rather than a true intermediate between HCC and CCC. is shown. Suggest. Claims to become cHCC-CCA patients showed similarities to HCC in terms of male preference, viral hepatitis status, serum alpha protein (AFP) levels, and non-tumor histology [6]. Primary biliary cholangitis (PBC) also appeared to be a rare prerequisite for the development of cHCC-CCA. However, these results are controversial. CCC-like demographic and clinical features have been reported in several small cohorts. The prognostic impact of cHCC-CCA included sex, tumor size, and treatment status, with poor prognosis in patients who did not undergo surgical resection, radiotherapy, or chemotherapy. Progressive disease with nodules and distant metastases also compromised survival chances. Explain why African Americans with lower disease-specific survival rates are preferred [7].

Clinical aspects

The reported clinical features were mainly based on small cohorts and statistically inadequate retrospective studies. In general, cHCC-CCA usually presents with symptoms typical of progressive disease and HCC or CCC, including painless jaundice, fatigue, abdominal discomfort, weight loss, pruritus, ascites, acute cholangitis, fever, and hepatomegaly [8]. Until the combined cHCC-CCA has different imaging features and is difficult to interpret depending on the dominant differentiation, I will remain silent. Staging of cHCC-CCA is compatible with staging of cholangiocarcinoma. Bile duct cancer can be classified according to the Bismuth-Corlette classification. This includes hilar cholangiocarcinoma. Indeed, in collaboration with the American Joint Committee on Cancer (AJCC)/ Union International Cancer Control (UICC)

Cancer Staging Manual, new classification proposals have been published that include the classification of tumors of the distal bile duct [9]. System included Perihilar and intrahepatic tumors. However, the Bismuth-Corlett classification and the TNM staging system for information on vascular encapsulation and distant metastasis have been criticized because vascular invasion affects the T stage, thus staging should be considered as the choice of local therapy. become. As a result, a new staging system for perihilar tumors has been proposed. These include tumor size, degree of biliary disease, hepatic artery and portal vein involvement, lymph node involvement, distant metastasis, and tumor volume Suspected residual liver after resection.

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Ultrastructural features

Inflammatory changes have been described as primary sclerosing cholangitis-associated cholangiocarcinoma. In one study, COX-2 was significantly upregulated in contrast to non-neoplastic biliary epithelial cells and sporadic ICC. Hepatitis B infection may be associated with p53 mutations. Mutation patterns are also site-specific. IDH1/2, BRAF mutations, and FGFR2 fusions have been found in canalicular ICC and are associated with progenitor cell expansion and the development of bile duct precancerous lesions [13]. The molecular alterations in cHCC-CCA and the identification of driver mutations that drive cHCC-CCA progression have long been neglected and unclear, probably because they occur infrequently. The landscape of molecular pathology shows significant heterogeneity and conflicting findings [14]. Molecular features of stem cells in cHCC-CCA led us to favor putative stem/progenitor cells as a common cellular origin in this mixed tumor. That his cHCC-CCA has properties of parental/progenitor cells at the molecular level, downregulation of the hepatocyte differentiation program, and binding to bile ducts controlled primarily by her TGFbeta and Wnt/beta-catenin signaling pathways indicates show. This signature is associated with redesigning the microenvironment. These findings were significantly different from well-differentiated HCC and showed features of poorly-differentiated HCC with stem cell features and poor prognosis. The stem cell-like trait was confirmed by genomic analysis, demonstrating positive groove-like transcripts [15].

Discussion

This overview describes the tortuous diagnostic pathway for rare primary liver lesions. Despite great advances in the detection of this highly aggressive tumor over the past decades, combined hepatocellular cholangiocarcinoma urgently requires further research efforts to dissect its underlying characteristics. The first critical step was the establishment of diagnostic criteria. Moreover, differential diagnosis, especially based on biopsy specimens, has pitfalls and should be performed by experts

in the field.

Currently used immunohistochemical markers lack sensitivity and specificity for unambiguous diagnosis. This group of tumors combines morphological and immunophenotypic hepatocellular and cholangiocytic features with mixed features of intratumoral lineages. For this reason, the current consensus of international experts recommends regular histopathological diagnosis with hematoxylin and eosin (H&E). Immunostaining is complementary but not essential for diagnosis. Established immunohistochemical markers such as hepatocyte paraffin 1 and arginase 1 can be used to confirm hepatocyte differentiation, whereas type I and type II cytokeratins 7 and 19 can be used to confirm ductal and bile duct differentiation, respectively. You can check in addition to the usual markers of lineage differentiation, numerous markers are used to identify cell lines with various specific outcomes. Nestin has been shown to be expressed only in intermediate-type stem-like cells, so expression should be considered when performing a differential diagnosis. In addition to specific diagnostic functions, comprehensive knowledge of key regulatory molecular phylogenies in intracellular signaling pathways is of great importance for effective therapeutic approaches.

Conclusions

Despite advances in defining criteria and classifications, diagnosis of liver tumors remains a challenge. Although great strides have been made in molecular characterization, further research is essential to elucidate new state-of-the-art therapeutic approaches. In recent years, several efforts have been made to noninvasively pursue diagnosis and reveal predictive and prognostic factors for hepatocellular carcinoma. Liquid biopsy describes a technique to detect circulating tumor cells (CTCs) by either indirect immunolabeling or reverse transcription-polymerase chain reaction (RT-PCR)-based methods. An approach that combines serum markers and their CTC measurements has shown promising results. Two studies significantly improved detection sensitivity in relatively large cohorts of 222 and 395 HCC patients.

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