Alpha-Fetoprotein : Its Diagnostic Role in Hepatocellular Carcinoma

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Hepatocellular carcinoma (HCC) is the most common cancer of the liver in the world with hepatitis viral infection as the most common etiology globally[1,2]. These are hepatitis B virus (HBV) 53% and hepatitis C virus (HCV) 25%[1] . The other risk factors are obesity, alcohol and diabetes but less common than hepatitis B or C viral infection[2]. Patients with high risk of HCC should be evaluated periodically (every 6 months) with abdominal ultrasound as the first imaging modality and combine with alpha-fetoprotein (AFP)[3].

ALPHA-FETOPROTEIN AS A DIAGNOSTIC TOOL OF HCC

Alpha-Fetoprotein (AFP) is an alpha-1 globulin containing glycoprotein. It's level increase not only in HCC but also in other conditions, such as pregnancy, chronic liver inflammation, and acute liver injury, so that it's not specific for HCC itself.[1] Based on its binding capability to lectin Lens Culinaris Agglutinin (LCA) the AFP is separated into three different glycoforms, AFP-L1, AFP-L2, AFP-L3. AFP-L1 does not bind LCA and mostly produced by non malignant hepatocytes in chronic hepatitis B infection or liver cirrhosis[1,5]. AFP-L2 has intermediate binding affinity to LCA and this glycoform is produced by yolk sac tumors and also can be detected in normal pregnancy[1]. AFP-L3 does bind LCA and this marker is produced by malignant hepatocyte with current cut off value more than 10%[1,5]. AFP-L3 can be detected in 35% patients with small HCC (less than 2 cm)[3,5]. Imaging techniques combined with AFP-L3 showed the 56% sensitivity and 95% specificity[3]. Nevertheless, it is not common to use AFP-L3 as HCC tumor marker in daily clinical practice.[15,16]

DIAGNOSIS OF HEPATOCELLULAR CARCINOMA BASED ON GUIDELINES

Most guidelines recommend only total AFP, not AFP-L3, in combination with abdominal ultrasound (US) for HCC surveillance. APASL guideline determined AFP 200 ng/mL as the cut off value in combination with US for HCC surveillance but not as a diagnostic tool. In its current HCC guideline[6], AASLD also did not recommend AFP as the only diagnostic tool to establish the diagnosis of HCC, eventhough the cut-off 400ng/mL was previously recommended as diagnostic criterion of HCC[3,7,8] . The reasons are that elevated AFP levels can be found in other malignancy including intrahepatic cholangiocarcinoma and germ cell tumors[3,9]. However, abdominal US plus AFP examination biannually is recommended for surveillance with sensitivity 61% and specificity 95%[3,5]. Imaging tools such as Multiphase CT or MRI is the main diagnostic tool to establish the diagnosis of HCC and if the patients have non characteristic of imaging it is advised to undergo liver biopsy, independent of AFP level[3,10,11,12,13]. EASL guideline,unequivocally, did not mention AFP level as a diagnostic tool to establish the HCC diagnosis[5]. The prognostic value of AFP also inconclusive. The latest Japan Society of Hepatology (JSH) Consensus Statement (2021) also did not mention AFP as a diagnostic tool of HCC[14]. Cross -sectional study in Indonesia showed that AFP still can be used for HCC surveillance[9]

CONCLUSION

AFP plus abdominal ultrasound have an important role in HCC surveillance of high risk patients, eventhough AFP doesn't have a definitive role to establish the diagnosis of HCC.

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