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HCV RELATED CLD- LIFELONG SURVELLIANCE FOR HCC IS MUST

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ABSTRACT **Introduction-**.HCV-related hepatocellular carcinoma (HCC) is a major cause of cancer mortality, often arising 20–40 years after infection, almost always in the presence of cirrhosis. While direct-acting antivirals (DAAs) offer a high cure rate (sustained virological response, SVR), reducing HCC risk, it is not completely eliminated. HCV induces chronic inflammation, oxidative stress, and cirrhosis, which drive carcinogenesis. The risk factors are increased risks include male gender, older age at infection, alcohol abuse, metabolic syndrome (diabetes, steatosis), and genotype 1b or 3. Patients with HCV-associated cirrhosis require regular monitoring (typically 6-month ultrasound). **Case Report-** We report a sixty-six-year-old female, a known case chronic hepatitis C related chronic liver disease and was treated nine years back with oral antiviral for 24 weeks with sofosbuvir 400 mg and velpatasvir 100 mg. She achieved sustained virological response after 12 weeks of treatment. Her ultrasonogram abdomen showed altered echotexture with moderate ascites and upper gastro-intestinal endoscopy revealed grade two oesophageal varices for which she was started on tablet carvedilol 3.125 mg twice daily with diuretics and other supportive therapy. Her baseline alphafeto protein level was in normal range. She was advised for every six monthly ultrasonogram (USG) abdomen with serum alphafeto protein level, as a part of HCC surveillance which was done regularly. She remained well for next nine years on regular medications. For last three months, she developed anorexia, generalized fatigue, increased decompensation as evidenced by increased abdominal distension due to ascites and development of bilateral edema. There was no history of fever, weight loss, haematemesis, melena, altered sleep pattern or behaviour, bladder or bowel symptoms, breathlessness on exertion or rest. On biochemical evaluation complete hemogram revealed pancytopenia, liver function test was deranged i.e. there was mild hyper bilirubinaemia, transaminitis, hypoproteinaemia and hypoalbunemia. The complete lipid profile was in below normal range but renal function test, serum electrolytes and blood sugar level were in normal range. The patient was referred for medical and surgical oncological consultation but later on lost to follow-up. **Conclusion-** HCV patients who have significant fibrosis or cirrhosis, even after achieving SVR have to be mandatory on surveillance for HCC by six monthly ultrasonogram abdomen and alphafeto protein level or earlier, if development of any new symptoms or on occurrence of deterioration. The achievement of SVR does not guarantee against development of HCC; hence lifelong vigil is required for the same.

KEYWORDS : Hepatocellular Carcinoma, Chronic Liver Disease, Hepatitis C Virus, Triple Phase Ct Scan, Alpha Fetoprotein Level

INTRODUCTION

Chronic hepatitis C virus (HCV) infection is a major cause of hepatic fibrosis and cirrhosis, with a risk for the development of hepatocellular carcinoma (HCC). Although highly effective direct-acting antivirals (DAAs) are available, the incidence, morbidity, and mortality of HCV-associated HCC are still high [1]. HCV is an uncommon for RNA viruses, as it manages to persist in up to 80% of cases, leading to chronic hepatitis C (CHC) with a high risk of developing fibrosis, cirrhosis, and eventually hepatocellular carcinoma (HCC). Annually, 1–4% of cirrhotic CHC patients develop HCC, the most common form of primary liver cancer, which has the third highest mortality among all cancer entities [2,3]. While cirrhotic liver disease generally increases the risk of developing neoplastic lesions, the annual incidence of de novo HCC is reported to be up to twofold higher in patients with HCV-related cirrhosis compared to other etiologies, such as autoimmune hepatitis [4], metabolic-associated fatty liver disease, and alcoholic fatty liver disease [5]. Furthermore, HCV-associated HCC can develop even in the absence of cirrhosis [6]. Thus, HCV poses a specific and significant risk for cancer development.

Case Report

We report a sixty-six-year-old female, a known case chronic hepatitis C related chronic liver disease and was treated nine years back with oral antiviral for 24 weeks with sofosbuvir 400 mg and velpatasvir 100 mg. She achieved sustained virological response after 12 weeks of treatment. Her ultrasonogram abdomen showed altered echotexture with moderate ascites and upper gastro-intestinal endoscopy revealed grade two oesophageal varices for which she was started on tablet carvedilol 3.125 mg twice daily with diuretics and other supportive therapy. Her baseline alphafeto protein level was in normal range. She was advised for every six monthly ultrasonogram (USG) abdomen with serum alphafeto protein level, as a part of HCC surveillance which was done regularly. She remained well for next nine years on regular medications. For last three months, she developed anorexia, generalized fatigue, increased decompensation as evidenced by increased abdominal distension due to ascites and development of bilateral edema. There was no history of fever, weight loss, haematemesis, melena, altered sleep pattern or behaviour, bladder or bowel symptoms, breathlessness on exertion or rest. On biochemical evaluation complete hemogram revealed pancytopenia, liver function test was deranged i.e. there was mild hyper bilirubinaemia, transaminitis, hypoproteinaemia and hypoalbunemia. The complete lipid profile was in below normal range but renal function test, serum electrolytes and blood sugar level were in normal range. The patient was referred for medical and surgical oncological consultation but later on lost to follow-up.

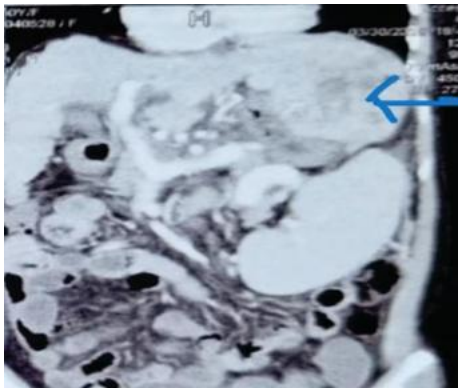

Figure 1- Triple Phase CT Scan Abdomen Showing Hepatocellular Carcinoma in Left Lobe Liver in SVR Achieved HCV Related Chronic Liver Disease Patient

DISCUSSION

Hepatitis C virus (HCV) is an RNA virus responsible for liver inflammation and the development of hepatocellular carcinoma (HCC). It is estimated that 1.5 million individuals are infected with HCV every year. However, only 20%–30% develop liver cirrhosis, of which 1%–4% develop HCC. Cancer induction appears to be rather indirect, crucially involving chronic inflammation and the establishment of a pro-tumorigenic environment, with a potentially stable and self-sustaining metabolic and epigenetic reprogramming. The remaining risk for patients to develop HCC even after SVR, hence, appears to be due to a sustainable impact on liver homeostasis as a consequence of infection. While direct interactions of HCV RNA or proteins with oncogenic pathways within the infected hepatocytes themselves might still contribute to carcinogenesis to a certain degree [7, 8]. HCV-associated HCC typically develops after years to decades of chronic infection. Ongoing elimination of infected hepatocytes by immune cells and cell death upon virus-induced stress continuously trigger regenerative hepatocyte proliferation [9]. The inherent risk of genetic mutations due to erroneous DNA replication is aggravated by oxidative damage [10]. This is mainly caused by reactive oxygen species (ROS), secreted by immune cells [11] or released from the mitochondria of infected hepatocytes [11,12]. HCV severely interferes with the host fat metabolism not only in infected cells in vitro but also in patients [13]. It alters the lipid composition in the circulation [14,15] and frequently induces steatosis [16,17], which is associated with a significantly higher incidence of HCC and mortality [18]. Steatosis is furthermore a major predictor of poor outcomes after SVR [19] as it often persists or even deteriorates [20, 21] after viral clearance. In combination with dysregulated lipid metabolism and steatosis, the resulting hyperinsulinemia can lead to an antiapoptotic, proproliferative, and, thus, tumor-promoting environment in the liver [22]. During tumor evolution, cancer cells may then adapt and develop their own strategies of immune evasion [23]. Chronic inflammation induces fibrosis and ultimately cirrhosis. This process is associated with the secretion of growth factors, immune suppression, and angiogenesis and is, therefore, tightly linked to HCC development [24]. Indeed, the degree of fibrosis is an important risk factor for HCC development in CHC, even after SVR [25]. There is evidence that in addition to chronic inflammation, HCV directly contributes to fibrogenesis. For patients treated in advanced stages of liver disease, the American Association for the Study of Liver Diseases (AASLD) recommends surveillance for HCC in SVR patients with cirrhosis [26], while the European Association for the Study of the Liver (EASL) recommends screening already from advanced fibrosis (METAVIR score F3) onwards [27]. Hepatocellular carcinoma (HCC) is more common in the right lobe of the liver. Based on a study of 322 HCC nodules, 72.7% (234 nodules) were situated in the right lobe, compared to 24.5% (79 nodules) in the left lobe and 2.8% (9 nodules) in the caudate lobe. HCC is most common in segment 8 (the superior-posterior segment of the right lobe). The right lobe is more frequently affected due to its larger size and the higher volume of blood it receives from the superior mesenteric vein, which carries pathogens and toxic substances directly into the right liver parenchyma, potentially causing higher rates of cirrhosis, which is a major precursor to HCC. While less common, left-sided tumours (segments 2, 3, and 4) are associated with a poorer prognosis in some studies, often due to later diagnosis, larger tumor size, or increased microvascular invasion. Though rare, HCC can occur in an accessory liver lobe, with most reported cases also located on the right. Our case was also on left lobe of liver which is uncommon and occurred after even after successful achievement of SVR.

CONCLUSION

HCV patients who have significant fibrosis or cirrhosis, even after achieving SVR have to be mandatory on surveillance for HCC by six monthly ultrasonogram abdomen and alphafeto protein level or earlier, if development of any new symptoms or on occurrence of deterioration. The achievement of SVR does not guarantee against development of HCC; hence lifelong vigil is required for the same.

Conflict of Interest

The authors declare that there was no conflict of interest or any kind of funding was taken for publishing this case report.

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