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De Novo Hepatocellular Carcinoma (HCC) in Non-Cirrhotic Chronic Viral Hepatitis C (HCV) Patients: A Case Series

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INTRODUCTION

Chronic hepatitis C (HCV) is a primary risk factor for hepatocellular carcinoma (HCC), typically associated with advanced fibrosis and cirrhosis. However, the development of HCC in non-cirrhotic patients with chronic HCV is exceedingly rare, occurring in less than 1.5% of cases. We present a case series highlighting two instances of HCC in non-cirrhotic HCV patients..

CASE 1

A 67-year-old male with a history of chronic myeloid leukemia (CML) in remission and treatment-naive chronic HCV (genotype 1b) was referred for HCV treatment. Imaging revealed five LIRADS-5 liver lesions and liver biopsy confirmed mild portal fibrosis without septa (F1) and moderately differentiated HCC. The patient underwent hepatic resection followed by successful HCV treatment.

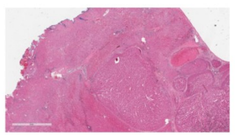

Figure 1: HE show Polygonal cells with nuclear atypia, including high N/C ratio, irregular nuclear membrane, multinucleation and prominent nuclei(scanning lower power)

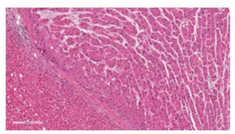

Figure 2: HE show polygonal cells with nuclear atypia, including high N/C ratio, irregular nuclear membrane, multinucleation and prominent nuclei(scanning higher power)

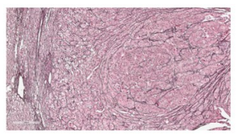

Figure 3: A reticulin stain performed highlights the thickened hepatocyte plates (> 3 cell thick) supports the diagnosis of hepatocellular carcinoma (scanning higher power).

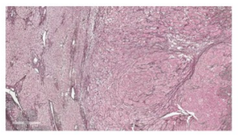

Figure 4: A reticulin stain performed highlights the thickened hepatocyte plates (> 3 cell thick) supports the diagnosis of hepatocellular carcinoma (scanning lower power).

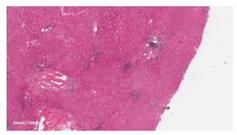

Figure 5: HE staining show periportal fibrosis, focal bridging and lymphocytes infiltration (scanning power).

CASE 2

A 69-year-old male with chronic HCV (genotype 3) achieved sustained virological response (SVR) four years prior, and presented with two LIRADS-5 liver lesions. A liver biopsy revealed mild portal fibrosis without septa (F1) and confirmed HCC. Yttrium-90 radioembolization was performed with a favorable response.

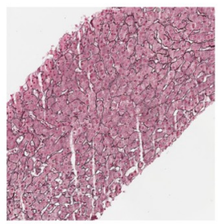

Figure 6: Liver Reticulin Normal

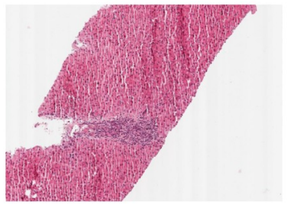

Figure 7: Liver Biopsy with Inflammation and pathology

DISCUSSION

- Chronic viral infections, particularly hepatitis B (HBV) and hepatitis C (HCV), are leading causes of primary hepatocellular carcinoma (HCC).
- HBV can cause HCC in non-cirrhotic individuals due to its ability to integrate with the host genome, leading to cell cycle dysregulation.
- HCV, being an RNA virus, cannot integrate with host DNA but can promote hepatocyte immortalization, potentially leading to HCC.
- Alcohol use, toxin exposure, and cirrhosis are major risk factors for HCC development.
- Rare cases of HCC in non-cirrhotics with HBV have been reported, while HCC in non-cirrhotics with chronic HCV is less common.
- Some cases of HCC in non-cirrhotics occur after achieving sustained virologic response (SVR) post-HCV treatment.
- The incidence of HCC in non-cirrhotic HCV patients is low but not negligible.
- Co-infection with HBV could contribute to HCC development in non-cirrhotics, although ruled out in the presented cases.
- Retrospective studies have shown a higher prevalence of HCC in non-cirrhotics with chronic HCV infection, especially among men.
- Screening guidelines post-HCV treatment in non-cirrhotics vary, with some advocating for routine screening in certain risk groups to detect HCC early.
- Latest guidelines (as of 2023) may not recommend routine follow-up for non-cirrhotic patients post-HCV treatment unless they have specific risk factors.
- Small sample size notwithstanding, the presence of Lirads-5 lesions in the presented cases adds to the understanding of HCC in non-cirrhotics.

CONCLUSION

The possibility of developing HCC in non-cirrhotic HCV patients even without advanced fibrosis raises the question regarding the need to perform closer screening/follow-up of these patients, even after SVR. Further studies with considerations given to genotype and gender to confirm these findings are needed.

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