5-2020

Development of Hepatocellular Carcinoma after Achieving Sustained HCVVirologic Response and Regression of Cirrhosis

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Development of Hepatocellular Carcinoma after Achieving Sustained HCV-Virologic Response and Regression of Cirrhosis

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Abstract

Introduction: Hepatocellular carcinoma (HCC) in a background of chronic Hepatitis C virus (HCV) infection is an emerging cause of cancer mortality. Interferon/ribavirin and direct acting antiviral (DAA) therapy have successfully treated HCV infection and may halt the progression of fibrosis. It is generally believed that achieving sustained viral response (SVR) could decrease the incidence of HCC by slowing down fibrosing process; hence preventing progression of cirrhosis.

Method:
Sixty-four-year-old female who was successfully treated for HCV infection with interferon and achieved sustained viral response (SVR) with regular follow-up. She presented with abdominal pain after more than 20 years. CT scan revealed a liver mass which was subsequently biopsied and proven to be HCC. Patient was treated with partial hepatectomy and histologic examination of the resected liver mass revealed well-differentiated HCC; non-neoplastic liver demonstrated features of regression of cirrhosis/fibrosis with fibrous expansion of few portal tracts and scattered very fine curvilinear fibrous septa; no portal/lobular inflammation was present.

Results:
The patient developed HCC more than 20 years after achieving SVR. Significant regression of cirrhosis/fibrosis in the non-neoplastic liver argues against the usual course of HCC development in cirrhotic/advanced fibrotic setting, and suggests the possibility of an alternative phenomenon, e.g., latency of HCV and/or oncologic potential of HCV at the genomic level.

Conclusion:
This rare event raises questions regarding relationship between regression of cirrhosis/fibrosis and developing HCC which are currently under investigation.

Background

- Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related deaths worldwide[1].
- Patients with HCV-induced cirrhosis are at particularly high risk for the development of HCC, with an annual incidence of HCC ranging from 0.5% to 10%[2].
- It is generally believed that HCC primarily occurs in the background of HCV- related cirrhosis; theoretically, achieving sustained viral response (SVR) could decrease the incidence of HCC by slowing down fibrosing process; hence preventing progression of cirrhosis.
- Interferon/ribavirin and direct acting antiviral (DAA) therapy have successfully treated HCV infection and may halt the progression of fibrosis.
- Sustained virologic response (SVR) with DAA has emerged as the most dominant modifier of HCC in patients with HCV[2].

Methods

- 64-year-old female initially presented with chronic hepatitis C viral infection with progressive cirrhosis and fibrosis.
- She was successfully treated for HCV infection with interferon in 1994 and achieved sustained viral response (SVR) with regular follow-up.
- Twenty-three years after achieving SVR, she presented to the gastroenterology clinic with abdominal pain in June 2017.
- Physical examination was unremarkable.
- CT scan revealed a 2 cm hyperattenuating liver mass which was subsequently biopsied and proved to be well-differentiated hepatocellular carcinoma (HCC).

Photos

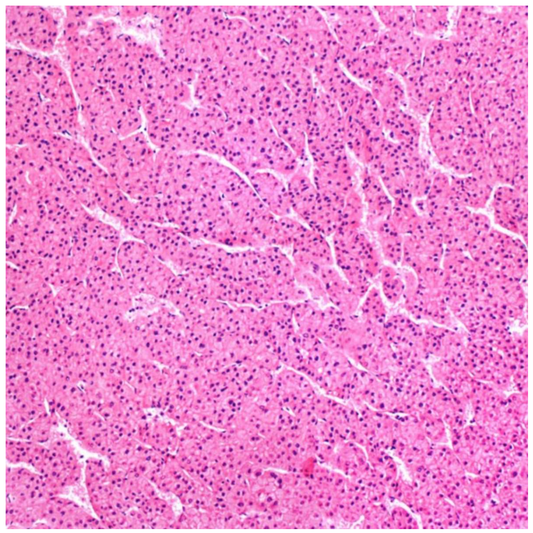

Figure 1. H&E demonstrating well differentiated hepatocellular carcinoma.

Results

- Patient was treated with partial hepatectomy.
- Histologic examination of the resected liver mass revealed well-differentiated HCC.
- Non-neoplastic liver demonstrated features of regression of cirrhosis/fibrosis with fibrous expansion of few portal tracts and scattered very fine curvilinear fibrous septa; no portal/lobular inflammation was present.

Conclusions

- The patient developed HCC twenty-three years after achieving SVR.
- Significant regression of cirrhosis/fibrosis in the non-neoplastic liver argues against the usual course of HCC development in cirrhotic/advanced fibrotic setting, and suggests the possibility of an alternative phenomenon, e.g., latency of HCV and/or oncologic potential of HCV at the genomic level.
- This rare event raises certain questions which have not been properly investigated in the course of HCC development, such as:
  - Relationship between regression of cirrhosis/fibrosis and developing HCC;
  - Does absence and regression of cirrhosis/fibrosis carry the same value;
  - Necessity of updating the surveillance criteria in patient with SVR lacking cirrhosis; and
  - Oncologic potential of HCV acquired at the genomic level; these questions/issues are currently under investigation.

Sample Bibliography

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010(127):2893–917.
2. Kulik L, El-Serag HB. Epidemiology and Management of Hepatocellular Carcinoma. Gastroenterology. 2019;156(2):477-491.e1. doi:10.1053/j.gastro.2018.08.065