Steatohepatic Hepatocellular Carcinoma—A Case Report with Literature Review

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Abstract We report a case of a 65 year old male who presented with complaints of pain right upper abdomen for past 3 months. He was a known diabetic and hypertensive. On evaluation he was found to have space occupying lesion in the right lobe of the liver. USG Guided FNC done showed a Hepatocellular Carcinoma with predominant steatosis. He underwent Right Hepatectomy for the same and Histopathological examination revealed a Steatohepatic Hepatocellular Carcinoma with background liver showing minimal steatosis and no significant fibrosis. This case is reported to provide better insight into the understanding of pathophysiology of metabolic syndrome as an etiological agent for development of HCC.

Keywords Steatohepatic Hepatocellular Carcinoma (SH-HCC) · Hepatocellular Carcinoma (HCC) · Metabolic syndrome · Non alcoholic fatty liver disease (NAFLD) · Non alcoholic steatohepatitis (NASH)

Introduction

SH-HCC is a recently described morphological variant of HCC. Only three case series of SH-HCC have been published in the indexed English literature till date. Most cases of SH-HCC in these series were found to be associated with NAFLD/NASH with an underlying metabolic syndrome. We report a case of SH-HCC in a patient of metabolic syndrome but without any significant liver dysfunction or fibrosis.

This case also emphasizes the need for cancer surveillance in patients of metabolic syndrome.

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Case Report

We report a case of a 65 year old male who is a known diabetic and hypertensive for last 20 years and had been on regular medication. Patient presented with complaints of pain upper abdomen for last 3 months. There was no history of jaundice/fever/weight loss. On examination there was no icterus. On Per abdomen examination abdomen was soft, non tender, with no organomegaly or free fluid. Lab Investigations done showed a serum bilirubin of 0.7 mg/dl (0.3–1.2), AST 46 IU/L (5–40), ALT 73 IU/L (10–40), Serum alkaline phosphatase was 62 IU/L (32–92), GGT 62 IU/L (7–64) and Albumin/Globulin ratio 1.6 (1.5–2.5) with an INR of 1.1. However his AFP and PIVKA II levels were elevated 9.91 ng/ml (0–8.5) n and 16 ng/ml (0–2) respectively. His lipid profile showed serum cholesterol as 250 mg/dl (<200) and triglycerides 160 mg/dl (35–150), HDL Cholesterol 44.4 mg/dl (35–85) and LDL Cholesterol was 110 mg/dl (<150). His viral markers done for Hepatitis B and C were negative.

MRI Abdomen done showed a relatively well margined nodular mass in the right lobe measuring 4.6×4.3×4.8 cm at segment V/VI junction displaying enhancement characteristics of Hepatocellular Carcinoma (Fig. 1).

USG Guided FNA had done from the mass showed a cellular smear with trabecular fragments of atypical hepatocytes with transgressing vessels. Mild to moderate steatotic vacuoles noted within the cytoplasm. Findings were consistent with HCC with predominant steatotic component (Fig. 2).

Patient underwent Right Hepatectomy for the same.

Histopathological Examination

Gross—Right Hepatectomy specimen measured 15×14×7 cm. Outer surface was well encapsulated. Serial sections revealed a tumor mass measuring 5×3.5×3 cm. located 2.5 cm away from the closest resected margin.

Fig. 1 MRI scan showing a well margined mass in right lobe of liver

The adjacent uninvolved liver parenchyma appears unremarkable.

Microscopic Examination—from the tumor mass showed a malignant neoplasm composed of atypical hepatocytes arranged predominantly in trabecular and pseudoacinar pattern having pleomorphic vesicular nuclei, prominent nucleoli and moderate cytoplasm. Focal areas of bizarre cells and tumor giant cell noted. Several areas within the neoplasm show prominent macrovesicular steatosis, ballooning degeneration and foci of inflammation seen occupying >50 % of the tumor area (Fig. 3). Adjacent liver tissue show minimal macrovesicular steatosis in perivenular region with no significant fibrosis. Immunohistochemistry did show positive staining for glutamine synthetase (Fig. 4), HepPar 1 and canalicul positivity for Polyclonal CEA.

Fig. 2 Cytological Smears showing atypical epithelial cell with pleomorphic nuclei, prominent nucleoli and moderate cytoplasm with steatosis (Geimsa $\times$ 40)

Fig. 3 Histopathological examination showing neoplastic hepatocytes with moderate steatosis and ballooning degeneration (H & E $\times$ 10)

Final diagnosis was rendered as Steatohepatic Hepatocellular Carcinoma with adjacent liver showing minimal steatosis.

Discussion

Most cases of HCC develop in cirrhosis resulting from chronic infection by hepatitis B virus and Hepatitis C Virus, alcoholic injury and lesser extent from genetically determined disorder like Hemochromatosis [1, 2]. However in about 15–50 % cases the etiology of HCC remains unclear.

NAFLD including NASH is rapidly evolving as a significant risk factor for development of primary Hepatocellular

Fig. 4 Immunohistochemical staining for Glutamine Synthetase (Original magnification $\times$ 10)

carcinoma as has been elaborated by a number of studies including a beautiful review by Baffy et al. of the same [3].

NAFLD has now emerged as a independent risk factor for HCC even without cirrhosis. This association is alarming due to global prevalence of NAFLD.

Salomao et al. in 2010 described a new variant of Hepatocellular carcinoma in explants liver of patient of chronic hepatitis C virus—Steatohepatic Hepatocellular carcinoma. Most cases of SH HCC showed features of NASH/NAFLD [4]. They first postulated a possible NAFLD/NASH pathway leading to SH-HCC.

In the subsequent years in 2012 Salomao et al. again reported another series of HCC in which SH-HCC constituted 16/118 of explants HCC's [5]. They also proposed a histological criteria for diagnosis of SH-HCC. The criteria states as 3 of the 5 features required in >50 % of the tumor mass to be diagnosed as SH-HCC. The five features included were steatosis, ballooning degeneration, Mallory Denk Bodies, inflammation and pericellular fibrosis. The criterion proposed was simple. However it lacks reproducibility among experienced and less experienced histopathologist. In our opinion steatosis and ballooning degeneration should be included into the major features and remaining three in minor features with the diagnosis of SH-HCC should include one major and two minor features.

Again in this series the authors emphasized that SH-HCC is strongly associated with steatohepatitis and metabolic syndrome.

Another study from India by Jain et al. in 2013 also illustrated similar association of SH-HCC with the metabolic syndrome [6].

The similar findings were also seen in our patient with SH-HCC developing in a background of metabolic syndrome in the absence of cirrhosis.

Conclusion

There are several growing portfolio work suggesting that metabolic syndrome can progress to Hepatocellular carcinoma even without the development of liver dysfunction. However, more epidemiological, clinical and molecular pathogenesis data are needed to determine the relative contribution of obesity, Diabetes Mellitus and NAFLD leading to development of HCC. These studies will open gates for development of a cancer surveillance plan for the potentially effected population.

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