Hepatocellular Carcinoma in a Patient with Huge Focal Nodular Hyperplasia (Case Report and Review of Literature)

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Abstract: Focal Nodular Hyperplasia (FNH) is a benign hepatic tumor usually affecting reproductive age of females and also has association with oral contraceptive. A few cases have been reported of co-existent FNH and Hepatocellular carcinoma (HCC) of the liver in the literature. We are dealing with a case of a 72-year-old, male patient , diagnosed HCC shortly after resection of a huge focal nodular hyperplasia of the liver.

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1. Introduction

Focal Nodular Hyperplasia (FNH) is hyperplasia of liver parenchyma characterized by the presence of central stellate scar (1,2,3,&5). Though it is the second most common benign tumor of the liver after venous hemangioma and its occurrence remains rare accounting for 21%-27% of all benign liver tumor (3-5% of all liver tumors). The presence of FNH simultaneously with fibrolamellar carcinoma (FL-HCC) or hepatocellular carcinoma (HCC) has been scarcely described. Almost, all the reported cases were females in the reproductive age (4-7). This is a report of an unusual huge; probably the largest reported FNH of the liver which was diagnosed in elderly man presented with right upper quadrant pain. HCC was diagnosed shortly after resection of the FNH in the same patient.

2. Case Report

A seventy-two- year-old man was presented to the emergency department complaining of upper abdominal pain after history of fall down from 4 meter height. He was diabetic and hypertensive for ten years on treatment. He denied any history of Alcohol intake. Physical examination on admission revealed abdominal tenderness and palpable right upper abdominal mass; there were no stigmata of chronic liver disease. Laboratory findings were entirely within normal range except for AST of 65 U/L and GGT: 1690 U/L. Serum Alfa-fetoprotein, CEA and CA19-9 were within normal range. Serology for hepatitis B and C was negative. Abdominal Ultrasound showed large solid mass of the liver measuring (11 x 10.4 x 15 cm) with central hypo echoic area. Contrast-enhanced abdominal computerized tomography (CT) scan revealed large (20 x 16 x 11cm) mass occupying the left liver lobe with central irregular hypo density and central scar consistent with Focal Nodular Hyperplasia (FNH). A follow up of Magnetic Resonance Imaging (MRI) of the liver was done and showed finding were again consistent with FNH **(Figure1)**. Two trial of embolization of the liver mass were failed. The patient was then operated upon where left hepatectomy was performed **(Figure2)**. Histopathology assessment of the resected mass revealed; grossly huge (24cm) well-demarcated, sub-capsular, light brown bulging solitary nodule that has central gray-white stellate scar with hemorrhagic and necrotic areas. Formalin fixed paraffin embedded sections were examined microscopically; the tumor showed hepatocytes' nodules surrounded by fibrous septa with the classic features of abnormal architecture, bile ductular proliferation and malformed vessels. **(Figure-3a)**; findings confirming FNH. Patient had completely uneventful post-operative course,

Three months later, the patient presented with abdominal pain, heart burn and weight loss of 15 Kilograms over a period of 3 months. His Physical examination findings were hepatomegaly, 6 cm below costal margin and significant loss of weight. Serum Alfa-FP and CA19-9 were slightly elevated (7.14 IU/ml and 39.64 IU/ml respectively). Patient underwent upper gastrointestinal endoscopy which revealed barrette's esophagus, grade 2 esophageal varices and gastritis. Abdominal CT scan was performed and has shown right hepatic lobe is studded with enumerable different small size hyper vascular lesions suggestive of Hepatocellular carcinoma (HCC) **(Figure 4)** and right basal pulmonary nodules. A needle core biopsy was taken from the liver lesion and sent for histopathology examination. Formalin fixed paraffin embedded

sections' examination confirmed the presence of thin plates of small hepatocytes with minimal nuclear atypia and abnormal reticulin network. A diagnosis of well differentiated HCC was made. **(Figure3b)** CT scan of the chest showed multiple pulmonary nodules in keeping with metastasis. Decision was made for palliative treatment, currently the Patient is following up with the gastroenterology team undergoing cessions of esophageal banding and taking Propranolol as secondary prophylaxis for esophageal varicies.

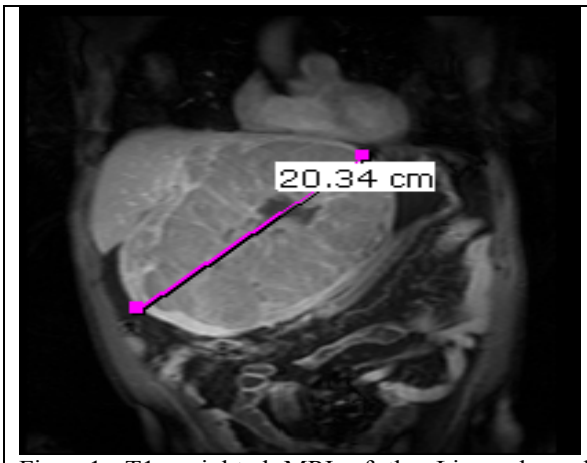

Figure1: T1 weighted MRI of the Liver showed defined rounded structure in the lift lobe of the liver with a central area of low segment intensity, consistent with FNH

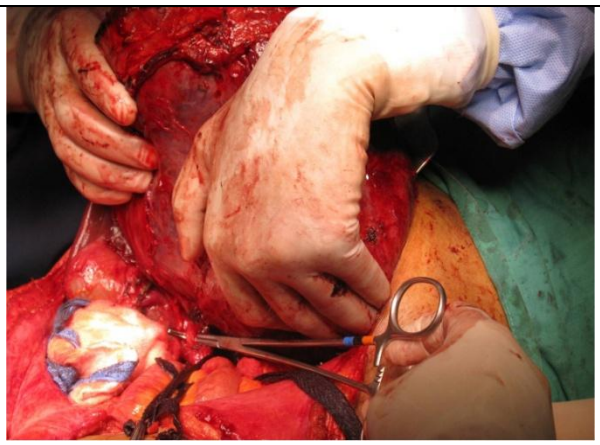

Figure 2: Intra-operative view of the mass.

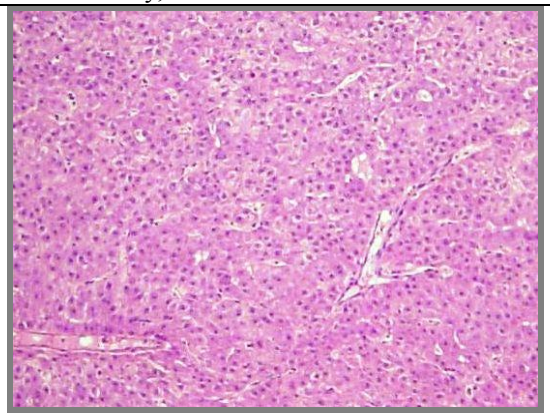

Figure 3A: Histopathology of the mass showed a benign hepatocytes separated by a fibrous setae with a mild sinusoidal dilatation with absence of portal vein branches and bile duct, consistent with FNH

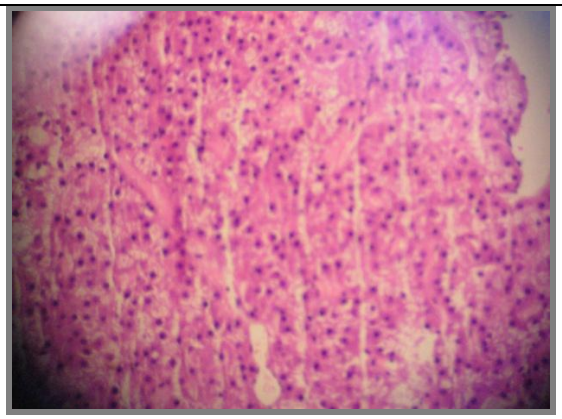

Figure 3B: Histopathology of the core biopsy from one of the new lesions discovered 3months after resection of the huge FNH, showed Hepatic tissue which is devoid of portal tract. Hepatic plates are thickened and the cells exhibit increase in N: C ratio with nuclear polymorphisms consistent with hepatocellular carcinoma.

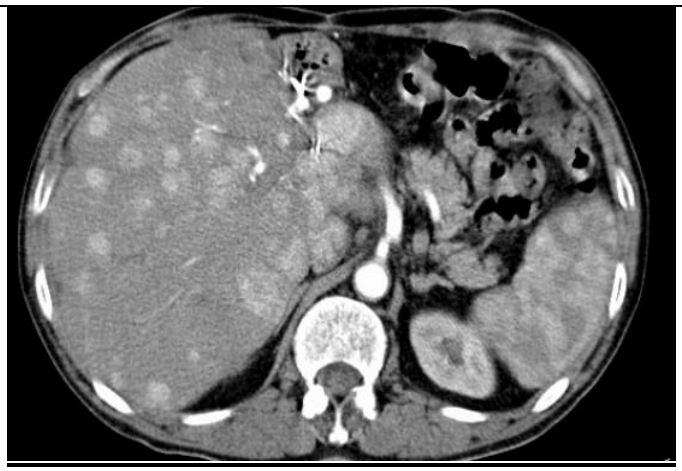

Figure 4: Arterial phase CT-scan of the liver post resection of the huge FNH, which showed multiple hypervascular hepatic lesions consistent with multiple HCC

3. Discussion

FNH, firstly described by Edmnson in 1956, It is the second most common benign tumor of the liver after hepatic hemangioma. (8). Up till now the nature and pathogenesis of FNH is still surrounded with a degree of controversy. However, in analysis of FNH cells in focus revealed that FNH is considered as type of reactive hyperplasia of liver cells to local liver lesion rather than a true tumor. While diagnosis of FNH depend largely on Doppler flow imaging (CDFI), computed tomography (CT) scan and magnetic resonance imaging MRI, all of these modalities have some limitation.(2,8,9,10 & 11). There is some difficulty in making the provisional diagnosis before operation. Because of the benign nature of FNH, therapy other than operation is the standard treatment especially if the patient is asymptomatic. However, invasive therapy like resection or embolization of the mass is recommended if there are symptoms. (9 & 10) as the case with our patient

Malignant transformation of benign liver tumor has been largely discussed in the literatures, with a considerable risk of hepatic adenoma to malignant transformation. Therefore, resection of the hepatic adenoma is recommended even if asymptomatic. On the other hand, FNH has no proven malignant potential so far. Nevertheless, presence of HCC lesions in the liver in close approximate to FNH lesion have been reported in the literatures, mostly in females of reproductive age using OCP (5, 12). Though no clear malignant potential of FNH lesion is evident, the noticeable accumulation of such cases in the literature justifies the need for further studies and assessment to identify any possible association between FNH and HCC and/or HCC and the use of OCP.

In the present case, FNH and HCC were diagnosed in an elderly man who retrospectively may have underlying compensating cryptogenic liver cirrhosis. No evidence of HCC lesion seen on images (CT) was done at initial presentation when FNH was diagnosed. Repeated CT at second presentation 3 months after the resection of huge FNH demonstrated multiple liver lesions consistent with HCC and the patient liver disease was clinically decompensating at this stage with bleeding varicies that needed band ligation. Whether presence of FNH or its size may mask imaging characteristics of co-existing HCC lesions, this needs further observation and studies.

There has been no reported association of FNH and cryptogenic cirrhosis in the literature to our knowledge and the literature we reviewed. The size of the FNH lesion in our patient is among the large if not the largest lesions reported in the literature.

In conclusion, differentiation between FNH and HCC needs a correct diagnosis and takes a appropriate therapeutic action. The reach to final diagnosis in the examined case does not exclude the others. The association between FNH and HCC is still an area of uncertainty but worth further meticulous observation and studies. Anticipation of HCC and meticulous search for it during the work up of FNH lesion and after the operative resection may be wise especially in females of reproductive age, who are using OCP and have FNH lesion and requiring resection and perhaps more so in elderly patients.

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