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Case Study

Hepatocellular Carcinoma in a non-B non-C Non-alcoholic Steatohepatitis (NBNC-NASH HCC)

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ABSTRACT

Introduction: Hepatocellular carcinoma (HCC) is the most common primary malignant liver tumour, which commonly occurs in those with underlying chronic liver problems mainly cirrhotic liver, with viral hepatitis (HBV and HCV) as the most common aetiological agent. HCC could also arise from non-cirrhotic liver, which include non-B non-C (NBNC) hepatitis, which is different in pathogenesis, epidemiology and prognosis. This disease entity would include the commonly benign fatty liver leading to non-alcoholic steatohepatitis (NASH) and HCC as sequelae. **Methods:** We present a case of non-B non-C HCC arising from a fatty liver in a non-alcoholic patient. Literature search was done with special emphasis on this disease. **Conclusion:** The incidence of NBNC HCC demonstrates an increasing trend, making it an important entity to be recognised early. A good understanding of this incidence would make it possible to predict the outcome, especially as the prognosis of non-B non-C HCC is fairly good if the HCC is found at an early stage.

Keywords: Hepatocellular carcinoma (HCC), imaging features, non-alcoholic steatohepatitis (NASH), non-B, non-C

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary malignant liver tumour with the majority of cases (50 – 80 %) arising from a setting of chronic liver parenchymal disease, mainly in a cirrhotic liver. Hepatitis B (HBV) and C (HCV) viruses have been implicated as the most common aetiological agent particularly in Asian and African subcontinents, whereas in the West, it is attributed to excessive alcohol consumption. In a minority of cases, HCC arises from a non-cirrhotic liver. Those with no known aetiological agent are duped as non-B non-C (NBNC) HCC. This would include the previously assumed benign condition, non-alcoholic steatohepatitis (NASH). We report a case of NBNC non-cirrhotic fatty liver which presented with left lobe HCC.

THE CASE

A 66-year-old Malay man presented to the emergency department, complaining of left hypochondrial and epigastric pain of one year duration, which worsened on the day of

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admission. He was previously diagnosed to have gastritis and managed at a local clinic. There was no history of blood transfusion, intravenous drug abuse, exposure to toxins, or alcohol intake. He also denied any significant loss of weight. Clinical examinations revealed an epigastric mass. No stigmata of chronic liver disease were noted.

Routine laboratory investigations and liver function tests were normal. Serum Alpha fetoprotein had a normal value of 3.03ng/ml (normal range: <8.2ng/ml). Hepatitis B and C serology tests were negative. An abdominal multislice computed tomography (MSCT) with dynamic contrast scanning revealed a large mass involving the left lobe of the liver measuring 8.9 x 9.2 x 9.1 cm in diameter. The mass was heterogenous in appearance and showed arterialised enhancement with significant contrast wash out during the portal venous phase (Figure 1(a) – 1 (c)). There was no evidence of vascular involvement or thrombosis. The presence of multiple hypo-attenuation in the centre suggested necrosis. The rest of the liver showed generalised hypo-attenuation in keeping with fatty liver. There were no features to suggest liver cirrhosis.

A diagnosis of left lobe liver lesion, either fibrolamellar HCC, focal nodular hyperplasia or metastases, was given as the differential diagnoses. Diagnosis of HCC was not prioritised in view of non-cirrhotic liver and negative hepatitis screening.

Lateral hepatic segmentectomy was carried out. The tissue sample was sent for histopathological examination. Grossly, a well-defined encapsulated mass with a yellow tan due to fatty metamorphosis, with focal haemorrhage and firm in consistency was found. No evidence to suggest tumour thrombo-emboli was noted. Evidence of background liver cirrhosis was not demonstrable. No involvement of liver capsule was observed. Histopathologically, the tumour was well encapsulated with cytological malignant features (as evidenced by nuclear pleomorphism and mitoses). Cholestasis was absent. There were patchy areas of tumour necrosis. The surrounding liver parenchyma showd an increase in

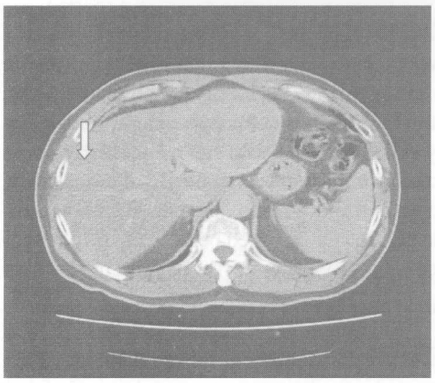

Figure 1 (a). Plain image of the liver showing diffuse hypodensity, in keeping with fatty change (arrow).

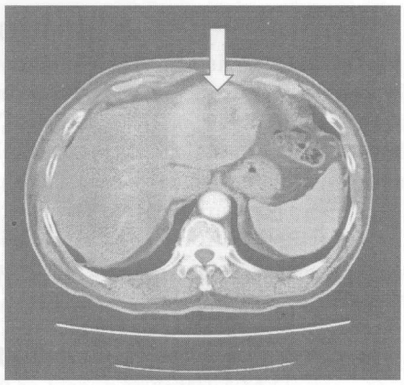

Figure 1 (b). Dynamic scanning in hepatic arterial phase, showing the mass enhanced intensely following i.v contrast (white arrow)

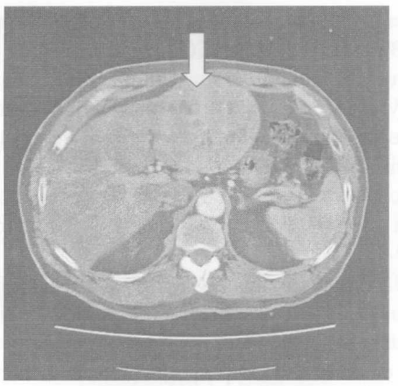

Figure 1 (c). Dynamic scanning in porto-venous phase, showing the mass appear isodense to the surrounding liver parenchyma.

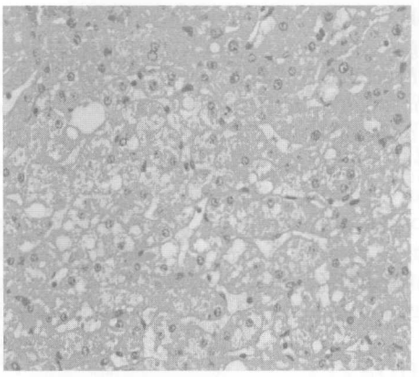

Figure 2 (a). The surrounding liver tissue shows microvesicular steatosis (fatty change), (20 x magnification)

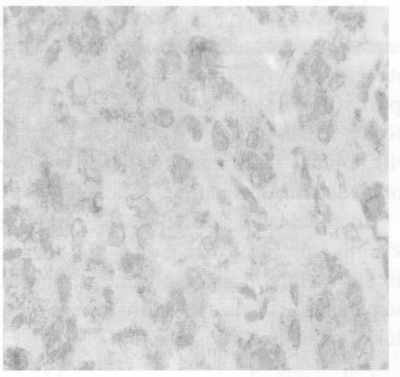

Figure 2 (b). Positive for alphafetoprotein immuno-histochemical stain (40 x magnifications) of the cells taken from the mass.

fibrosis and areas of steatosis with features of chronic hepatitis (Figure 2 (a)). Excision margins were free from the tumour. Immunostains tested positive for alpha fetoprotein which confirmed the diagnosis of HCC (Figure 2 (b)).

He was well during discharge and no complications or evidence of recurrence was noted at 3 months follow-up.

DISCUSSION

In this patient, an absence of history of alcohol consumption and normal liver function tests were noted. The histological findings did not meet the criteria for viral hepatitis, haemochromatosis, autoimmune hepatitis or primary biliary cirrhosis as the aetiologies

ɔonsible for HCC. Imaging features showed absence of cirrhosis. Excluding all the above ıtioned causes, non-B non-C (NBNC) HCC were considered.

NBNC HCC is frequently found in cases without underlying liver cirrhosis (as in this e). Epidemiologically, it tends to be in older age groups and associated with alcohol ıse. Histologically, the hepatic inflammation and fibrosis were less severe. In early stage, ɜNC patients show significantly better prognosis than HBV-HCC and HCV-HCC. Although difference in recurrence rate post-resection, the survival after detection of HCC recurrence ıs markedly better than that of HBV or HCV patients attributed to good liver function (less sociation of liver cirrhosis). [1,2]

The incidence of NBNC is approximately 5-15% of all HCC. There is evidence showing ɔn-alcoholic steatohepatitis (NASH) as the causitive factor for NBNC HCC.[3, 4] As part of ıe spectrum of previously thought benign non-alcoholic fatty liver disease (NAFLD), lASH was first used to describe the morphologic pattern of liver injury with evidence of lcoholic hepatitis and steatosis on liver biopsy, with no history of alcohol abuse. The ıajority of the patients were obese with some of them showing evidence of hyperlipo- ɔroteineamia and adult-onset diabetes mellitus or both.

Unfortunately, the natural history of NASH is poorly defined and often detected late as :here are no serum markers for NASH. Cryptogenic cirrhosis may be the representative of a late stage of NASH, which loses its features of necroinflammatory activity and steatosis in up to 80% of patients (i.e., burnt-out NASH). A definitive diagnosis would require liver biopsy, which shows the hallmark feature of moderate to severe macrovesicular steatosis with lobular inflammation, which was present in our patient's biopsy. Thus, it can be concluded that this patient is most likely a case of NBNC NASH HCC.

In conclusion, NBNC HCC should be considered as a known complication that can develop from a NASH patient. Further studies would be helpful in understanding the disease including its pathogenesis, and thus, prognostication and better management of the patients. This is especially true as the prognosis of NBNC HCC is good if the HCC is picked up at an early stage.

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