A Case of Multiple Hypervascular Hyperplastic Liver Nodules in a Patient with No History of Alcohol Abuse or Chronic Liver Diseases

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Up-to-date imaging modalities such as three-dimensional dynamic contrast-enhanced CT (3D CT) and MRI may contribute to detection of hypervascular nodules in the liver. Nevertheless, distinguishing a malignancy such as hepatocellular carcinoma from benign hypervascular hyperplastic nodules (HHN) based on the radiological findings is sometimes difficult. Multiple incidental liver masses were detected via abdominal ultrasonography (US) in a 65-year-old male patient. He had no history of alcohol intake and no remarkable past medical history or relevant family history, and his physical examination results and laboratory findings were normal. 3D CT and MRI showed numerous enhanced nodules with hypervascularity during the arterial phase. After US guided liver biopsy, the pathological diagnosis was HHN. To date, several cases of HHN have been reported in patients with chronic alcoholic liver disease or cirrhosis. Herein, we report on a case of HHN in a patient with no history of alcoholic liver disease or cirrhosis. (Korean J Gastroenterol 2015;65:321-325)

Key Words: Liver; Nodule; Hyperplasia; Hypervascular

INTRODUCTION

With the recent progress of imaging modalities, detection of liver nodules is common. In particular, three-dimensional dynamic contrast-enhanced CT (3D CT) and MRI contribute mainly to making a differential diagnosis of nodules. Diagnostic imaging with 3D CT and MRI, however, shows hypervascularity in both hepatic malignancy, such as hepatocellular carcinoma (HCC), and benign hypervascular hepatic nodules, such as focal nodular hyperplasia (FNH), hepatocellular adenoma (HCA) and, rarely, hypervascular hyperplastic nodule (HHN). Therefore, distinguishing these two conditions based on the radiologic findings is sometimes difficult. In clinical situations, however, differential diagnosis to exclude malignancy is important in order to avoid needless therapeutic interventions. Therefore, in a difficult case of differentiating benign from malignant nodules based on the radiologic findings, there is an occasional need to perform biopsy for histological confirmation.

To date, only a few cases of HHN have been reported, and...
all of the patients had chronic alcoholic liver disease or cirrhosis.\textsuperscript{2-6} Herein, we report on a case of multiple HHN in a patient with no history of alcohol drinking or chronic liver disease.

**CASE REPORT**

A 65-year-old man was referred from the local clinic due to multiple variable-sized liver masses detected incidentally on abdominal ultrasonography (US) for the patient’s regular health screening examination. He had no symptoms or signs on the referred area of the abdomen. He had no history of alcohol intake, smoking, or drug intake, and no remarkable past medical history or relevant family history. His physical examination results were also normal. His height was 155.3 cm.

![Fig. 1. Abdominal ultrasonography. Multiple-numerous hypoechoic nodules are seen in both lobes of the liver (arrows).](image1)

![Fig. 2. Abdominal three-dimensional dynamic contrast-enhanced CT images. (A) Pre-enhancement. Multiple nodules are highly enhanced in the arterial phase (B), with decreased enhancement in the portal phase (C), followed by iso-attenuation in the delayed phase (D).](image2)
cm, body weight was 55 kg, and body mass index was 22.8 kg/m². The laboratory findings upon admission were as follows: hemoglobin 13.3 g/dL, hematocrit 39%, white blood cell count 4,300/μL, platelet count 187,000/μL, AST 30 IU/L, ALT 33 IU/L, total protein 7.4 g/dL, albumin 4.5 g/dL, total bilirubin 0.6 mg/dL, ALP 79 IU/L, GGT 51 IU/L, PT 95.3%, CRP 0.4 mg/dL, AFP 2.41 ng/mL, and protein induced by vitamin K absence II 19 mAU/mL. The patient’s HBsAg, anti-HBs, anti-HBc IgG, and anti-HCV were all negative. Esophagogastroduodenoscopy showed no evidence of portal hypertension or varices.

The abdominal US showed variable-sized multiple-nodular lesions, ranging from 5 to 15 mm in diameter, throughout the liver, appearing as hypoechoic nodules (Fig. 1). The subsequent 3D CT showed multiple enhanced nodular lesions in the arterial and portal phase and isodense nodules in the delayed phase, which were well-matched with those found on the US (Fig. 2). The MRI showed an iso-intense signal on T1- and T2-weighted images. Following gadoxetate acid (Gd-EOB-DTPA, Primovist; Bayer Schering Pharma, Berlin, Germany) enhancement, numerous nodules were highly enhanced in the arterial phase (Fig. 3).

US-guided liver gun biopsy was performed six times on separate lesions to confirm the nature of the hypervascular nodules histologically. The liver biopsy showed hepatocellular nodules with mild fatty changes and slightly increased cellular densities without cellular or structural atypia and mitotic figure (Fig. 4). It also showed hypervascularity of the unpaired arteries and sinusoidal dilatation with congestion. In immunohistochemistry, the endothelial cells of the sinusoids were positive to CD34, indicating the capillarization of the sinusoids (Fig. 4). The background liver was normal except for the findings mentioned above (Fig. 4).

In this patient with no history of chronic alcoholic liver disease or cirrhosis, the diagnosis of multiple HHN was made based on the aforementioned radiologic and pathologic findings.
DISCUSSION

Hypervascular nodules in the liver include hemangioma, FNH, HCA, fibrolamellar carcinoma, HCC and metastases from primary tumors such as islet cell tumor, carcinoid, renal cell carcinoma, melanoma, and thyroid carcinoma. Angiosarcoma, infantile hemangioendothelioma, peliosis hepatis, and intrahepatic splenosis rarely present as hypervascular hepatic masses.7 Besides these, the HHN in the current case is also considered a rare entity showing hypervascularity.

The most common benign hypervascular nodule is hemangioma. Histology shows a series of vascular lakes and channels, with larger lesions developing areas of thrombosis and fibrosis.7 The second one is FNH. A well circumscribed lesion consisting of a stellate scar or a fibrous body surrounded by multiple benign nodules appearing as hepatocytes is the characteristic feature of FNH.1 The third one is HCA, which consists of a sheet of hepatocytes and is formed as a pseudocapsule related to compression of the adjacent hepatic parenchyma. In contrast to FNH, however, HCA does not form bile ducts.7 On the other hand, HHN shows increased cellular density compared to that of the normal liver but less than that of HCC. In addition, it has an unpaired artery and shows increased sinusoidal capillarization.

International Working Party Classification8 and/or World Health Organization classification9 has been widely used for classification of hepatocytic nodular lesions. However, HHN is not described in either classification. One of the clinical concerns regarding the absence of a uniform classification scheme is the inability of determining the probability of premalignancy or malignancy.

In the aspect of prognosis, HHN appears to be benign, thus requiring no specific therapeutic intervention. Eight HHNs in the liver were recently reported in seven patients with chronic alcoholic liver disease or cirrhosis.4 In six of the eight cases with follow-up CT, five nodules showed a decrease in size within 36 months, and one disappeared within eight months. Park et al.3 reported a case of HHN in alcoholic liver cirrhosis, in which the nodules showed no change in size and number after four months from the initial diagnosis. In the case reported herein, 3D CT was performed after six months, and the follow-up 3D CT showed that the nodules had the same
sizes and numbers. However, due to the limited number of reported cases, the prognosis of HHN remains undetermined. The pathogenesis of HHN in the liver has not yet been clearly established. A recent hypothesis considers abnormal hepatic circulation, including changes in the portal venous or arterial system as the possible etiology.10

As described above, to date, reported patients with HHN had chronic liver diseases or at least a history of heavy drinking.11 Another few cases of HHN have been reported in patients with Budd-Chiari syndrome.12 In the current case, however, the patient had neither symptoms and signs nor risk factors of chronic liver disease, such as those that modify hepatic blood circulation. To the best of these authors’ knowledge, this is the first reported case in South Korea of multiple HHN with a normal background liver in a patient with no history of alcohol abuse or chronic liver disease.

It is still not clear what kinds of surveillance protocols are needed for HHN patients. Accumulation of data will be necessary in order to clarify the etiologies, risk factors, prognosis, and strategy for management that is evidence-based. It is hoped that the current report will serve as an educational case for physicians listing HHN as a differential diagnosis of hypervascular liver nodule and as the first step in accumulation of HHN in a patient with no history of alcohol abuse or chronic liver disease so as to elucidate the etiologies, risk factors, prognosis, and evaluation protocols.

REFERENCES