

Nodular Regenerative Hyperplasia of the Liver : Radiologic Findings¹

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Nodular regenerative hyperplasia (NRH) of the liver is not common, and no MR imaging of this condition has been reported. We describe a case of NRH with findings of US, CT, MR and angiography. US showed hypoechoic nodules; spiral CT showed enhancing nodules during the arterial phase; MR showed no detectable masses on T1 and T2-weighted images, and angiography showed hypervascular masses during arterial phases.

Index Words : Liver neoplasms, US
Liver neoplasms, CT
Liver neoplasms, MR
Liver neoplasms, angiography

Nodular regenerative hyperplasia (NRH) of the liver is characterized by many hyperplastic nodules composed of cells resembling normal hepatocytes (1, 2). The size of the nodule is usually very small, ranging from a few millimeters to one centimeter, but in some cases, the mass may be large. Microscopically the cells resemble normal hepatocytes and no fibrosis is noted; this is an important difference between NRH and regenerative nodules. The radiologic findings of this tumor disclose multiple hepatic nodules that resemble the diffuse involvement of metastatic carcinoma or multifocal hepatocellular carcinoma, and with the aid of a liver biopsy, a clinician may thus be able to correctly diagnose the condition (3). We describe the sonographic, CT, MR and angiographic findings, with correlative pathology, of a case of nodular regenerative hyperplasia of the liver.

Case Report

A 56-year-old woman with a history of diabetes mellitus presented with a 20-day history of abdominal

pain. On physical examination, there was no abnormality. Laboratory findings revealed elevated levels of serum alkaline phosphatase (246 U/l), serum gamma glutamyl transpeptidase (84 U/l), and serum glucose (389 mg/dl). The results of other liver function tests were normal. Viral markers for hepatitis were negative. The level of serum alpha-fetoprotein was 1.1 ng/ml.

Sonographic examination showed multiple, small, discrete hypoechoic nodules scattered in both lobes with diffuse fatty change (Fig. 1A). During the arterial phase, spiral CT scans with bolus injection (3 ml/sec by mechanical injector) of 120 ml of contrast material showed multiple and variable-sized enhanced masses of varying size (Fig. 1B). During the portal and delayed phases, mass enhancement had almost disappeared (Fig. 1C). Collimation was 5 mm, table feed was 7 mm/sec, and reconstruction interval was 5 mm. On MRI examination, T1-weighted (TR/TE; 200/4.8, 2D FLASH) (Fig. 1D) and T2-weighted images (TR/TE; 4386/138, Turbo spin echo) (Fig. 1E), revealed no masses in the liver. Hepatic arteriography showed multiple, scattered hypervascular masses during the arterial and capillary phases (Fig. 1F), but these masses disappeared during the delayed phase. There was no evidence of irregular tumor vessels, vascular encasement, or arterioportal shunt.

Using an 18-gauge needle, we twice performed

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sono-guided gun biopsy on the hepatic mass. On microscopic examination, the nodules were seen to be composed of hyperplastic hepatocytes with abundant clear cytoplasm forming plates two or more cells thick. The interface of the nodules and adjacent parenchyma showed atrophic hepatocytes and compressed veins

with congestion. Compressed reticulin fibers outlined the margin of the nodules (Fig. 1G). Trichrome stain revealed no fibrous septa. The final pathologic diagnosis was NRH of the liver.

The patient was discharged after treatment for diabetes mellitus.

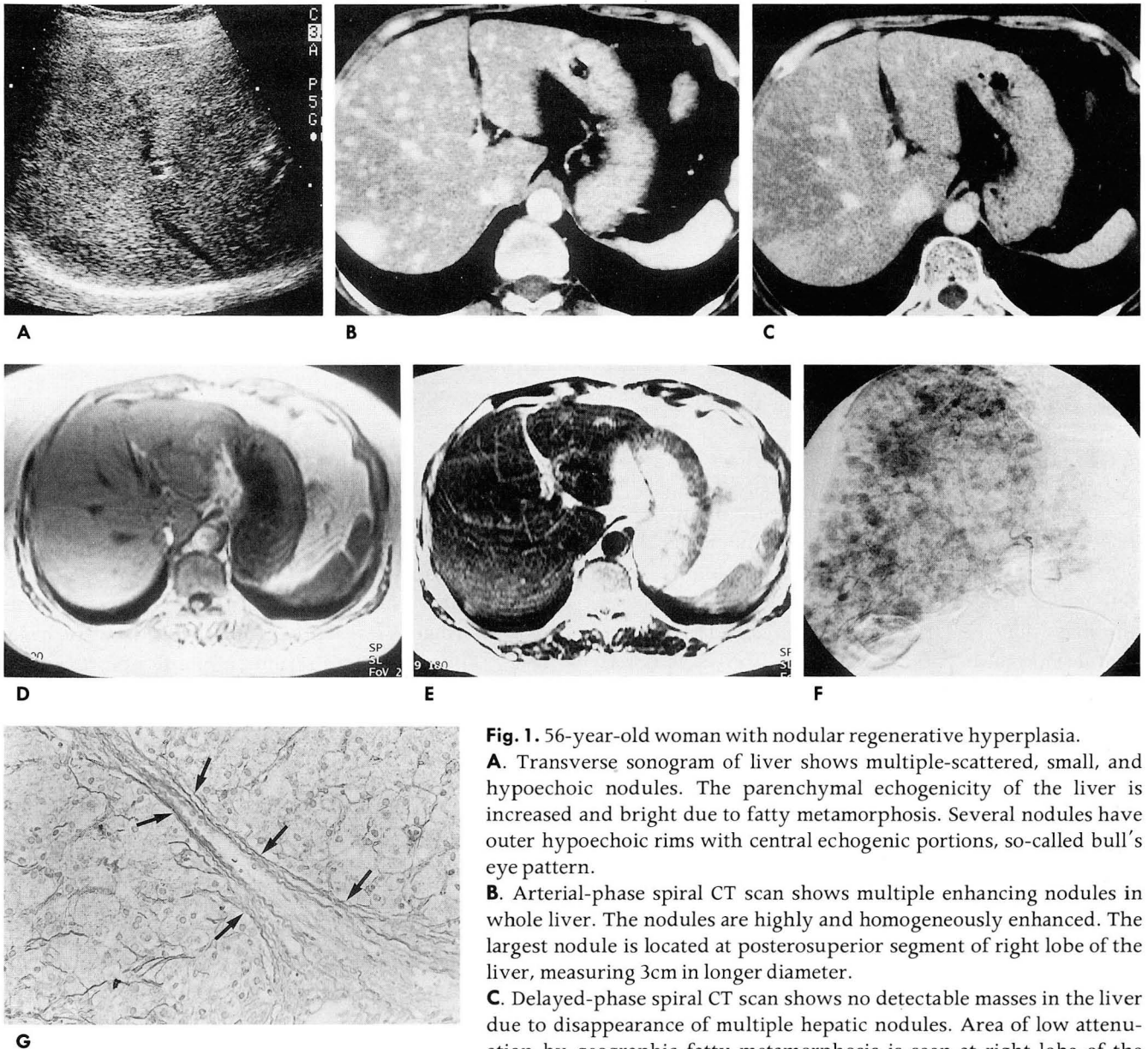


Fig. 1. 56-year-old woman with nodular regenerative hyperplasia.

A. Transverse sonogram of liver shows multiple-scattered, small, and hypoechoic nodules. The parenchymal echogenicity of the liver is increased and bright due to fatty metamorphosis. Several nodules have outer hypoechoic rims with central echogenic portions, so-called bull's eye pattern.

B. Arterial-phase spiral CT scan shows multiple enhancing nodules in whole liver. The nodules are highly and homogeneously enhanced. The largest nodule is located at posterosuperior segment of right lobe of the liver, measuring 3cm in longer diameter.

C. Delayed-phase spiral CT scan shows no detectable masses in the liver due to disappearance of multiple hepatic nodules. Area of low attenuation by geographic fatty metamorphosis is seen at right lobe of the liver.

D. Axial T1-weighted 2D FLASH MR (TR/TE; 200/4.8) image shows normal liver parenchyma without detectable tumor mass.

E. Axial T2-weighted fast spin-echo MR (TR/TE; 4368/138) image shows no definite evidence of high signal mass in liver parenchyma.

F. Capillary-phase hepatic angiography shows hypervascular nodules in whole liver parenchyma. The size of mass is variable from a few millimeters to several centimeters.

G. Microscopic examination shows nodules with thick hepatocyte plates surrounded by atrophic parenchyma and vein with compressed reticulin fibers (arrows) (Reticulin stain, $\times 200$).

Discussion

NRH is a rare benign hepatic disease in which diffuse regenerative liver nodules, unassociated with fibrosis are seen(1, 2). The condition is often detected as an incidental finding at autopsy, because many patients with NRH may be asymptomatic or may present with mild portal hypertension(2).

NRH has numerous synonyms, including nodular transformation, noncirrhotic nodulation, hepatocellular adenomatosis, adenomatous hyperplasia, and diffuse nodular hyperplasia(1, 2).

It is associated with a variety of diseases, including rheumatoid arthritis, Felty's syndrome, subacute bacterial endocarditis, multiple myeloma, macroglobulinemia, myelofibrosis, polycythemia vera, hereditary hemorrhagic telangiectasia, polyarteritis nodosa, diabetes mellitus, and toxic oil syndrome(1). Our case was combined with diabetes mellitus.

The pathogenesis of NRH is not obvious; vascular, immune, hormonal and drug effects have been hypothesized(3). One theory is that a vascular change occurs at the level of the acinus; the hepatic arterial inflammation may involve the portal venous branches, and cause ischemic atrophy of the involved acinus. Adjacent acini with an intact blood supply then undergo compensatory hyperplasia causing nodular hepatocellular growth(1), and the coalescence of small nodules leads to the formation of macroscopic nodules. Portal hypertension which was not involved in our case, may be related to compression of terminal hepatic venules, portal veins or sinusoids by vasculitis or by small nodules(3).

The incidence of NRH is equal in men and in women. Many cases are found incidentally during physical or radiologic examination, autopsy, or workup for associated disease(3).

The radiologic features of NRH resemble those of focal nodular hyperplasia, hepatocellular adenomas, metastasis or multifocal hepatocellular carcinomas(2, 3). Sonographic images of NRH revealed a wide range of liver conditions; in some, the liver appeared to be normal, while in others, focal nodules of variable echogenicity were visible. In our case, the masses were seen as hypoechoic nodules, and were accentuated due to surrounding bright and increased parenchymal echogenicity caused by fatty infiltration of diabetes mellitus. CT imaging of NRH showed multiple nodules of low attenuation, but in our case, multiple highly attenuated enhancing nodules were seen. There is thus a discrepancy between reported cases and ours. CT

images of reported cases were obtained by conventional CT, but in our case, spiral CT was used. The low attenuation seen in nodule images obtained by conventional CT may be explained by delayed image after washout of contrast material. In our case, the nodules were highly enhanced during the arterial phase (30 seconds after the start of infusion of contrast material), but were isodense to liver parenchyma during the portal and delayed phases (70 seconds and three minutes, respectively, after the start of infusion of contrast material). To date, MR imaging of NRH has not been reported, and in our case, MRI failed to detect the masses. The reason is not certain, but may be connected to the fact that hepatic nodules are composed of hyperplastic hepatocytes. Angiographic imaging of NRH showed a vascular mass filled from the periphery. In our case, the masses were hypervascular and scattered in both lobes during the arterial phase (two seconds after the start of infusion of contrast material), and contrast material washed out during the 12-second delayed phase.

The gross findings of NRH are multiple bulging nodules on the external surface, and the cut surface of the liver has multiple and discrete nodules that resemble metastatic carcinoma(1). Microscopic examination of NRH shows hyperplastic nodules without fibrosis(1). A biopsy specimen of NRH shows a diffuse, thick hepatocyte plate, micronodule and erythrocyte in sinusoids(4). In our case, the nodules were composed of thick hyperplastic hepatocytes and there was no evidence of fibrous septa; tumor cells were not seen within the nodules. This was therefore a case of NRH of the liver.

Findings of multiple discrete nodules in the liver suggests that hepatic metastasis has occurred. Although the US and CT features of NRH resemble such metastasis, a difference is seen in MR images. In hepatic metastasis, tumor nodules show low signal intensity on T1-weighted, and high signal intensity on T2-weighted spin echo imaging. In this case, however, the isointensity of nodules, compared with liver parenchyma, probably prevented their detection.

Treatment is not necessary unless a nodule bleeds or ruptures.

In summary, NRH is an underdiagnosed disease that has variable radiologic findings; in some images, the liver appears to be normal, while others reveal a single large nodule or multiple tiny nodules. If multiple hepatic nodules similar to those found in NRH are detected by radiologic examination, particularly in a patient with idiopathic portal hypertension or a disease known to be associated with NRH, the

radiologist should recommend gun biopsy of the mass, rather than searching for occult cancer.

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간에 생긴 결절성 재생증식은 흔하지 않은 질환으로 아직 MR 소견은 문헌에 보고된 바가 없다. 저자들은 초음파검사, CT, MR, 혈관조영술을 시행한 후 조직생검에 의하여 확진된 1예의 결절성 재생증식을 경험하였기에 보고한다. 방사선학적 소견으로는 초음파검사상에서 여러 개의 저 에코 결절로, 나선식 CT 동맥조영기에서 조영증강이 매우 잘 되는 다수의 작은 결절로 보였고, MR의 T1과 T2 강조영상에서는 전혀 종괴를 발견할 수 없었으며, 혈관조영술상 동맥기에서 과혈관성 종괴로 나타났다.