Abdom Imaging 24:258–261 (1999)

Abdominal Imaging

Imaging features of nodular regenerative hyperplasia of the liver mimicking hepatic metastases

M. Clouet,[1] **I. Boulay,**[1] **M. Boudiaf,**[1] **P. Soyer,**[1] **J. Nemeth,**[2] **R. Kiselman,**[1] **R. Rymer**[1]

[1]Department of Radiology, Institut Curie, 26 rue d'Ulm, 75231 Paris Cedex 05, France
[2]Department of Pathology, Lariboisière Hospital, 2 rue Ambroise Paré, 75010 Paris, France

Received: 9 October 1997/Revision accepted: 25 February 1998

Abstract
We described the sonographic, computed tomographic (CT), and magnetic resonance (MR) imaging features of one atypical case of nodular regenerative hyperplasia of the liver. The presence of multiple hepatic nodules suggested the diagnosis of metastatic disease to the liver because of a peripheral rim of enhancement on CT obtained after intravenous administration of contrast material and a halo sign on T2-weighted spin-echo MR imaging. Examination of the pathologic specimen obtained after surgical biopsy showed that the nodules were made of hepatocytes, with a nodular arrangement surrounded by peliosis, without fibrosis or cirrhosis. These findings suggested that peliosis may cause peripheral rim of enhancement on CT and halo sign on MR imaging. In light of this case, nodular regenerative hyperplasia of the liver should be considered in the differential diagnosis of hepatic metastases.

Key words: Liver, neoplasms—Liver, magnetic resonance imaging—Liver, computed tomography.

Noduar regenerative hyperplasia of the liver (NRH) is a rare benign hepatic lesion characterized histologically by diffuse involvement of the liver by nodules of regenerative hepatocytes without cirrhosis. Although this is a well-known and well-defined histological entity, it is less familiar to radiologists [1]. One reason may be that imaging findings are often normal, so that only a few cases have been reported in the radiologic literature.

We describe one atypical case of NRH of the liver in which imaging findings demonstrated diffuse involvement of the liver by multiple nodules, which was pathologically documented after surgical biopsy of the liver.

Correspondence to: M. Clouet

Case report

A 39-year-old woman was admitted to our hospital for nausea, vomiting, and epigastric pain. She had had a splenectomy after an abdominal trauma 20 years before. Clinical examination and esophagogastroduodenoscopy were normal. Biologically, aspartamate transaminase (184 IU/L, normal = 0–15 IU/L) and alkaline phosphatase (391 IU/L, normal = 20–75 IU/L) levels were elevated. Hepatitis B virus surface antigen and hepatitis C antibody were negative. The patient did not have acquired immunodeficiency syndrome or infected with HIV virus. Serum bilirubin and α-fetoprotein levels were normal.

Sonographic examination of the liver showed five hypoechoic and well-delineated nodules in the right lobe. All were homogeneous or slightly heterogeneous, with a hypoechoic rim (Fig. 1). Diameters were 15–32 mm. The left lobe was heterogeneous without a definable nodule. Computed tomography (CT; Tomoscan LX, Philips, Best, The Netherlands) was performed with 10-mm contiguous slices before and after intravenous administration (IV) of a iodinated contrast material. On plain CT, no real hepatic lesion could be depicted; only hypodense subcapsular areas could be seen. In addition, no change in hepatic morphology and especially no enlargement of the caudate lobe were seen. After IV administration of iodinated contrast material, the hepatic parenchyma was heterogeneous, with multiple hypoattenuating subcapsular nodules in the left lobe and segment VII. In addition, some nodules showed peripheral rim of enhancement (Fig. 2). CT images obtained 5 min later showed homogeneous nodules that became isoattenuating relative to the adjacent hepatic parenchyma. Magnetic resonance (MR) imaging examination (MR Max, General Electric Medical Systems, Milwaukee, WI) was performed at 0.5 T by using T1-weighted short time inversion recovery (STIR) pulse sequence [repetition time (TR) = 1180 ms, time inversion (TI) = 380 ms, echo time (TE) = 20 ms] and T2-weighted conventional spin-echo (SE) imaging (TR = 2060 ms, TE = 120 ms). Multiple nodules with different MR imaging features were depicted in both lobes. More nodules were seen with MR imaging than with sonography and CT (12 nodules in the right lobe with MR imaging vs. five and seven with US and CT). On T1-weighted STIR imaging, the main nodules were isointense relative to the liver and some were hyperintense. Some had a hypointense rim (Fig. 3). On T2-

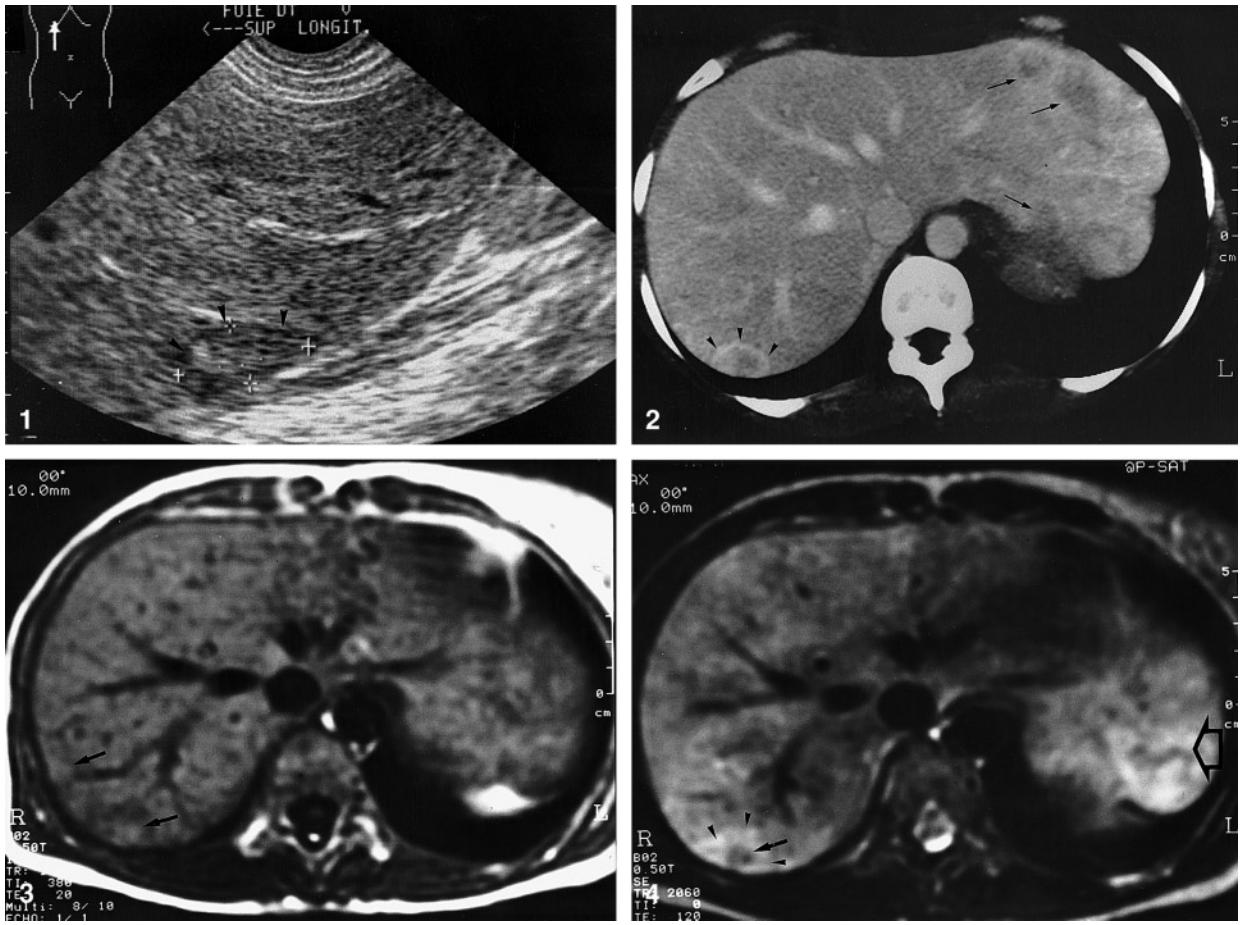

Fig. 1. Sonogram of the liver shows well-defined, homogeneous, isoechoic nodule with a slightly hypoechoic rim (*arrowheads*) in the right lobe of the liver (segment VII).

Fig. 2. CT obtained after intravenous administration of iodinated contrast material during the portal dominant phase demonstrates multiple "nodules" in the left lobe featuring peripheral rim of enhancement (*arrows*). At this level of slice, the nodule in segment VII shown in Figure 1 (*arrowheads*) displays peripheral rim of enhancement.

Fig. 3. T1-weighted STIR MR imaging (TR = 1180 ms, TI = 380 ms, TE = 20 ms) shows subcapsular, poorly defined nodules in the right lobe of the liver, which are isointense relative to the adjacent parenchyma (*arrows*).

Fig. 4. T2-weighted SE MR imaging (TR = 2060 ms, TE = 180 ms) shows a hyperintense and heterogeneous left lobe (*open arrow*). Some hypointense nodules (*arrow*) display a hyperintense rim ("halo" sign; *arrowheads*).

weighted SE imaging, the left lobe was heterogeneous and diffusely hyperintense relative to the remaining hepatic parenchyma, without any definable nodule (Fig. 4). The right lobe was found to contain multiple nodules with different appearances: some were hypointense or hyperintense with a hyperintense rim ("halo" sign; Fig. 4) and some were markedly hyperintense. Analysis of histological material obtained from percutaneous biopsy of the liver was inconclusive because it showed normal hepatocytes and dilated sinusoids without fibrosis or malignant cells. After a 6-month follow-up period, the patient was in excellent clinical condition. Aspartamate transaminase and alkaline phosphatase levels were still elevated (377 IU/L and 473 IU/L, respectively). Imaging examinations showed multiple hepatic nodules. Histological examination of the pathologic specimen obtained after surgical biopsy in segment III showed nodules made of normal hepatocytes in a nodular arrangement. Peliosis with dilated vascular structures was observed around the nodules. No fibrosis was seen, and portal spaces were markedly distorted. All these findings were consistent with NRH of the liver (Fig. 5).

Discussion

NRH is a distinct pathologic entity characterized by the presence of diffuse regenerative nodules of hepatocytes in the periportal areas without hepatic cirrhosis or fibrosis [1, 2]. Liver biopsy with a large tissue sample is necessary to ascertain the diagnosis. In our case, percutaneous biopsy provided insufficient pathologic material. Macroscopically, NRH of the liver may be normal or very similar to hepatic cirrhosis, with multiple regenerative nodules [3].

The actual frequency of NRH of the liver is 0.6–2.6% in autopsy series. NRH is a very common histologic entity, and this contrasts with the relatively small number of papers reporting imaging features of NRH of the liver.

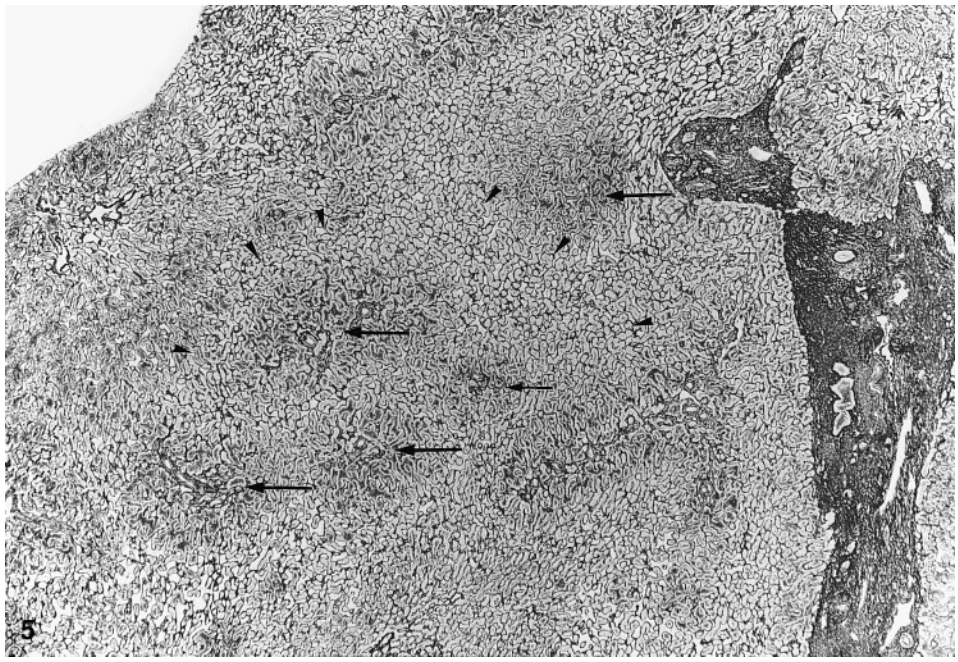

Fig. 5. Pathologic examination (Gordon Sweet) shows multiple hyperplastic parenchyma nodules (*arrows*) surrounded by peliosis (*arrowheads*) without fibrosis. Original magnification ×180.

One reason is that NRH is most often asymptomatic. NRH is mostly found incidentally on biopsy specimens, during laparotomy performed for another reason, or from autopsies [1, 4].

The physiopathologic mechanism of NRH remains unclear. At present, NRH is considered to be a consequence of an abnormality of the portal blood flow [5]. NRH of the liver is often associated with systemic vasculariti, hematologic disease (myeloma or lymphoma), hepatic metastases from breast carcinoma, primary pulmonary hypertension, primary biliary cirrhosis, chronic Budd–Chiari syndrome, or secondary to organ transplantation [1, 3, 5–7]. Clinically, patients with NRH of the liver may be asymptomatic or may suffer from portal hypertension. In patients without cirrhosis, NRH is the second cause of portal hypertension after portal thrombosis [5, 8]. Slight increase in serum liver enzyme levels often indicates the disease. Jaundice is very rare.

Imaging findings of NRH are not specific. In most cases, imaging examinations show normal findings. In most cases, sonography shows normal hepatic parenchyma. In a few cases, well-delineated hypoechoic or isoechoic nodules can be depicted [1, 3, 6, 9, 10]. Hyperechoic nodules have been reported in very rare cases [5]. Sometimes a diffusely heterogeneous hepatic parenchyma can be seen. In some cases, sonography can depict multiple nodules, whereas CT and MR examination show normal findings. CT can show normal findings in half of the cases or hypoattenuating nodules relative to the adjacent hepatic parenchyma in the other cases [1, 9–12]. Rarely, spontaneously hyperattenuating nodules can be depicted [1]. Usually the nodules do not enhance after IV, but hyperenhancing nodules with arterioportal shunting have been reported [6]. MR imaging usually shows normal findings [9, 10]. It may show heterogeneous hepatic parenchyma with nodules compressing portal branches, similar to findings seen in cirrhosis [3]. These latter findings, however, have been reported in only one case. In our case, we observed some nodules with peripheral rim of enhancement, similar to findings observed in malignant tumor or encapsulated tumor. To our knowledge, this finding in NRH of the liver has never been reported.

In most cases, the differential diagnoses of NRH of the liver include cirrhosis with diffuse hepatocellular carcinoma, regenerative nodules, and borderline nodule. Regenerative nodules can be distinghished from NHR by the fact that they appear hypointense on T1- and T2-weighted sequences. In our case, the multiple nodules suggested the diagnosis of metastatic disease because of peripheral rim of enhancement on CT or a halo sign on T2-weighted MR imaging [13]. Pathologic examination of the resected specimen showed hepatocytes with a nodular arrangement surrounded by peliosis [14]. Peliosis is defined by the presence of cystic hepatic sinusoidal dilatation with multiple blood-filled lacunar spaces of different sizes. Sonographically, when this entity is diffuse to the liver, it can show an inhomogeneous pattern with hyper- and hypoechoic regions [15]. CT may demonstrate spontaneous hyperdense lesions in relation to higher density aggregation of large blood-filled spaces. After bolus administration of contrast material, these lesions first appear as hypodense and then as iso- or hyperdense [15]. Rim of enhancement on CT and the halo sign on MR imaging in our case may be explained by the peripheral peliosis.

In conclusion, our case shows that NRH of the liver may simulate metastatic disease to the liver. Imaging fails to characterize this histological entity definitely. Liver biopsy with a large tissue sample is necessary to make the diagnosis; thus, surgical biopsy is mandatory.

References

1. Dachman AH, Ros PR, Goodman ZD, et al. Nodular regenerative hyperplasia of the liver: clinical and radiologic observations. *AJR* 1987;146:717–722
2. Steiner PE. Nodular regenerative hyperplasia of the liver. *Am J Pathol* 1959;35:943–953
3. Trauner M, Stepan KM, Resch M, et al. Diagnostic problems in nodular regenerative hyperplasia (nodular transformation) of the liver. *Z Gastroenterol* 1992;30:187–194
4. Wanless IR. Micronodular transformation (nodular regenerative hyperplasia) of the liver: a report of 64 cases among 2500 autopsies and a new classification of benign hepatocellular nodules. *Hepatology* 1990;11:787–797
5. Buffet C, Altman C. Regenerative nodular hyperplasia [in French]. *Gastroenterol Clin Biol* 1994;18:123–132
6. Feng W, Takayasu K, Konda C, et al. CT of nodular hyperplasia of the liver in non-hodgkin lymphoma. *J Comput Assist Tomogr* 1991; 15:1031–1034
7. Young ST, Paulson EK, Washington K, et al. CT of the liver in patients with metastatic breast carcinoma treated by chemotherapy: findings simulating cirrhosis. *AJR* 1994;163:1385–1388
8. Naber AHJ, Van Haelst U, Yap SH. Nodular regenerative hyperplasia of the liver: an importance cause of portal hypertension in non-cirrhotic patients. *J Hepatol* 1991;12:94–99
9. Pelletier G, Roche A, Boccaccio F, et al. Imagerie de l'hyperplasie nodulaire régénérative du foie étude de 9 cas. *Gastroenterol Clin Biol* 1988;12:687–690
10. Patriarche C, Pelletier G, Attali P, et al. Ultrasonography, angiography, computed tomography and magnetic resonance in nodular regenerative hyperplasia of the liver: report of a pseudo-tumoral case. *Radiat Med* 1988;6:111–114
11. Nguyen TD, Oakes D, Fogel MR, et al. Hepatocellular adenoma and nodular regenerative hyperplasia of the liver in a young man. *J Clin Gastroenterol* 1978;8:478–482
12. Thung SN, Gerber MA, Bodenheimer HG. Nodular regenerative hyperplasia of the liver in a patient with diabetes mellitus. *Cancer* 1982;49:543–546
13. Hahn PF, Stark DD, Saini S, et al. The differential diagnosis of ringed hepatic lesions in MR imaging. *AJR* 1990;154:287–290
14. Kruskal JB, Kane RA, Thomas P, et al. Clinical and prognostic significance of the halo surrounding metastatic liver tumors seen on US and MRI [abstract]. *AJR* 1995;164:117
15. Gore RM. Peliosis hepatis. In: Gore RM, Levine MS, Laufer I, eds. *Textbook of gastrointestinal radiology*. Philadelphia: WB Saunders, 1994:2029–2031