Turk J Gastroenterol 2004; 15 (3): 173-177

Contrast-enhanced MR Angiography of Benign Regenerative nodules following TIPS shunt procedure in Budd-Chiari syndrome

Budd-Chiari sendromunda TIPS şant işlemi sonrasında gelişen benign rejeneratif nodüllerin kontrastlı MR anjiografi ile görüntülenmesi

Sumru TANJU[1], Ayşe ERDEN[1], Koray CEYHAN[1], Işıl TÜRKMEN SOYGÜR[1], Hakan BOZKAYA[2], İlhan ERDEN[1]

Ankara University, Department of Radiology[1], Department of Gastroenterology[2], Ankara

In this report we describe the magnetic resonance (MR) angiographic features of benign hepatic nodules that developed in a patient with Budd-Chiari syndrome, and present the distinguishing features of benign regenerative nodules from hepatocellular cancer. In a 27-year-old woman with chronic Budd-Chiari syndrome, previously non-existing benign nodules developed in the liver parenchyma during the 10-month period following transjugular intrahepatic portosystemic (TIPS) shunt placement. The liver had been examined with gray-scale and Doppler sonography in addition to the MR imaging and MR angiography. On MR angiography, more hepatic nodules became visible in the portal venous phase compared to that of the arterial phase. Delayed washout of contrast medium in nodules was considered to be due to stasis in hepatic sinusoids. Hypervascularization, appearance after portosystemic shunt creation, multiplicity, small size (< 2 cm in diameter in our patient), presence of peripheral rim, and high signal intensity on T1-weighted images are important imaging features of benign hepatic nodules that develop in patients with Budd-Chiari syndrome.

Keywords: Budd-Chiari syndrome, liver nodules, contrast-enhanced MR angiography

Budd-Chiari sendromunda TIPS şant işlemi sonrasında gelişen benign rejeneratif nodüllerin kontrastlı MR anjiografi ile görüntülenmesi Budd-Chiari sendromu olan bu olguda, karaciğerde gelişen benign rejenerasyon nodüllerin daha önce literatürde tanımlanmayan kontrastlı MR anjiografi bulguları vurgulanmış ve benign nodüllerin hepatosellüler karsinomadan ayırtıcı özellikleri sunulmuştur. Budd-Chiari sendromu tanısı ile TIPS yapılan 27 yaşındaki kadın hastada 10 ay sonra karaciğerde benign rejeneratif nodüller ortaya çıkmıştır. Hastanın karaciğeri, ultrasonografi, renkli Doppler ultrasonografi, MR görüntüleme ve MR anjiografi ile incelenmiştir. MR anjiografide, IV kontrast madde uygulamasını takiben portal venöz evrede, arteriyel evreye göre daha fazla nodul boyanarak görünür hale gelmiştir. Muhtemelen hepatik sinüzoidlerdeki staz nedeniyle, nodüllerin kontrast maddeyi bırakması gecikmiştir. Nodüllerin hipervasküler, çok sayıda ve küçük boyutta (bizim hastamızda 2 cm'den küçük) olmaları, portosistemik şant sonrası ortaya çıkmaları, periferlerinde halkasal sinyal intensite farkı bulunması ve Tl ağırlıklı görüntülerde yüksek sinyal şiddeti göstermeleri Budd-Chiari sendromunda gelişen hepatik benign rejenerasyon nodüllerinin özellikleridir.

Anahtar kelimeler: Budd-Chiari sendromu, karaciğer nodülleri, kontrastlı MR anjiografi

INTRODUCTION

Budd-Chiari syndrome is caused by the obstruction of the hepatic venous outflow. Causes of this syndrome vary, including tumoral invasion, hypercoagulable states, birth control pills, abdominal trauma and webs of the inferior vena cava and hepatic veins. However, the exact etiology cannot be determined in 25% to 75% of cases (1, 2).

Benign regenerative nodules (previously termed as adenomatous hyperplastic nodules), nodular regenerative hyperplasia, and macroregenerative nodules have been described in the literature in association with chronic Budd-Chiari syndrome (3-6). Hepatocellular carcinoma (HCC) can also develop in patients with Budd-Chiari syndrome

Address for correspondence: Ayşe ERDEN

Ankara University, Department of Radiology, Ankara, Turkey
Fax: +90 312 310 08 08
E-mail: ayse.erden@medicine.ankara.edu.tr

Manuscript received: 23.12.2003 **Accepted:** 16.03.2004

(4-6) and accounts for 0.7% of all the cases of HCC (4). It is important to distinguish benign regenerative nodules from HCC'since their management differs radically.

In this report we describe the magnetic resonance (MR) imaging and MR angiographic features of benign hepatic nodules that developed in a patient with Budd-Chiari syndrome.

CASE REPORT

A 27-year-old woman was admitted to our hospital with drowsiness, confusion and disorientation. She had no serious health problems until 15 days previously. On physical examination, abdominal distention due to massive ascites was detected and the liver was tender. Hepatitis markers were negative. Ultrasonography (US) and computed tomography (CT) showed obstruction of three main hepatic veins. No nodules within the liver were detected by imaging methods during this period. Fulminant hepatic failure due to Budd-Chiari syndrome was diagnosed. The patient underwent a transjugular intrahepatic portosystemic (TIPS) shunt placement, interposed between the right portal vein and the inferior vena cava.

Ten months later, she was readmitted with abdominal pain and progressive abdominal distention. The patient had normal serum alpha-fetoprotein level. US demonstrated multiple isoechoic to hypoechoic nodules (Figure 1). Doppler sonography showed no TIPS shunt dysfunction. MR imaging depicted multiple nodules ranging from a few millimeters to 2 cm within the liver. On gradient-echo Tl-weighted MR images, nodular lesions were hyperintense compared to hepatic parenchyma (Figure 2a). The nodules were hypointense on fast spin-echo (FSE) T2-weighted images (Figure 2b). Large nodules had a rim around them (Figures 2a-b). MR angiography showed focal narrowing of the inferior vena cava at the subdiaphragmatic level. The middle and left hepatic veins were not visuali-

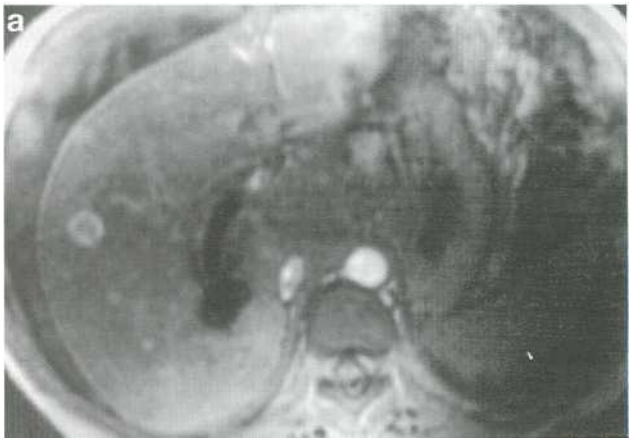

Figure 2a. MR images of the liver in axial plane. Gradient-echo Tl-weighted image (TR/TE/flip angle: 100 msec/6.3 msec/90^0) shows multiple hyperintense nodular lesions of various size. No signal was received from TIPS stent due to its metallic content

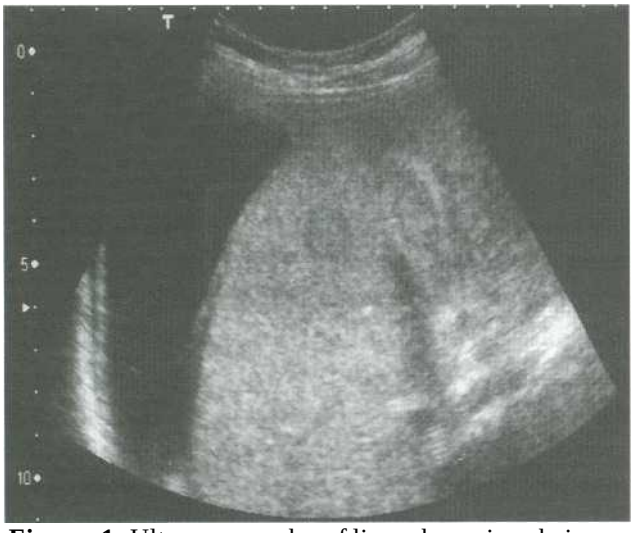

Figure 1. Ultrasonography of liver shows isoechoic nodule (arrow) which has peripheral hypoechoic rim. Ascites is also present

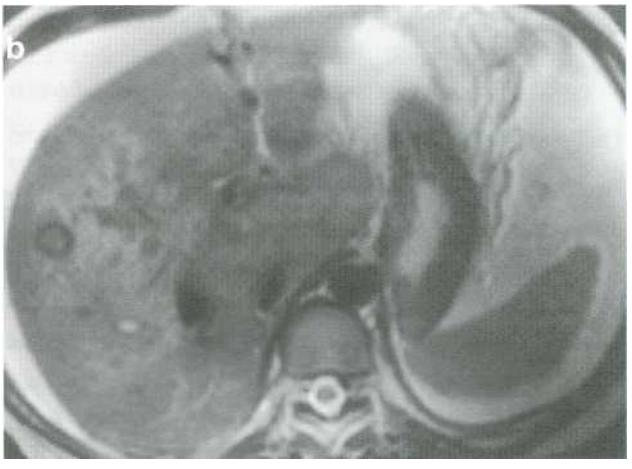

Figure 2b. MR images of the liver in axial plane. On T2-weighted FSE image (TR/TE: 3000 msec /83.9 msec), the nodules are hypointense compared to surrounding liver parenchyma. Large nodule has peripheral rim (arrow)

zed due to chronic thrombosis. TIPS stent was present at the plane of the right hepatic vein. TIPS stent due to its metallic content cause localized magnetic field distortions and signal loss. Thus, the flow in its lumen could not be evaluated with MR imaging. The parenchymal nodules enhanced intensely and homogeneously on arterial and venous phases of MR angiography (Figures 3a-b). On portal venous and delayed phases, numerous additional nodules enhanced. The washout of contrast medium in nodules was delayed, probably due to stasis in the sinusoidal bed.

Ultrasonography-guided fine needle aspiration biopsy of two nodules was performed. Cytologic examination of the biopsy specimens showed signs of the benign nodules. Biopsy smears were hypocellular and composed of reactive hepatocytes that occurred as small monolayered sheets, in cohesive groupings with irregular jagged outlines, and as single cells. These cells had round-to-oval, centrally placed nuclei with prominent nucleoli, well-defined abundant granular cytoplasm and maintenance of low nuclear-to-cytoplasmic ratio. Mild nuclear pleomorphism was also noted in reactive hepatocytes. No feature that could be considered consistent with primary or metastatic malignancy of liver was observed on smears.

DISCUSSION

The pathogenesis of benign regenerative nodules in Budd-Chiari syndrome is unclear. Some authors have suggested that the disturbance of hepatic microcirculation secondary to obstruction of the hepatic veins and the elevation of hepatocellular growth factors may play a role in their development (1, 3, 4). Surgical portocaval shunt can also be a risk factor in the etiology (4, 6). Maetani et al. suggested that decreased portal venous flow may be one of the possible risk factors since most of the regenerative nodules are located at poorly enhanced areas on CT during arterial portography (6). The nodules presented in our case also developed after TIPS procedure. Since the amount of shunted portal blood flow increases following the portosystemic anastomotic intervention, the interaction between the hepatocytes and portal flow decreases. The lessened portal flow may be the triggering factor in development of the nodules.

Hepatic nodules in Budd-Chiari syndrome are typically multiple (>10), small (< 4 cm) and hypervascular (1, 3-6). They do not have a specific location in the liver (4). The nodules have an increased arterial supply corresponding to their dense enhancement on MR imaging. Hypervascularization of benign regenerative nodules associated with

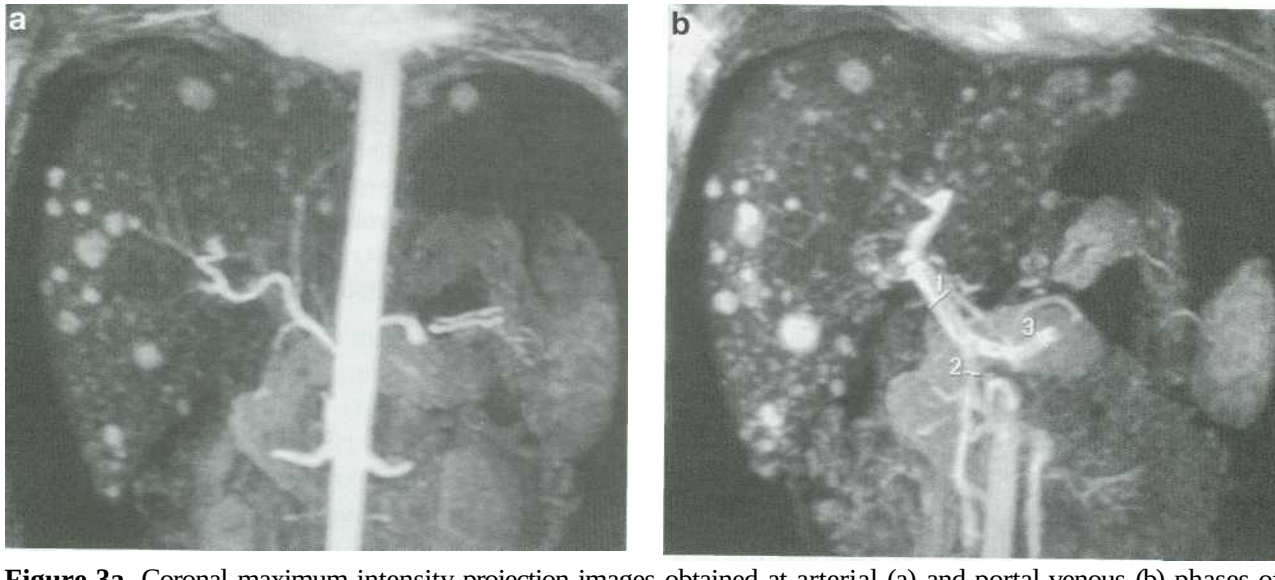

Figure 3a. Coronal maximum intensity projection images obtained at arterial (a) and portal venous (b) phases of MR angiography (TR/TE/flip angle: 5 msec/ 1 msec/ 20°) show multiple, homogeneous contrast enhanced nodules. Note progressively visualized additional small nodules in portal venous phase. Delayed washout of contrast medium in nodules may have been a result of stasis in sinusoids and portal venous bed secondary to hepatic outflow obstruction (b). 1: portal vein; 2: superior mesenteric vein and 3: splenic vein. Image incompletely demonstrates splenic vein due to reconstruction technique

Budd-Chiari syndrome probably does not have the same pathogenesis as of those observed in HCC. A progressive increase in the number of the visible hepatic nodules and persistence of their enhancement during the late venous phase of MR angiography may have been secondary to portal venous stasis in this patient. However, Vilgrain et al. reported that congestion is absent histopathologically in the nodules themselves despite the presence of congestion in the extranodular liver parenchyma (4).

On MR imaging, the benign hepatic nodules in Budd-Chiari syndrome are often noted as hyperintense on Tl-weighted images (3-6) and iso-/hypointense on T2-weighted images (5,6). However, their signal intensity on T2-weighted MR imaging is variable and the nodules can be hyperintense on T2-weighted images (3,4). The regenerative nodules, drained by the hepatic veins, are prone to congestion and infarction if their venous drainage is impaired. Infarcted regenerative nodules in cirrhosis are described as hyperintense on T2-weighted images (5). Infarction can therefore be an explanation for the few cases of hyperintense regenerative nodules on T2-weighted images. The reason for hyperintensity on Tl-weighted images remains unclear. Although congested perinodular parenchyma (6) may give a relatively hyperintense appearance to the nodules, fat and copper depositions in these nodules may also be responsible for their high signal intensity (4, 5).

In patients with chronic liver parenchymal disease, HCC should be considered in the differential diagnosis of the benign nodules. The HCC lesions are usually hypointense compared to the liver parenchyma on Tl-weighted images and mild-to-moderately hyperintense on T2-weighted images (6, 7). It has been reported that dysplastic nodules and regenerative nodules in cirrhosis generally do not exhibit high signal intensity on T2-weighted images (7). Hypervascular nodules in Budd-Chiari syndrome, which have low signal intensity on T2-weighted images, are likely benign lesions (6). However, benign hepatic nodules in this syndrome are not always hypointense on T2-weighted images. The distinction between HCC and benign nodules in Budd-Chiari syndrome cannot be made on the basis of MR signal intensity (4). Dynamic imaging after bolus injection of contrast medium is particularly important for detection of HCCs. The typical pattern of enhancement of HCC includes rapid homogeneous enhancement on arterial phase images. Most often, HCC is isointense on portal venous phase and hypointense on delayed phase images. If present, the capsule surrounding HCC enhances considerably on later images, which is typical of fibrous tissue (7).

In the literature, a peripheral rim is described around the large benign regenerative nodules in Budd-Chiari syndrome. This peripheral ring was also present around the large nodules in our patient. According to our observations, perinodular ring around the regenerative nodules is unlikely in cirrhosis with other etiologies. Soyer et al. suggested that a perinodular rim can develop as a result of parenchymal pressure atrophy at the periphery of the expanding nodules (3). They may be caused by sinusoidal dilatation, congestion or recent hemorrhage (5). Maetani et al. reported that a peripheral rim may reflect the presence of a large central scar, which is a characteristic finding of benign regenerative nodules larger than 1 cm in Budd-Chiari syndrome. On MR imaging, a central scar is shown as a central hypointensity area on Tl-weighted images and as a central hyperintensity area on T2-weighted images. In the delayed phase of contrast enhancement, the central scar shows prominent enhancement (6). The nodules should be sufficiently large so as to exhibit a different signal intensity in their center. We believe that the regressive changes inside the nodules may create an appearance of a so-called peripheral rim. However, the concepts of perinodular ring or central scar have not been clarified yet and perceptional and interpretational differences still exist. In our case, probably owing to their small size, no signal intensity differences at the center of the majority of the nodules were detected.

To our knowledge, contrast-enhanced MR angiographic findings of benign hepatic nodules in Budd-Chiari syndrome have not been reported previously. Hypervascularization, appearance after portosystemic shunt creation, multiplicity, small size (< 2 cm in diameter in our patient), presence of peripheral rim around the large nodules, and high signal intensity on Tl-weighted images, which have been reported (3-6) as the characteristic features of benign regenerative nodules in Budd-Chiari syndrome, were also present in liver MR and MR angiography of our case.

REFERENCES

1. Castellano G, Canga F, Solis-Herruzo JA, et al. Budd-Chiari syndrome associated with nodular regenerative hyperplasia of the liver. J Clin Gastroenterol 1989; 11: 698-702.
2. Dilawari JB, Bambery P, Chawla Y, et al. Hepatic outflow obstruction (Budd-Chiari syndrome). Experience with 177 patients and a review of the literature. Medicine 1994; 73: 21-36.
3. Soyer P, Lacheheb D, Caudron C, Levesque M. MRI of adenomatous hyperplastic nodules of the liver in Budd-Chiari syndrome. J Comput Assist Tomogr 1993; 17: 86-9.
4. Vilgrain V, Lewin M, Vons C, et al. Hepatic nodules in Budd-Chiari syndrome: imaging features. Radiology 1999; 210: 443-50.
5. Brancatelli G, Federle MP, Grazioli L, et al. Large regenerative nodules in Budd-Chiari syndrome and other vascular disorders of the liver: CT and MR imaging findings with clinicopathologic correlation. AJR Am J Roentgenol 2002; 178: 877-83.
6. Maetani Y, Itoh K, Egawa H, et al. Benign hepatic nodules in Budd-Chiari syndrome: radiologic-pathologic correlation with emphasis on the central scar. AJR Am J Roentgenol 2002; 178: 869-75.
7. Krinsky GA, Lee VS, Theise ND, et al. Hepatocellular carcinoma and dysplastic nodules in patients with cirrhosis: prospective diagnosis with MR imaging and explantation correlation. Radiology 2001; 219: 445-54.