Case 5095

Nodule-within-a-nodule sign
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Patient: 33 years, male

Clinical History:

We present a case of a 33 years old male with chronic Budd-Chiari and TIPS. Hepatic ultrasound revealed multiple hypoechoic nodules. At CT nodules were hypervascular. Beside this characteristic, MR showed that at T1 and T2 weighted images they have nodule-within-a-nodule morphology. Final diagnosis was high-grade dysplastic nodules without HCC

Imaging Findings:

Our patient was a 33 years old male with a chronic Budd-Chiari for 8 years and a TIPS inserted 3 years ago. A routine ultrasound showed multiple hypoechoic nodules between 1 and 2 cm in liver parenchyma. At this time patient was asymptomatic and laboratorial evaluation was normal (namely ? -fetoprotein). CT at arterial phase depicted multiple hypervascular nodules that became less conspicuous at portal phase: some isodense with a hypodense halo, others only isodense. TIPS and portal vein were patent. There wasn’t ascite or lymphadenopathy (Fig 1, 2). T1 weighted images were obtained in phase and out of phase and didn’t revealed steatosis. At this sequence nodules were slightly hyperintense to the parenchyma and have a central dot of low signal (Fig 3). T2 weighted images with fat saturation revealed that this central dot is hyperintense and the marginal halo more hypointense than the liver (Fig 4). After gadolinium nodules enhancement was rapid and homogeneous in arterial phase. At portal phase we could see a little washout, but the nodules still were more intense than the liver, aspect that remained in late phase (fig 5, 6, 7). The diagnosis of high-grade dysplastic nodules was proposed. Liver transplantation has been done, and pathologic analysis stated the existence of cirrhosis with regenerative nodules ranging from 1 to 20 mm, some with central clusters of hepatocytes with nucleus of various size and shape associated with increased amount of cytoplasmic glycogen, but without evidence of nuclear atypia.

Discussion:

Various parenchymal liver diseases may lead to cirrhosis. Cirrhotic liver contains regenerative nodules and may also contain dysplastic nodules as well as hepatocellular carcinoma [1]. Regenerative nodules result from localized proliferation of hepatocytes and their supporting stroma. Dysplastic or neoplastic lesions are composed of hepatocytes that show histologic characteristics of abnormal growth caused by a presumed genetic alteration [1, 2]. Dysplasia is indicated by the presence of nuclear and cytoplasmic changes, such as minimal to severe nuclear atypia and increased amount of fat of glycogen. Dysplastic nodules can be low grade or high grade. Most hepatocellular carcinomas (HCC) cannot be distinguished histologically from dysplastic nodules with certainty. In addition, foci of carcinoma can be found in otherwise benign dysplastic nodules. These and other findings support the theory of stepwise carcinogenesis of HCC [1, 2]. Regenerative nodules show low signal on T2 weighted images, variable signal on T1 weighted images and no enhancement on arterial phase of examinations [2]. HCC shows high signal intensity on T2 weighted images, intense enhancement on arterial phase and variable sign on T1 weighted [2, 3]. Dysplastic nodules are a step between regenerative nodules and HCC, so signal intensity and enhancement are not definitive. Although this problem image techniques can detect with confidence high-grade dysplastic nodules and
small HCC. It's documented in the literature that high-grade dysplastic nodules and small HCC may have a nodule-within-a-nodule appearance on MR images, especially if a focus of HCC originates within a siderotic regenerative nodule. These nodules have a target configuration with a central dot of high signal on T2 weighted images, and low signal on T1 weighted images. On arterial phase nodules show intense enhancement [2, 3]. Brancatelli et col described large regenerative nodules that are frequently seen in Budd-Chiari syndrome and less commonly in other vascular disorders of the liver. They are usually multiple, with a typical diameter of 0.5–4 cm. At pathologic analysis, are well-circumscribed, round lesions that may distort the contour of the liver. At multiphasic helical computed tomography, large regenerative nodules are markedly and homogeneously hyperattenuating on arterial dominant phase images and remain slightly hyperattenuating on portal venous phase images. Large regenerative nodules are bright on T1-weighted magnetic resonance images and show the same enhancement characteristics after intravenous bolus administration of gadolinium contrast material. They are predominantly isointense or hypointense relative to the liver on T2-weighted images [4]. Brancatelli also stated that there is no evidence that large regenerative nodules degenerate into malignancy [4]. Despite the knowledge that Brancatelli studies don’t describe malignant nodules in patients with Budd-Chiari and hypervascular nodules, and the fact that we couldn’t see morphologic changes in radiological studies that suggest cirrhosis (like regenerative nodules), the clinical context and the morphology of nodules in our patient (nodule-within-a-nodule configuration) directed the radiological diagnosis to a high suspicion of malignancy (dysplastic nodules versus HCC). Since the patient had serious coagulation disorders, biopsy was impossible, and clinicians decide to give priority to this patient in the transplant list.

**Differential Diagnosis List:** High-grade dysplastic nodules without HCC

**Final Diagnosis:** High-grade dysplastic nodules without HCC

**References:**


Description: Arterial phase shows hypervascular nodules in the left lobe of the liver, and a TIPS in inferior vena cava. Origin:
**Description:** phase shows heterogeneous enhancement in liver parenchyma, mainly peripheric, aspect secondary to chronic Budd-Chiari. Nodules became less conspicuous, some became isodense with a hypodense halo, others isodense. **Origin:**
Description: In-phase T1 weighted image. Grossly liver was a normal signal intensity, but with some heterogeneity in the right lobe. Multiple nodules in left lobe with a nodule-within-a-nodule morphology. The outer halo has higher signal than the liver and the inner dot lower signal. Origin:
Description: T2 weighted with fat saturation. The nodules retain the same morphology, but now the central dot has a higher signal than the periphery. Origin:
Figure 5

*Description:* T1 weighted image after gadolinium in arterial phase. Nodules showed intense and homogeneous enhancement.

*Origin:*
Description: T1 weighted image after gadolinium in portal phase. Nodules remain more intense than the liver. Origin:
Description: T1 weighted image after gadolinium in late phase. Nodules remain more intense than the liver. Origin:
Description: T1 weighted image after gadolinium in late phase. Nodules remain more intense than the liver. Origin: