Nodules in Liver Cirrhosis

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Regenerative Nodules
Regenerative nodules result from grossly distorted hepatic architecture, heterogeneous regeneration and hepatocellular dysplasia. Cirrhosis can be divided by gross pathology into micronodular, macronodular, and mixed form according to appearances of regenerative nodules. The typical appearance of regenerative nodules on MR images includes isointensity or relatively hyperintensity on T1-weighted images and iso or low signal intensity on T2-weighted images. These appearances may be due to the prolonged T1 and T2 values of fibrous septa, because of infiltration by inflammatory cells and development of pseudo bile ducts in the fibrous septa surrounding the regenerative nodules. Regenerative nodules often accumulate iron more than the surrounding hepatic parenchyma. As gradient-echo MR imaging is particularly susceptible to magnetic field heterogeneity, siderotic regenerative nodules may cause artifactual enlargement of the regenerative nodules with low signal intensity. It is controversial whether the detection of siderotic regenerative nodules at MR imaging should be considered a significant risk factor for HCC. However, pathologic observations suggest a role for iron-accumulated regenerative nodules in carcinogenesis. The findings of studies published in the pathology literature have suggested that the presence of iron in large (> 8mm) regenerative nodules is a significant risk factor for the presence of dysplastic or frank malignant changes.

Dysplastic Nodules
Dysplastic nodule is a nodular region of hepatocytes with dysplasia but without definite histologic criteria of malignancy. Dysplastic nodules can be low- or high-grade. Low-grade dysplastic nodules have commonly been referred to as ordinary adenomatous hyperplasia. High grade dysplastic nodules have commonly been referred to as atypical adenomatous hyperplasia. Dysplastic nodules without atypia tend to be hypointense on T2-weighted images and hyperintense on T1-weighted images. This combination of intensities on T1- and T2-weighted images was a finding specific to the
dysplastic nodule, although there are some overlaps with well-differentiated HCC. Most dysplastic nodules are hypovascular without arterial enhancement on dynamic MR imaging. A dysplastic nodule may also contain a microscopic area of HCC, and it is then called a dysplastic nodule with subfocus of HCC.

Early HCCs

Many HCCs develop in a step-wise fashion from dysplastic nodules to dysplastic nodules with malignant foci, and to early HCC (well-differentiated) on the basis of gradually increasing size and cellular density, although a de novo pathway for HCC has been also proposed. Dysplastic nodules with malignant foci (HCC) are observed as the evolution of a tumor from a large dominant dysplastic nodule to frank HCC, and can be seen at MR imaging with the so-called nodule-in-a-nodule appearance. The small foci of HCC within the dysplastic nodule have signal-intensity characteristics exactly opposite those of the nodule. On T1-weighted images, such lesions typically show high signal intensity of a large nodule, with internal foci that are slightly low signal intensity to the liver. On the arterial-phase dynamic images, malignant foci show early enhancement. In many cases, these small foci of HCC grow rapidly, so aggressive follow-up or treatment should be considered when these small foci are initially detected. Early HCCs are usually small and well-differentiated, classified as Edmonson Grades I or II. The most well differentiated HCCs may have vascularity similar to that of the adjacent liver, indicating combined perfusion by hepatic artery and portal vein similar to that of benign parenchyma. Therefore, despite optimal arterial-phase imaging, a large number of early HCCs (well-differentiated) remain isointense relative to the background and go undetected at MR imaging. These early HCCs with hypovascularity are best seen at portal-venous-phase or equilibrium-phase imaging.

Advanced HCC

Advanced HCCs have variable appearances in signal intensity at MR imaging, although they are usually hypointense on T1-weighted images and hyperintense on T2-weighted images. Nevertheless, MR imaging is a useful modality for the diagnosis of advanced HCC because of its demonstration of characteristic morphologic features. T2-weighted MR images may show a "mosaic" pattern of signal intensity as a characteristic finding of HCC, produced by multiple centers of growth. The septum or fibrous capsule with 0.5 to 3.0 mm thickness can often be identified as low signal structures on T1-weighted MR images. The intratumoral fibrous septum is seen as low intensity on T2-weighted images because of its less water content. Advanced HCCs
sometimes have necrosis and hemorrhage and/or invasion of hepatic and portal veins. When HCC is complicated by portal vein thrombus, the peripheral liver segment shows high signal intensity on T2-weighted image due to edematous change of liver parenchyma. The blood supply of HCCs is primarily from hepatic arteries, providing a potential mechanism for improved detection. Therefore, it is essential to use a dynamic contrast-enhanced arterial-phase technique to show the arterial enhancement in HCCs. Most advanced HCC nodules are hypervascular, become enhanced at MR imaging, are optimized with arterial-phase imaging, and show a washout of tumoral contrast material during the portal-venous or equilibrium phase. Early enhancement of HCC is usually diffuse, multi-nodular or heterogeneous. HCC is usually less intense than liver on portal phase images. On equilibrium-phase images, the HCCs are usually iso- or hypointense to surrounding liver, but fibrous capsules surrounding focal HCC are often hyperintense, due to the large interstitial space of fibrous tissue.