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MINI REVIEW

Imaging of benign hepatocellular lesions: Current concepts and recent updates

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Summary Focal nodular hyperplasia (FNH) and hepatocellular adenoma (HCA) are a variety of solid lesions mostly found in the absence of underlying chronic liver disease in young patients. HCA is no longer to be considered as a unique lesion but as a recollection of different entities sharing common points but most of all separated by different typical morphological aspects. Accurate diagnosis is of clinical importance as the management is most of the time conservative for FNH, whereas HCAs expose patients to hemorrhage and malignant transformation, and may lead to a more invasive treatment, mainly surgical resection. Moreover, the different HCA subtypes expose to different risks of complication. The best imaging techniques for the differentiation between FNH and HCAs and for the subtyping of HCAs are contrast-enhanced ultrasound (CEUS) and magnetic resonance imaging (MRI), as specific combinations of imaging features have been associated with the different lesions. They should be considered as complementary examinations. Atypical or multiple lesions, lesions containing fat or presence of an associated steatosis represent diagnostic challenges. Recently, MR hepatospecific contrast agents have been shown to be useful. Emergent elastography techniques might also be helpful in the near future. Biopsy should always be performed in case of uncertain diagnosis to reach a final diagnosis and avoid unnecessary invasive treatment.

Introduction

Benign hepatocellular lesions are rare epithelial solid entities encountered mostly in young women. They are classically divided into two groups that do not share the same pathogenesis or course of evolution and do not expose to the same complications. Focal nodular hyperplasias (FNH) are regenerative polyclonal formations that generally

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remain asymptomatic and follow a very benign course of evolution, while hepatocellular adenomas (HCA) correspond to neoplastic monoclonal lesions [1,2], subject to hemorrhage and rare malignant transformation [3,4].

Differentiating these two entities has been an issue for many years because management is different for each. Most FNH are managed conservatively and treatments are indicated only for the few symptomatic ones. HCAs, on the other hand, may lead more frequently to an invasive treatment, mainly surgical resection.

Final diagnosis relies on pathological analysis performed on biopsy. However, as most of these lesions are discovered fortuitously in young patients and develop on normal liver parenchyma, non-invasive characterization techniques shall be preferred. This is why imaging plays a central role in the diagnosis of these lesions. In the present review, we will detail the imaging features of FNH and HCAs, as recent advances in imaging studies allow an accurate diagnosis in the majority of cases, thus limiting the need for liver biopsies. Pathogenesis and pathological considerations are beyond the scope of the present text.

Focal nodular hyperplasia

FNH is the most frequent benign hepatocellular lesion (.9%), with a sex ratio around nine women for one man [5]. They are most of the time asymptomatic, and, when large or pediculated, may result in non-specific abdominal symptoms. In more than half of all cases, hepatic tests are normal. When not, isolated elevation of gammaglutamyl transpeptidase and/or alkalin phosphatases is found.

Ultrasound and computed tomography

Most lesions are fortuitously discovered on an ultrasound or CT. At ultrasound, FNH is usually slightly hypoechoic or isoechoic, and may only be detected because they displace the surrounding vessels. Hypoechoic halo or lobulated contours are often observed. The central scar is difficult to visualize at US (20% of the cases) [6]. When visible, it is slightly hyperechoic. Typical findings at color Doppler include the presence of a central feeding artery with a stellate or spoke-wheel pattern corresponding to the artery running from the central scar to fibrous septa. On CT scans, FNH spontaneously appears as a focal hypoattenuating mass. The central hypoattenuating scar is depicted in only one-third of the cases [6], and calcifications within the central scar, very rare, are observed in only about 1% of the cases [7] At the arterial phase of contrast-enhanced CT, the lesion enhances rapidly in most cases (95—100%) [8]. At the portal venous phase the lesion is either iso- or slightly hyperattenuating relative to normal liver. Furthermore, lesion is homogeneous in 90% of all cases, present with lobulated contour and no capsule. The central feeding artery is visible in the majority of cases [9] and the central element enhances is 89% on the late phase [9].

Contrast-enhanced ultrasound and magnetic resonance imaging

A second examination is often required for definite non-invasive diagnosis. It can be achieved with imaging using contrast-enhanced ultrasound (CEUS) or MR imaging, as specific features have been associated with both the techniques [10]. CEUS has been less studied, and imaging features still require prospective validation. This is why MRI is considered the best imaging tool with a sensitivity of 70% and a specificity of 98% [11].

With ultrasound contrast agents or non-linear continuous imaging, FNH enhances at the very arterial phase, and becomes homogeneously isoechoic after 30 seconds in the vast majority of the cases. They have been associated with two specific features:

- a spoke-wheel aspect, encountered in 20—25% of the lesions;
- a centrifugal filling, more frequent in lesion smaller than 3 cm [12].

The central scar is detected in around 40% of the lesion, mostly in FNHs larger than 3 cm [9], and appears hypoechoic on both arterial and portal phases. According to Kim et al., by showing centrifugal enhancement with radiated vascularisation, differentiation with adenoma is possible in most cases [13]. Recently, Wang et al. advocated that CEUS should be the first-line imaging technique for the diagnosis of FNH [9]. In our experience, the combination of CEUS and MR imaging is often performed [10].

On MR imaging, one has to remember that the diagnosis of FNH is based on a combination of features, none of them being specific of FNH. There are seven major criteria to assess a proper diagnosis:

- lesion not different from the liver before contrast injection, i.e. iso- or hypointense on T1-weighted images (94—100%) and iso- or slightly hyperintense on T2-weighted images (94—100%) [14];
- homogeneity apart the central scar;
- presence of a central scar, corresponding to a central hypointense area on T1-weighted images and strongly hyperintense on T2-weighted images (78—84%) [15];
- intense enhancement at arterial phase without washout;
- no capsule;
- lobulated aspect;
- absence of underlying chronic liver disease or clinical history of cancer.

When all the criteria are present, the diagnostic specificity is close to 100%. One point must be stressed: the prevalence of typical features of FNH in literature ranges from 22—70%, and may be explained by variations in the stringency of the criteria sets used to diagnose FNH, and recruitment bias.

Hepatobiliary contrast agents can be used to highlight the hepatocellular origin of the lesions. After injection of Gadolinium-BOPTA (Multihance, Bracco) FNH appears hyperintense in comparison to the surrounding liver [16,17]. After injection of Gadolinium-EOB-DTPA (Primovist/Eovist Scher-