Imaging approach in focal nodular hyperplasia: a case report and review of the literature

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Abstract:
We report a case of focal nodular hyperplasia in a 34-year-old man with no medical history. On clinical examination the patient seemed to be in good health but the image features showed a liver mass measuring about 2 × 2.5 cm. Imaging investigations showed typical features of focal nodular hyperplasia; consequently the biopsy was not necessary. A particular observation in this patient was the male sex (FNH usually appears in female patients), as well as the surprising disposition of the FNH inside a small island of normal tissue, surrounded by fatty liver. A review of the imaging appearance of focal nodular hyperplasia is also presented in detail, too.

Key words: Focal nodular hyperplasia, contrast-enhanced ultrasound (CEUS), computer tomography (CT), magnetic resonance imaging (MRI)

Background:
Focal nodular hyperplasia (FNH) is the second most common benign liver tumour and accounts for 8% of all primary hepatic tumours. It is more commonly found in young and middle-age women, although it can present with smaller lesions and atypical features in men [1]. FNH is usually asymptomatic and is often discovered incidentally. Imaging (MR, CT scan or contrast-enhanced ultrasound) is invaluable in diagnosing the condition, while liver biopsy is unnecessary in typical cases.

Case presentation:
A 34-year-old asymptomatic man presented in our department for a routine check-up. He did not report a history of meaningful disease. On physical examination, the liver was palpable, with normal consistency. Complete blood tests show haematological and biochemical values within normal range.

Abdominal ultrasound revealed a hypoechoic mass, within the right liver lobe, measuring about 2 × 2.5 cm (fig. 1a). Liver parenchyma appeared enlarged and hyperechoic (corresponding to fatty changes), while the spleen was not enlarged. In addition, power and colour Doppler ultrasound clearly showed the feeding arteries which surrounded the nodule and the radial shape of the intranodular vasculature (figure 1b, c). CEUS was further performed, using a classical protocol with bolus injection of 2.4 mL of second-generation contrast agent (Sonove) in the cubital vein. We used a Hitachi EUB 8500 ultrasound system, with an embedded contrast module, using specific dynamic contrast harmonic imaging (dCHI) software settings, with a mechanical index set to 0.22.
An intense enhancement of the lesion was observed during the arterial phase, with a central hypoechoic region that corresponds to the central scar (fig. 2a). Portal and late venous phase images show sustained enhancement of mass, which continued to show more enhancement than the adjacent liver tissue (fig. 2b, c). The persistent homogenous enhancement in the portal and late phase suggested a benign lesion. These features, as well as the presence of a central scar were consistent with the diagnosis of focal nodular hyperplasia.

Unenhanced CT scan revealed fatty infiltration of the liver with an island of remaining normal tissue. The FNH was observed as a hypo-attenuation nodule inside this island of normal liver, adjacent to the fatty liver parenchyma (fig. 3a). After contrast medium administration, the nodule enhanced rapidly and homogeneously during the arterial phase (fig. 3b). In the portal-venous and equilibrium phases, the area of focal nodular hyperplasia appeared iso-dense when compared to the normal liver parenchyma (fig. 3c), while in the equilibrium phase the central scar had hyper-attenuation.
Concerning MRI, on the unenhanced T2-weighted image, the FNH appeared as an iso-intense lesion with a hyper-intense central scar (fig. 4a). After specific contrast agent administration (Primovist), the lesion showed intense and homogeneous enhancement during the arterial phase (fig. 4b) and rapid wash-out in the portal-venous phase (fig. 4c). In the equilibrium phase the lesion was iso-intense as compared with the surrounding liver parenchyma (fig. 4d). The central scar was hypo-intense during the arterial and portal-venous phase; however it appeared hyper-intense in the equilibrium phase, alike to the CT imaging observation.

Fig. 3. CT images of FNH. Unenhanced CT scan revealed fatty infiltration of the liver with only an island of remaining normal tissue. FNH was observed as a hypo-attenuation nodule inside this island of normal liver, adjacent to the fatty liver parenchyma (a). After contrast medium administration, the nodule enhanced rapidly and homogeneously during the arterial phase (b). In the portal-venous and equilibrium phases, the area of focal nodular hyperplasia appeared iso-dense when compared to the normal liver parenchyma (c), while in the equilibrium phase the central scar had hyper-attenuation.

Fig. 4. MRI appearance of FNH. On the unenhanced T2-weighted image the FNH appeared as an iso-intense lesion with a hyper-intense central scar (a). After specific contrast agent administration, the lesion showed intense and homogeneous enhancement during the arterial phase (b) and rapid wash-out in the portal-venous phase (c). In the equilibrium phase the lesion was iso-intense as compared with the surrounding liver parenchyma (Fig. 4d).
Real-time virtual sonography, a new imaging technique that combines in real-time, transabdominal ultrasound with CT or MR, was also performed. The colour Doppler and power Doppler ultrasound image of the FNH lesion were simultaneously displayed with the contrast-enhanced MR (fig. 5a, b).

![Fig. 5. Real-time virtual sonography of the focal lesion, with simultaneous display of the contrast-enhanced MR section and real-time ultrasound image: power Doppler (a) and colour Doppler (b).](image)

Discussion:

Along with haemangiomas, FNH is second between benign lesions of the liver and has a reported prevalence of 0.9% [3]. FNH represents hyperplastic responses to a hemodynamic disturbance related to vascular abnormalities. Molecular pathways altered in this tumor is poorly understood [4]. Pathologically, FNH usually presents as a firm, coarsely nodular mass of variable size, with a dense, central stellate scar and radiating fibrous septa that divide the lesion into lobules. Microscopically, the lesion closely resembles inactive cirrhosis. Hepatocytes appear normal, but they lack the normal cord arrangement. Kupffer cells are present, and the fibrous septa contain numerous bile ductules and vessels [5]. A recent study suggests that the central part of FNH suffers from hypoxic conditions due to arterial hyper-perfusion; and the resultant oxidative stress may activate hepatic stellate cells, leading to central scar formation [6].

Vascularity of the focal nodular hyperplasia is particular. Anomalous arteries join to the capillaries that, in turn, connect with venulae that drain into hepatic veins of the surrounding parenchyma, without connections to portal vessels [7].

Currently, FNH is divided into two types, classic and non-classic. Classic FNH is characterized by the presence of abnormal nodular architecture, malformed vessels, and cholangiocellular proliferation. The non-classic type comprises three subtypes: a) telangiectatic FNH, b) FNH with cytological atypia and c) mixed hyperplasic and adenomatous FNH [8].

Sonographically, the lesions usually appear homogeneous and isoechoic, but they can also be hyper- or hypoechoic nodules. A central scar has been seldom depicted, appearing as an echogenic linear or stellate structure within the central portion of the mass. However, demonstration of the central scar is infrequent and may be seen in other liver tumors. Colour Doppler US shows a characteristic vascular pattern, including hypervascularity of the mass, centrifugal arterial flow originating from central portion of the tumor and, in some cases, radiating peripherally from a central vessel in a stellate configuration [5].

At real-time CEUS, FNH shows a typical stellate or spoke wheel pattern, followed by complete enhancement during the arterial phase and remain hyper- or iso-vascular in the portal and late phase. A recent study evaluates the presence of typical signs of FNH in relation to lesion size. The results show stellate vascular enhancement in 95% of lesions larger than 3 cm, in only 30% of lesions smaller than 3 cm, while lesions smaller than 2 cm practically did not show this phenomenon at all. Also, the central scar was present in 85% of lesions larger than 3 cm and in only 20% of lesions smaller than 3 cm. Therefore, CEUS can be the final diagnostic method for FNH larger than 3 cm which has typical spoke-wheel vessel structure. If this phenomenon is not present and the central scar is not visible, specific diagnosis of FNH cannot be based solely on CEUS findings [9]. In generally, the typical pattern has been observed in 74-100% of FNH [10, 11]. In CEUS, the differentiation with adenoma is made by the presence of a central feeding artery, stellate vascularity with sustained enhancement in the portal venous phase, the absence of a capsule and the absence of areas of necrosis [12].

On unenhanced CT, FNH usually has iso-attenuation or slightly hypo-attenuation. A low-density central area, corresponding to the central scar can be seen in a third
of cases. During the arterial phase of contrast-enhanced CT, FNH rapidly enhances and becomes hyper-dense compared to the normal liver. In the portal-venous phase of enhancement, the difference in attenuation between FNH and normal liver decreases and FNH may become iso-dense with normal liver parenchyma. The central scar is almost always seen as a hypo-attenuation area to the ?? as compared with the remainder of FNH on both unenhanced and enhanced dynamic phase scans [8], while the fibrous scar may show early arterial enhancement [13]. A very useful tool in demonstrating the intratumoral vascularization of FNH is the 3D multidetector CT angiography, demonstrating the hepatic venous drainage and the absence of portal-venous supply. A pseudocapsular enhancement may be uncommonly seen surrounding the lesion in the parenchymal phase [13], but in our case this was absent.

On MR, FNH are considered classic when they appear as homogeneously iso-intense or slightly hyper-intense on T2-weighted images, and iso-intense or slightly hypo-intense on T1-weighted images, before contrast agent administration. An atypical MR imaging finding of FNH may consist of a marked T1 or T2 lesion hyper-intensity. The typical behavior during the dynamic phase of contrast enhancement consists of marked and homogeneous signal intensity enhancement during the arterial phase, rapid and homogeneous signal intensity wash-out during the portal venous phase, and signal iso-intensity (with the exception of the scar) during the equilibrium phase [13]. The fact that the lesion enhances to a higher degree than the surrounding liver tissue indicates the benign nature of the lesions, as well as the fact that the biliary system of FNH is malformed, slowing the biliary excretion [8].

A typical scar appears as a hyper-intense central stellate area on T2-weighted images and as a hypo-intense area on T1-weighted images. During the dynamic phase of contrast enhancement it is hypo-intense during the arterial and portal-venous phases and slightly hyper-intense in the equilibrium phase [8].

In our case, there was a typical enhancement, with the central scar retaining a hypo-attenuation appearance during the arterial phase. However, retention of contrast material within the fibrous scar can be observed on delayed scans, generating iso-attenuation or, more frequently, hyper-attenuation. Furthermore, on MR imaging, we noticed a hyper-intense focal nodule in T1/T2 developed in an area of normal hepatic tissue which, in turn, was surrounded by a fatty liver appearance (liver steatosis). Another particular observation in this patient was the male sex (FNH usually appears in female patients), as well as the surprising disposition of the FNH inside a small island of normal tissue in a largely fatty liver.

The use of contrast-enhanced dynamic MR imaging provides the greatest diagnostic sensitivity among the currently used imaging techniques, especially when combined with information available on pre-contrast T1 and T2-weighted images. However, the high frequency of atypical features does not allow accurate characterization of FNH in every case. In this regard, diagnosis on dynamic MR imaging with conventional extracellularly-distributed Gd agents relies on the same morphologic and hemodynamic features as helical CT [8]. A technique such as real-time virtual sonography, which combines the dynamic MR features with real-time ultrasound, including real-time CEUS, can certainly contribute to the accuracy of FNH diagnosis.

In conclusion, noninvasive imaging modalities, particularly CEUS and MRI, allow a reliable distinction of FNH from other focal liver lesions in most cases. Also, both methods represent ideal imaging modalities for work-up of these lesions in relatively young people suspected of having FNH, because radiation and iodine-based contrast media agents are not used.

References
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