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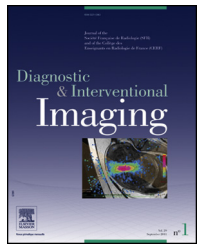

SHORT ORIGINAL ARTICLE / *Gastrointestinal imaging*

Interest of contrast-enhanced sonography to identify focal nodular hyperplasia with sinusoidal dilatation

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KEYWORDS
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Inflammatory hepatocellular adenoma;
Contrast-enhanced ultrasound;
Glutamine synthetase

Abstract
Background and aims: Focal nodular hyperplasia with major sinusoidal dilatation (FNH-sd) is a misleading entity, with some features resembling inflammatory hepatocellular adenoma (HCA). We aimed to assess the performance of contrast-enhanced ultrasound (CEUS) for the diagnosis of FNH-sd.
Methods: Four histologically proven FNH-sd nodules in four patients were investigated with both MRI and CEUS imaging. Sinusoidal dilatation was focally visible in all cases in histology.
Results: In MRI, in all the four cases, lesions were hypervascular in arterial phase, with high intensity in T2-weighted sequence imaging and persistent enhancement in the delayed gadolinium-enhanced phase. These MRI features were more indicative of HCA than FNH. On the other hand, CEUS showed a very specific centrifugal filling followed by a strong, homogeneous enhancement of the whole lesion.
Conclusion: CEUS seems to be an essential step for the diagnosis of non-typical FNH, such as FNH-sd. This small series highlights the interest of performing both CEUS and MRI for the diagnosis of atypical focal liver lesions, such as FNH-sd.

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Abbreviations

FNHa	focal nodular hyperplasia
HCA	hepatocellular adenoma
MRI	magnetic resonance imaging
FNH-sd	focal nodular hyperplasia with sinusoidal dilatation
TFNH	telangiectasic focal nodular hyperplasia
GS	glutamine synthetase
LFBAP	liver fatty acid-binding protein
CRP	C-reactive protein
SAA	serum amyloid A
HNF1 α	Hepatocyte nuclear factor-1 alpha
US	ultrasound
CEUS	contrast-enhanced ultrasound
AASLD	American Association for the Study of Liver Diseases
CK7	cytokeratins 7

Introduction

Majority of focal liver lesions are benign in non-cirrhotic liver. Focal nodular hyperplasia (FNH) is the second most common benign liver tumor after hemangioma [1]. The prevalence is estimated at 0.9% of the general population [2]. Although FNH may affect both sexes of all ages, it is more common in females (80%—95%) in their third or fourth decade of life [2]. FNH is often solitary but may be multiple in approximately 20% of cases. The pathogenesis of FNH is not well understood, but it is thought to be a non-specific response to locally increased blood flow. This hypothesis is strengthened by the fact that FNH can also be associated with vascular abnormalities as hepatic hemangiomas [3]. In 1995, the International Working Party classified FNH with other regenerative lesions, in contrast to adenoma (HCA), which is known as a neoplastic lesion [4].

FNH is usually asymptomatic, and most cases are discovered incidentally on abdominal imaging. Clinical symptoms due to mass effect are infrequent. These lesions must still be correctly diagnosed because surgical resection is limited to symptomatic FNH, while the others are left untreated.

FNH in its typical form is an easy diagnosis with cross-sectional contrast-enhanced imaging. Thus, the imaging features of FNH include homogenous lesions, significant enhancement on the arterial phase with a lack of washout during the portal venous and delayed phases, peripheral lobulation and the presence of a central scar. Based on these criteria, CT and/or MRI have a sensitivity of 70% and a specificity of 100% for the diagnosis of FNH.

However, in daily practice, there are still some difficulties concerning less typical forms, such as pre/incomplete FNH, absence of central scar, presence of steatosis and sinusoidal dilatation. The so-called ''telangiectasic FNH'' (TFNH) was shown to be, at the histological level, closer to the family of hepatocellular adenomas (HCA) than to FNH itself [5,6]. Subsequently, it was shown that most of the so-called TFNH were inflammatory HCA [7]. More recently, the distinction between FNH and other lesions, like inflammatory HCA, has been largely solved with the progresses of molecular biology and its application in immunohistochemistry. Indeed, glutamine synthetase (GS), markedly overexpressed in FNH in a particular ''map-like pattern'', was used as a useful immunohistological marker to differentiate FNH from HCA [8]. Moreover, FNH does not express markers of HCA subtypes: particularly C-reactive protein (CRP) and serum amyloid (SAA) are negative, whereas they are overexpressed in inflammatory HCA. In addition, liver fatty acid-binding protein (LFABP) is normally expressed in FNH contrary to its absence in hepatocyte nuclear factor-1 alpha (HNF1α) mutated adenoma [7—9].

In this short article, we report four cases of histologically confirmed FNH with sinusoidal dilatation (FNH-sd). MRI and contrast-enhanced ultrasound (CEUS) data were retrospectively analysed to determine specific semiological pattern of these particular FNH type.

Methods

This retrospective and monocentric study had the approval of our Research Ethics Board for chart review.

We identified four patients with FNH-sd from December 2008 to November 2011 in the database of our pathology department. Histological, medical (including blood liver tests) and radiological data were collected and analyzed.

Histological analysis

Percutaneous needle biopsies were performed under ultrasonographic guidance using a 16—18 Gauge needle, according to the recommendations of the American Association for the Study of Liver Diseases (AASLD). At least two cores of liver tissue were obtained per patient.

The biopsy specimens were processed and paraffin sections were stained with H&E, Masson's trichrome, Perls. Additional immunostaining was performed, such as cytokeratins (K) 7 and 19, as well as glutamine synthetase (GS), serum amyloid A (SAA), C-reactive protein (CRP) and β-catenin.

MRI

MRI was performed on a 1.5 T MRI system (Achieva, Phillips Medical System, Best, The Netherlands), in our radiology department. For all MRI examination, the following sequences were acquired and analysed: axial in-phase and out-of-phase chemical-shift GRE T1-weighted (T1 W) images (repetition time/echo time, 208/2.3 and 4.6 msec; flip angle, 80°; field of view, 430 mm; matrix, 292 × 178; number of sections, 30; section thickness, 5.4 mm; two signals acquired); a respiratory-triggered, fat-suppressed, T2-weighted (T2 W) fast spin-echo pulse sequence (repetition time/echo time, 1,287/70 msec; flip angle, 90°; field of view, 450 mm; matrix, 308 × 156; number of sections, 30; section thickness, 5 mm; one signal acquired); a T2 W fast spin-echo pulse sequence (repetition time/echo time, 531/60 msec; flip angle, 90°; field of view, 395 mm; matrix, 256 × 136; number of sections, 25; section thickness, 6 mm; one signal acquired); and fat-suppressed dynamic gadolinium-enhanced T1 W gradient echo sequences during the arterial phase, late arterial phase, portal venous phase, and delayed phase, with manual administration of gadolinium-based contrast medium (repetition time/echo time, 4/1.92 msec; flip angle, 10°; field of view, 430 mm;