Focal nodular hyperplasia of the liver with pseudo-angiomatous appearance of the central area: MRI findings and physiopathological insights

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Radiology Case. 2008 Oct; 2(4):8-12 :: DOI: 10.3941/jrcr.v2i4.47

ABSTRACT

We report an unusual case of focal nodular hyperplasia (FNH) with angioma-like vascularity in the central scar illustrated on MRI and proven by histopathology. The vascular theory of common causative factors in FNH and haemangioma is discussed.

CASE REPORT

An incidental nodular lesion of the liver was identified in an asymptomatic 30-year-old woman during screening abdominal ultrasonography. The patient had no symptom, especially no abdominal pain. She reported no surgical or medical history. She had taken oral contraceptives during 10 years. Liver function test and tumour markers were within normal limits.

An abdominal MRI was decided to be performed by the family physician. A 1.5 T clinical imaging system (Symphony, Siemens, Erlangen, Germany.) was used to perform liver study. Sequences included T2-weighted fast spin echo and T1-weighted gradient echo with and without fat suppression. A T1-weighted gradient echo MR sequence was performed during the hepatic arterial, portal and venous phases after administration of gadolinium. Delayed-phase imaging was performed at 3 and 5 minutes after contrast injection.

MR Images revealed the presence of a 3 cm lesion in the right lobe of the liver (segment V). Axial T2-weighted image identified an iso intense lesion relative to the surrounding liver parenchyma. Furthermore, we identified a nodular zone, hyperintense on T2 weighted images (Fig. 1a) and becomes brighter as the time to echo is lengthened (Fig. 1b). On in phase T1-weighted images, the lesion appeared slightly hypo intense to the liver less than the center. Axial gadolinium-enhanced T1-weighted GRE image obtained during arterial phase shows intense homogeneous enhancement except in the nodular zone (Fig. 1c). In the portal phase, the lesion was intense relative to the surrounding liver parenchyma. Whereas the enhancement of the lesion progressively decreased, the nodular zone demonstrated peripheral puddling of contrast (Fig. 1d). A pseudo-capsule appeared like a thick ring around the lesion in slightly hypo signal on T1 and T2-weighted images, and was enhanced during the delayed phase.

MRI results provided uncertain diagnosis' and a surgical resection was performed without post operative complication. Intra-operative ultrasonography showed a hypo-echogenic 3 cm nodular mass at the junction of liver segments VII/VIII. There were no central scars neither radial fibrous bands. Enucleo-resection was done after a short hepatotomy using ultrasonic dissection and TissueLink□. Post-operative course was uneventful and patient was discharged on post-operative day 8.

Macroscopically, the lesion was well limited, measured 25 mm in diameter. Its overall architecture was that of a classical FNH, with the presence of a small, but fully developed, central scar; however, the central scar contained a small area of unusual appearance, characterized by the presence of blood-

filled cavities. The histological examination made it possible to confirm the nature of the lesion and to better analyze the unusual alterations of the central scar. The lesion had all the characteristics of a FNH, organized around a central scar containing large dystrophic vessels, small bile ductules and focal inflammatory infiltrates; fibrous bands, radiating from the central scar, separated nodules of hyperplastic, normal-appearing hepatocytes; in periphery, the lesion was not encapsulated but well limited by a pseudo-capsule (Fig. 2a).

The only unusual feature was the presence of a large, nodular area containing dilated, blood-filled vascular cavities; this area was located between the central scar and the adjacent hyperplastic hepatocyte nodules. At closer examination, blood-filled vascular cavities were found to correspond to preexisting, dilated capillary vessels running between hepatocyte plates (Fig. 2b). Hepatocyte plates were readily visible at the contact with adjacent hyper plastic nodules; they became progressively atrophic and disappeared in the vicinity of the central scar in which they were replaced by a dense fibrous tissue containing scattered inflammatory cells and small biliary ductules (Fig. 2c). In the vicinity of this area, a large dystrophic vessel with thrombotic obliteration of the lumen could be observed (Fig. 2d).

The final histological diagnosis was therefore typical FNH, with progressive destruction of a pre-existing hyperplastic nodule by an ischemic and congestive process.

DISCUSSION

FNH is the second most common benign tumour of the liver after venous haemangioma: its prevalence is reported to be 0, 9 % in the general population (1). In contrast to liver adenoma, FNH is considered to be a non neoplastic lesion, without risk for malignant transformation. Indeed, it is now largely assumed that FNH is a hyperplastic pseudo-tumor, secondary to vascular malformations or local disturbances in arterial blood flow. FNH occurs predominantly in women (ratio male to female 1:8) and in the third to fifth decades of the life (1,2). Most commonly, FNH is discovered in asymptomatic patients. Its radiological appearance is usually highly characteristic: imaging features are specific enough to allow a definitive diagnosis. No treatment is usually required, except for very large or painful tumors. Only cases with atypical features are submitted to histological evaluation and/or surgical resection.

On MR imaging, Hemangioma is iso- or hypointense on T1-weighted images, is hyperintense on T2-weighted images. Hemangioma shows either an homogeneous enhancement in arterial and portal phases for lesion less than 2 cm or peripheral, nodular discontinuous enhancement with progressive centripetal filling on delayed phase. Adenoma is a mass with heterogeneous signal intensity on T1and T2-weighted images due to fat and recent hemorrhage. Heterogeneous enhancement mass on arterial phase with presence of pseudocapsule on delayed phase. For the diagnosis of HCC on MR imaging, lesion is variable on T1-weighted images and hyperintense on T2-weighted images. HCC is typically an hypervascular lesion on arterial phase and a wash out on portal phase. For cholangiocarcinoma, lesion is heterogeneous hypointense on T1-weighted images and hyperintense with large central hypointensity on T2-weighted images. Enhancement is variable without specificity.

We here report a case of FNH with atypical imaging features raising diagnostic problems. The atypical imaging aspects were found to correspond to the existence of unusual histological lesions which may cast some light on the pathophysiology of this lesion and its growth pattern. The same case was reported by Saito in short communication and possible mechanism of pathogenesis of the FNH was suggested (3, 4).

Typical FNH can be diagnosed by US bidimensionnal Doppler or with injection of contrast, computed tomography (CT) and Magnetic Resonance Imaging (MRI). MRI has higher sensitivity (70%) and specificity (98%) (5). Typically, FNH is iso- or hypo-intense on T1 weighted images, slightly hyper- or iso-intense on T2 weighted images. Typical FNH shows an intense homogenous enhancement in arterial phase and an enhancement of the central scar in the later phase of gadolinium imaging. The central scar could be seen hyper-intense on T2-weighted images and low in signal intensity on T1-weighted images. A pseudo-capsule may be sometimes prominent; it results from the compression of the surrounding liver parenchyma, the presence of peritumoral vessels and of an inflammatory reaction. The pseudo-capsule is usually a few millimetres thick and typically shows high signal intensity on T2-weighted images and enhancement on delayed contrast-enhanced images.

Despite the atypical imaging features seen in this case, the macroscopical and microscopical appearances of the lesion were highly characteristic. Indeed, the lesion presented all the features of a typical FNH. It contained a typical central scar, from which radiated fibrous septa separating hyperplastic nodules made of normal-appearing hepatocytes. The central scar was formed by a dense fibrous connective tissue containing abnormal vessels, some degree of cholangiolar proliferation and scattered inflammatory infiltrates. The only unusual histological feature, likely to be responsible for the atypical imaging appearance of the tumor, was the presence of a large pre-existing hyperplastic nodule, containing dilated blood vessels running between atrophic hepatocellular plates, progressively replaced by a fibrous, inflammatory tissue. The presence, in the vicinity of this lesion, of a large thrombotic vessel is in keeping with a process of ischemic and congestive nature.

Despite the presence of vascular alterations, the tumor reported here must not be confused with the so-called “telangiectatic FNH”, which is now considered to be a variant of liver cell adenoma. In “telangiectatic FNH”, the typical architectural features of typical FNH, such as the central scar, are absent; the vascular alterations include the presence of telangiectatic capillary vessels around the fibrous septa and of areas of pseudo-peliotic sinusoidal dilatation within the tumour (1,2). Vascular lesions are therefore very different from those observed in our case, which were focal in distribution and corresponded to the dilatation of pre-existing vessels associated with hepatocellular atrophy and progressive fibrosis.

Another differential diagnosis to consider was hemangioma associated with FNH. The presence of both lesions in the same patients is estimated to 20 % (6). At imaging studies and even at macroscopical examination, some features were confusing. The accumulation of blood within dilated pre-existing vessels resulted in imaging and gross features mimicking those of typical hemangiomas. However, the histological appearance of the lesion easily ruled out this diagnosis.

The unusual lesion observed in the present case of FNH may cast some light on the pathophysiology of this entity. Its overall appearance strongly recalls the features of the so-called parenchymal extinction which may be observed in cirrhosis. Parenchymal extinction corresponds to the progressive destruction of pre-existing cirrhotic nodules as a result of a focal ischemic process induced by local hemodynamic disturbances. It has been suggested that parenchymal extinction is one of the main determinants of the progression of fibrosis in chronic liver disease. Our observation strongly suggests that a comparable process may be operating in FNH and may play a role in the growth of the lesion. Indeed, it is now assumed that early FNH are small lesions essentially devoid of a central scar and formed by hyperplastic nodules separated by thin fibrous septa. The progressive growth of FNH is thought to be associated with the expansion of the central scar and the enlargement of hyperplastic nodules. Our observation suggests that one of the mechanisms responsible for the expansion of the central scar may be the progressive destruction of pre-existing hyperplastic nodules after intra-tumoral ischemic events.

In conclusion, we report here a case of atypical FNH, characterized by unusual imaging features due to the presence of an area of hyperplastic parenchyma undergoing a progressive process of extinction, secondary to vascular disturbances.

TEACHING POINT

This observation suggests that in FNH, intra-tumoral ischemic events may result in the progressive expansion of the central scar through the destruction of pre-existing adjacent hyperplastic nodules.

ABBREVIATIONS

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T = Tesla
FNH = Focal nodular hyperplasia
HCC = Hepatocellular carcinoma
US = Ultrasound
CT = Computed tomography
MRI = Magnetic resonance imaging
GRE = Gradient echo

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FIGURES

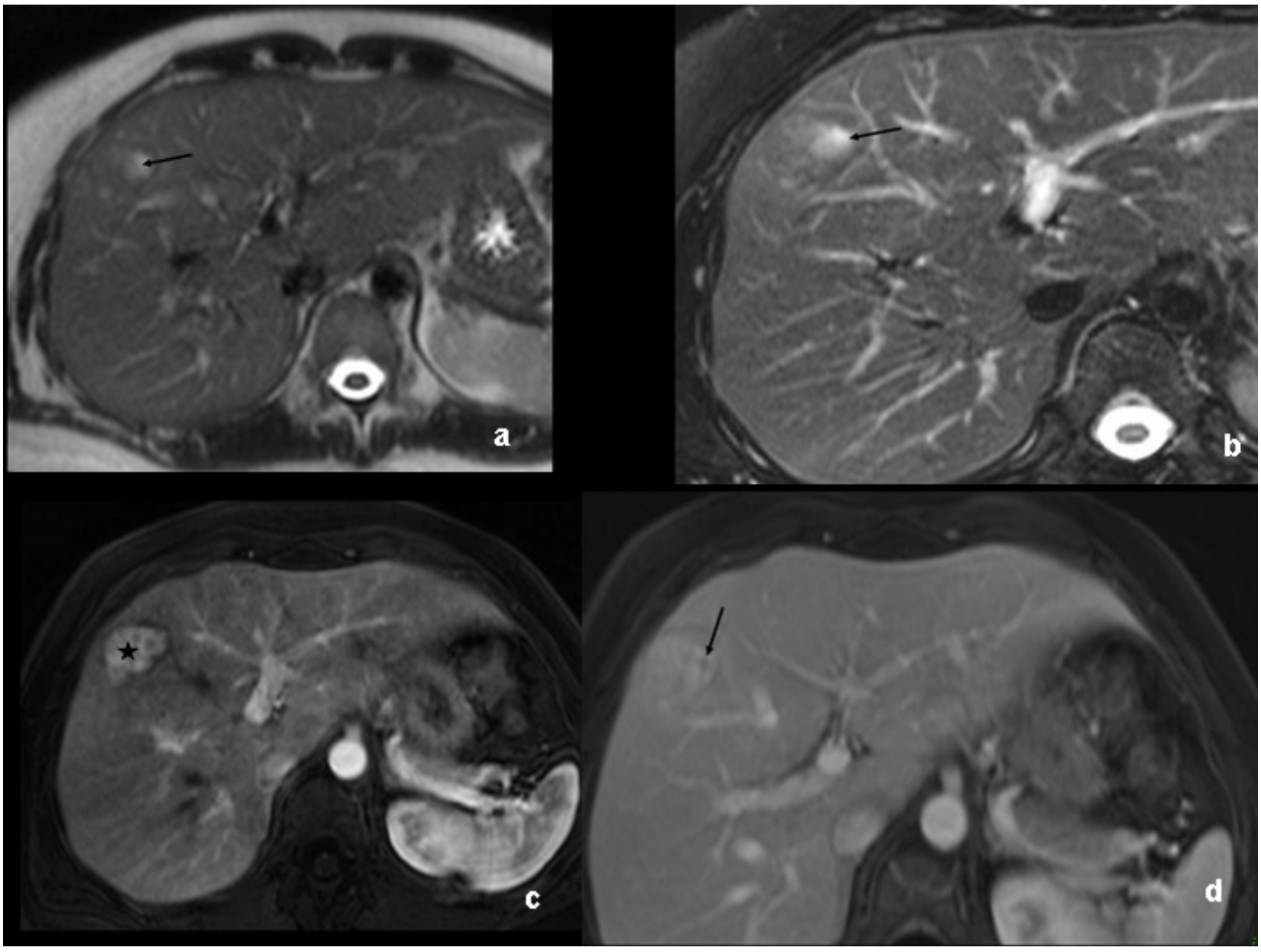

Figure 1: Magnetic Resonance features of the lesion. (a) Transverse T2-weighted fast spin-echo MR image shows a homogeneous lesion that is faintly hyperintense to surrounding liver parenchyma, except for a nodular zone which is hyperintense (black arrow). (b) Transverse T2-weighted fast spin-echo MR image with long TE (TE : 160 msec) shows a brighter nodular zone (black arrow) within the homogeneous lesion.

(c) Transverse T1-weighted gradient-echo MR image obtained during the hepatic arterial phase demonstrates strong homogeneous lesion enhancement (star) except for the central nodular area. (d) Transverse T1-weighted gradient-echo (TR/TE : 160/4.9 msec) MR image obtained during portal venous phase imaging shows the lesion as the same intensity compred to the surrounding liver parenchyma. The nodular zone shows peripheral puddling of contrast (black arrow).

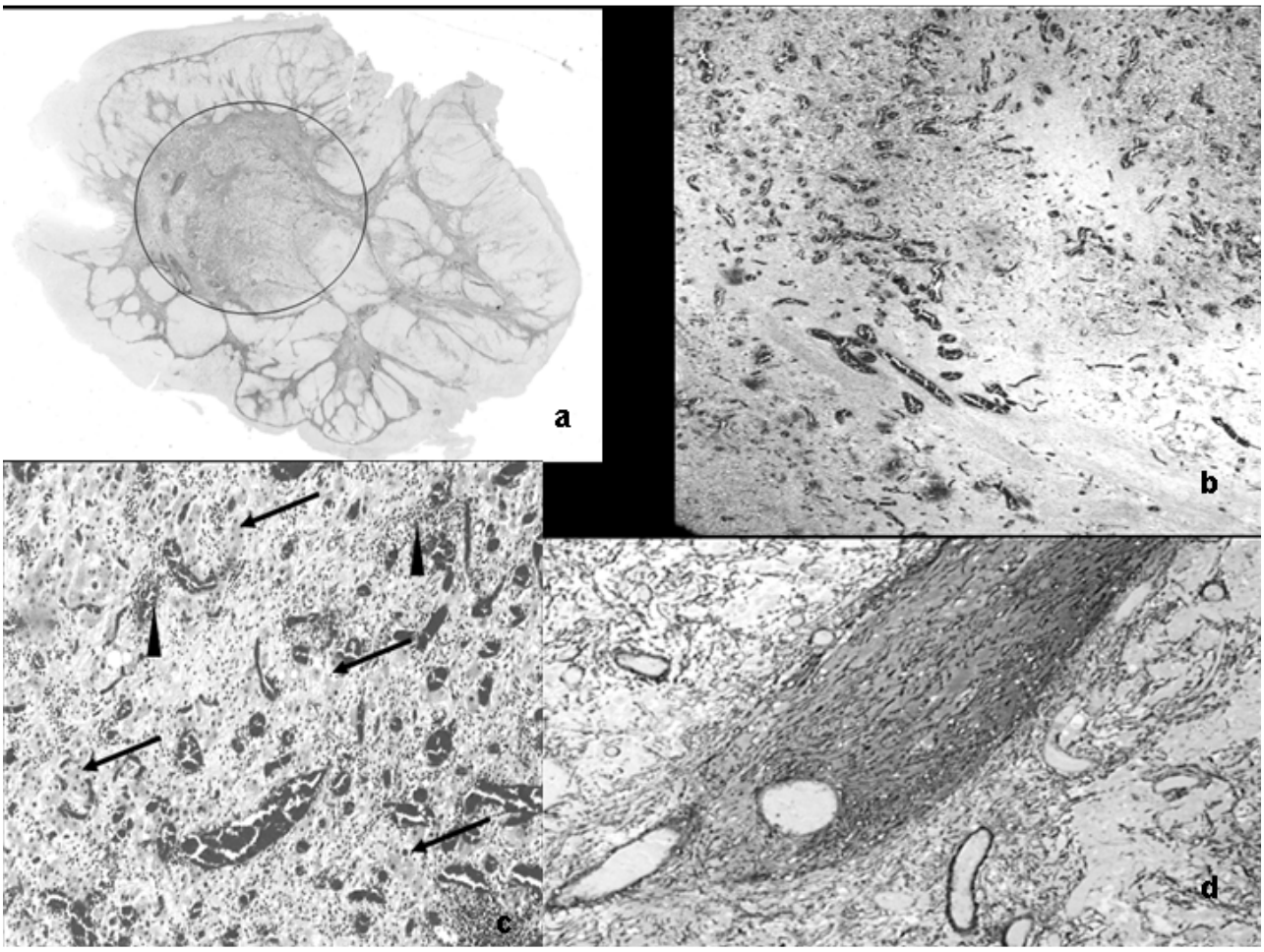

Figure 2: Histological features of the lesion. At low magnification (a), the overall architecture of the lesion, by alpha-SMA (alpha-Smooth Muscle Actin) immunodetection, is typical of a FNH: the central scar is well visible and fibrous septa separate hyperplastic nodules; in periphery, the lesion is well limited and a pseudo-capsule is visible; within this otherwise typical lesion, an area (encircled) shows unusual and distinctive histological features. At higher magnification (b), this area is characterized by the presence of dilated blood vessels scattered with a fibrous tissue. At even higher magnification (c), atrophic hepatocytes (arrowheads) are visible within the fibrous tissue, between dilated blood vessels; inflammatory cells are numerous (arrows). In the vicinity of the lesion (d), a large vessel with obliteration of the lumen by an organized thrombus, underlined by alpha-SMA immunodetection, is visible.

a, indirect immunoperoxidase, original magnification, x40; b, hematoxylin-eosin staining, original magnification, x160; c, hematoxylin-eosin staining, original magnification, x240; d, indirect immunoperoxidase, original magnification, x120.

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