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IMAGING FINDINGS OF HEPATIC FOCAL NODULAR HYPERPLASIA IN GD-EOB-DTPA VS. GD-BOPTA-ENHANCED MRI

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SUMMARY

Focal nodular hyperplasia (FNH) is a benign focal lesion of the liver. Magnetic resonance imaging (MRI) plays a key role in the detection and characterization of focal hepatic lesions, thanks to the widespread availability of conventional contrast media, especially liver-specific media such as Gd-BOPTA (Multihance, or Gadobenate Dimeglumine) and Gd-EOB-DTPA (Primovist, or Gadoxetic Acid) that are selectively accumulated in hepatocytes and partially excreted by the biliary system. There are no significant differences in FNH enhancement, neither during the dynamic phase nor during the liver-specific phase of MRI, following the infusion with GD-BOPTA or GD-EOB-DTPA.

Introduction

Focal nodular hyperplasia (FNH) is a benign focal lesion of the liver. It is considered a hyperplastic reaction of the hepatic parenchyma to abnormal arterial hyperperfusion of either congenital or acquired origin. It is found in 3 to 8% of the adult population, and represents the most frequently diagnosed benign lesion after hemangioma. Focal nodular hyperplasia is more common in young women (third-fourth decade of life), with a female/male ratio of 8:1. In most cases, FNH is asymptomatic. Symptomatic patients may complain of abdominal pain, and may sometimes present with hepatomegaly. Liver function markers are normal in about 50% of cases, while the remaining half show an increase of gamma-glutamil-transepeptidase. Due to the fact that the typical FNH remains stable over time and does not undergo malignant transformation or rupture, its treatment is conservative. Currently, it is thought that the use of oral contraceptives does not cause the development of FNH. However, their use may stimulate FNH growth, while suspension of oral contraceptives is often followed by a decrease in the size of the lesion. The classic form of FNH is a non-capsulated lesion, composed of nodules appearing as normal hepatocytes crowded around a fibrous core. From this core, septa containing dilated vessels and bile ducts (but no portal vessels) branches off radially. The central fibrotic area is rich in connective tissue, in which various abnormal arteries and an intense proliferation of biliary structures, surrounded by inflammatory cells, can be observed. Ultrasound, CT and MRI scans (sometimes combined with guided percutaneous biopsy) are widely used for liver investigations. Currently, MRI plays a key role in the detection and characterization of focal hepatic lesions, thanks to the widespread availability of conventional contrast media, especially liver-specific media, such as that are selectively picked up by hepatocytes with partial biliary excretion. These contrast agents

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can be employed to perform a classic dynamic MRI study (with arterial, portal venous and late phase imaging) and a liver-specific delayed phase study (after 1-3 hours and 20-40 minutes, respectively). The aim of our study was to assess, both qualitatively and quantitatively, FNH enhancement during the dynamic and liver-specific phases of MRI, obtained with the two most commonly used contrast media (Gd-BOPTA and Gd-EOB-DTPA, or Gadobenate Dimeglumine and Gadoxetic Acid), in order to compare their characteristics and behavior, as well as to detect any differences between these two agents.

Materials and methods

Study population

17 patients (15 female and 2 male), aged from 19 to 54 (average 41 years), with FNH of a mean size of 2,6 cm (max. 6 cm, min. 1,4 cm), underwent two MRI scans, one with Gd-BOPTA and the other with Gd-EOB-DTPA with a mean interval of about one year (min. 5 months, max. 14 months, average 10 months). 12 patients (1 male and 11 female) had a unique lesion, while 5 patients (1 male and 4 female) had multiple (2 or more) lesions, for a total of 24 FNH. Both MRI scans were performed by means of a 1.5 T system with phased array body coils. A standard protocol was been followed, involving acquiring imaging sequences both in basic conditions and after intravenous administration of 0.1 ml/kg of Multihance or Primovist. Arterial, portal and equilibrium phase images were acquired after 13 seconds, 120 seconds and 3-5 minutes from the automatic bolus detection, respectively. The liver-specific phase images were acquired 1-3 hours after Multihance injection, or 10-20 and 30 minutes after Primovist injection. Two radiologists valued three parameters for every lesion: lesion intensity compared to the surrounding hepatic parenchyma before contrast agent administration (hypo-intense, iso-intense or hyper-intense); during arterial, portal, equilibrium and liver-specific phases; as well as the presence of central scar presenting as a hypo-intense area after administration of a contrast agent.

Results

In 19 of 24 lesions, FNH behavior was similar with both contrast agents, appearing hyper-intense in the arterial, portal and equilibrium dynamic phases, and iso-intense in the liver-specific phase. In three of 24 lesions, FNH behavior was slightly different between the two agents, with a predominant iso-intensity during the portal -venous and equilibrium phases following the administration of Gadoxetic Acid compared to Gadobenate Dimeglumine. However, one lesion showed a predominant iso -intensity during the portal-venous and equilibrium phases following the administration of Gadobenate Dimuglimine compared to Gadoxetic Acid. In another patient, the lesion showed atypical characteristics, being hypo-intense during the liver-specific phase. A concordance of 79.2% ($p < 0.05$) was found between the two contrast agents, both qualitatively and in terms of liver-specific phase intensity signal.

Discussion

The MRI is an imaging method with high diagnostic and characterization capacity in FNH, as confirmed by our results. Notably, the application of liver-specific contrast agents (confirming the benign hepatospecific nature of FNH) increases the sensitivity and specifity of this technique considerably. The typical characteristics of a FNH lesion include iso-intensity or slight hyper- intensity, when compared to the remaining liver parenchyme in T2 sequences, and iso-intensity or slight hypo-intensity in T1 sequences. Gadolinium injection is followed by an immediate, intensive and homogeneous enhancement in T1w sequences during the arterial phase (Figure 1A), and a constant, but less evident hyper-intensity, during the subsequent portal phase (Figure 1B), tending to iso-intensity during the equilibrium phase (Figure 1C), due to the progressive drainage of the contrast media from the peripheral vein. The central scar is generally visible as a focal area of hyper-intensity in the T2w sequences due to the presence of myxomatous tissue and the hypo-intensity during the T1w sequences. The scar is generally hypo-intensive in the arterial and portal phases, with the progressive filling of contrast media making it hyper-intense in the equilibrium phase; this phenomenon is caused by the delayed draining of the gadolinium from the myxomatous tissue of the scar. After the administration of liver-specific contrast media, the lesion appears iso- or faintly hyper-intense in the T1w

sequences (Figure 1D), clearly different from angioma, adenoma as well as primitive and secondary malign hepatic lesions that do not accumulate the contrast media due to mutated or completely absent hepatocyte functionality (thus resulting hypointense).

From the analysis of the data obtained during this study, it is clear that there are no significant differences in the enhancement characteristics of FNH, neither during the dynamic phases nor during the liver-specific phases of MRI scans performed after infusion with GD-BOPTA and GD-EOB-DTPA. The application of Primovist allows, moreover, a considerably shorter acquisition time for the liver-specific phase (after 20-30 minutes and not after two hours like with Multihance), as well as the possibility of acquiring the T2 sequences during the time interval between the two delayed phases, resulting in a more efficient management and better patient compliance.

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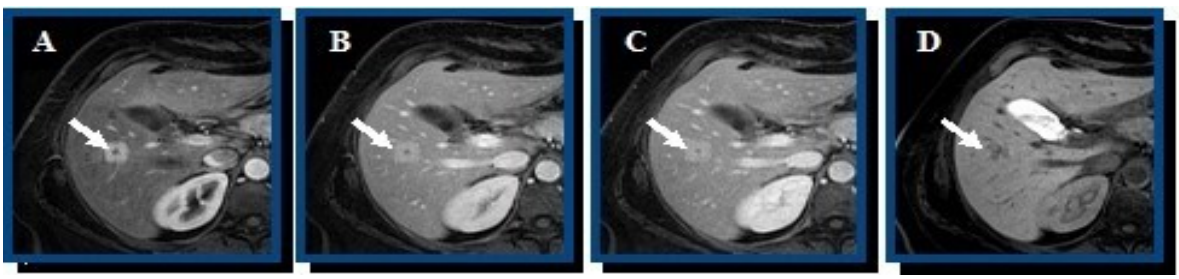

Figure 1: FNH enhancement after gadolinium injection: the lesion is visible as a focal area of hyper-intensity during the arterial phase (A), less evident hyper-intensity during the subsequent portal phase (B), tending to iso-intensity during the equilibrium phase (C). After the administration of liver-specific contrast media, the lesion appears iso- or faintly hyper-intense (D).

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