

Multiple focal liver lesions – diagnosis challenges. Case report

Cătălina Mihai^{1,2}, Bogdan Mihai^{1,3}, Felicia Crumpei³, Camelia Barr³, Dan Ferariu³, Ștefan Gergescu^{1,3}, Cristina Cijevschi Prelipcean^{1,2}

¹ „Gr. T. Popa” University of Medicine and Pharmacy, Iași, Romania

² Gastroenterology and Hepatology Institute, Iași, Romania

³ „Sf. Spiridon” University Hospital, Iași, Romania

Abstract

Multiple focal liver lesions can generate diagnosis difficulties in daily practice. This paper present the case of a 53 years old patient with multiple hyperechoic liver lesions suggestive for hepatic hemangiomas, detected during the ultrasonographic exam. Contrast enhanced ultrasonography indicated focal hepatic steatosis, while computed tomography proposed possible liver metastasis. The histological diagnosis was focal nodular hyperplasia associated with hepatic steatosis. The peculiarity of the case was the association of multiple focal nodular hyperplasia lesions with hepatic steatosis and atypical imaging findings that required histological confirmation.

Key words: multiple focal nodular hyperplasia, hepatic steatosis, ultrasonography, computed tomography.

Rezumat

Leziunile focale multiple hepatice pot crea dificultăți de diagnostic în practica clinică. Prezentăm cazul unei paciente în vârstă de 53 de ani la care examenul ecografic a decelat formațiuni hepatice hiperecogene multiple cu aspect de hemangioame hepatice. Ecografia cu substanță de contrast a sugerat diagnosticul de steatoză focală hepatică, în timp ce computer tomografia a indicat posibile metastaze hepatice. Diagnosticul de certitudine a fost cel histologic – hiperplazie nodulară focală multiplă asociată cu steatoză hepatică. Particularitatea cazului consta în asocierea leziunilor multiple de hiperplazie nodulară focală cu steatoză hepatică și aspecte atipic la explorarea imagistică a ceea ce a impus confirmare histologică.

Cuvinte cheie: hiperplazie nodulară focală multiplă, steatoză hepatică, ultrasonografie, computer tomografie

Introduction

The etiological diagnosis of multiple focal liver lesions may sometimes represent a real challenge for the physician. Focal nodular hyperplasia (FNH) is the second most frequent benign liver tumor after hemangioma [1]. Usually it appears as a solitary lesion, but in 20% of cases multiple lesions may occur [2]. Along with the development of high performance imaging techniques (contrast enhanced ultrasonography, computed tomogra-

phy, magnetic resonance imaging) the diagnosis accuracy of this pathology has increased. In most cases the imaging findings are characteristic, allowing a certain diagnosis, even without the histological exam. There are many situations mentioned in literature where the atypical imaging aspects may generate problems of differential diagnosis with other benign or malignant liver lesions [3,4].

Case presentation

A female patient 53 years old, without significant personal or family history, was admitted in the Gastroenterology and Hepatology Institute, Iasi, for right upper quadrant pain and asthenia, as part of an insidious onset that started few weeks earlier. The patient was non-smoker, did not use alcohol, oral contraceptives or other drugs. The physical exam revealed an increased

Received 24.11.2010 Accepted 17.01.2011

Med Ultrason

2011, Vol. 13, No 1, 72-75

Address for correspondence:

Dr. Cătălina Mihai

Bd. Independenței, nr. 1

700111, Iași

Tel: +40-745501967

Email: catalinamihai@yahoo.com

body mass index (26 kg/m²), the liver was slightly enlarged, 2 cm below the right costal margin, with soft consistency and it was not tender to palpation. The laboratory studies indicated mixed dyslipidemia (cholesterol levels 278 mg/dl, triglycerides levels 290 mg/dl). The hemogram, liver function tests, glycemia, kidney function tests, alpha-fetoprotein and lactate-dehydrogenase levels were within normal limits and viral serologies for B and C hepatitis (HBs antigen, anti-HCV antibodies) were negative.

The abdominal ultrasound exam showed a slightly enlarged liver (anterior-posterior diameter of the right lobe was 185 mm and of the left lobe 70 mm) with multiple hyperechoic, homogeneous, well-circumscribed masses, with no Doppler signal, suggesting liver hemangiomas: in segment 5 there was a 39 mm mass, close to the left hepatic vein; in segment 4 there were two lesions, 14.9 mm and 25 mm; in segment 6/7 an 8-10 mm lesion and in the caudate lobe there was a 10 mm mass (fig 1). The other abdominal organs (gall bladder, pancreas, spleen, kidneys, urinary bladder and ovaries) had a normal ultrasonographic appearance.

Contrast enhanced ultrasonography revealed normal enhancement in the arterial phase, without specific pattern. The lesions were isoechoic with the rest of the liver parenchyma in the portal and venous phase, an aspect that suggested focal hepatic steatosis (fig 2).

The contrast enhanced CT scan identified in both lobes of the liver multiple lesions, hypodense before and after contrast media administration, with moderate attenuation after contrast media injection (fig 3). The conclusion of the CT scan exam was that of metastasis from an unknown primary source.

The investigations that were performed in order to discover a possible primary tumor (upper GI endoscopy, colonoscopy, gynaecological exam, endocrinology consultation, thoracic X ray, tumor markers) were all negative and magnetic resonance imaging was not available due to technical reasons.

Since there were discrepancies between the imaging investigations an exploratory laparotomy followed by a histological exam was decided. The biopsy of a nodule from the 4th segment of the liver revealed an area of nodular regeneration suggesting focal nodular hyperplasia as well as macrovesicular steatosis with fatty cysts.

The final diagnosis was benign liver lesions: multiple FNH associated with hepatic steatosis.

Discussions

The presented case demonstrates the diagnostic challenges that multiple focal nodular hyperplasia raises.



Fig 1. Multiple focal nodular hyperplasia. Ultrasonographic aspect: hyperechoic, homogeneous, well-circumscribed liver lesions. The mass in segment 5 is close to the left hepatic vein.

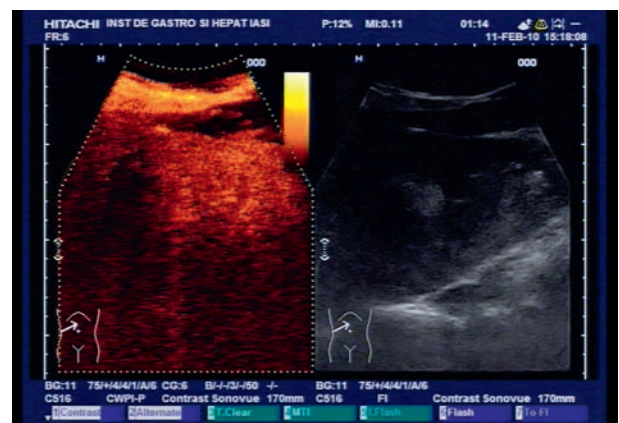


Fig 2. Focal nodular hyperplasia associated with hepatic steatosis. Contrast enhanced ultrasonography findings: the contrast media uptake is similar to that of the rest of the liver parenchyma in all three phases, arterial, portal and parenchymal phase.



Fig 3. Multiple focal nodular hyperplasia. CT scan aspect: low attenuating hepatic lesion relative to rest of the liver parenchyma. The density of the lesions becomes slightly increased after contrast media administration.

Focal nodular hyperplasia (FNH) is a congenital vascular anomaly accompanied by a hyperplastic reaction of the hepatocytes. It is characterized by an agglomeration of normal hepatocytes and mesenchymal cells in an abnormally organized pattern [5]. In the centre of the lesion there is a fibrous scar that contains arteries and veins. FNH represents 8% of all liver tumors and is the second most frequent benign liver tumor after hepatic hemangioma. It is more common in women and is associated with the use of oral contraceptives [6]. The lesion may be solitary or, in less than 20% of cases, multiple. In 23% of the situations it may be accompanied by liver hemangiomas or adenomas.

There are two categories of FNH: classic FNH (80%) (entails an abnormal nodular pattern, malformed vessels and cholangiolar proliferation) and nonclassic FNH (20%) which is divided into: teleangiectatic, with cell atypia and mixed – hyperplastic and adenomatous [7].

The ultrasonographic aspect of FNH is that of an iso- or hyperechoic lesion (it can be hypoechoic, too, if it has developed in a fatty liver); the central scar is considered the characteristic feature of FNH, but is visible in only one third of the cases [8].

Doppler sonograms reveal a hypervascular lesion (the aspect requires a differential diagnosis with hepatic hemangioma); the typical aspect, difficult to demonstrate in lesions smaller than 3 cm, is that of a “spoke-wheel-like” pattern where the vascular structures are identified in the centre of the mass, corresponding to the central scar [9].

Contrast enhanced ultrasonography identifies a rapid contrast uptake in the arterial phase. The filling takes place from the centre and spreads to the margins of the mass with a “spoke-wheel-like” pattern. In the portal phase the lesions remains hyperechoic compared to the rest of the liver parenchyma and in the late phase it is either hyper- or isoechoic [10,11].

In most cases of FNH the diagnosis is established through CT scan, MRI or histopathological examination.

The characteristic aspect on nonenhanced CT scan is that of a solitary, homogenous, slightly hypoattenuating nodule; in 20% of the situations the hypodense scar in the centre of the lesion may be observed [4]. During the arterial phase a rapid and intense fill is noticed, except in the central scar which presents a delayed uptake because of the myxomatous stroma [4]. In the venous phase the contrast agent washes out; in delayed acquisitions the lesion is isodense relative to the rest of the hepatic parenchyma, but the central scar has a delayed wash-out. Atypical features are lack of identification of the central scar, unhomogeneous uptake, pseudocapsular peripheral vascular ring and hypoattenuation after contrast media injection [12].

Magnetic resonance imaging identifies the lesion as hypointense in T1 and iso- or hyperintense and homogeneous in T2. The central scar appears hyperintense in T2 [4].

The typical imaging features are not found in all cases of FNH, as the previously presented case has just confirmed. Other studies in literature present cases of FNH with discordant findings without being able to fully elucidate the cause of these differences [13].

In our case, the central scar, considered the “mark” for FNH diagnosis, was not evident in either of the performed investigations. Literature studies show that the central scar cannot be visualized in 66% of the cases through ultrasonography, in 40% through CT scan and in 22 % through MRI [4].

Multiple lesions of FNH are found in only 20% of the cases. Hyperechoic hepatic nodules discovered ultrasonographically raise a series of differential diagnosis problems: multiple hepatic hemangiomas, focal hepatic steatosis, hepatic metastasis, multicentric hepatocellular carcinoma, lymphomatous infiltration, granulomatosis or FNH [14].

Doppler and contrast enhanced ultrasound both failed to demonstrate the hypervascular character of the lesions. Since it is known that the sensitivity of imaging techniques is related to the size of a lesion a possible explanation could be the rather small size of the nodules as most of them were between 10 and 20 mm [15]. In the case of contrast enhanced ultrasonography if image acquisition is performed after 20 seconds in the arterial phase the hypervascularity may be missed [16].

Another particularity of the case is represented by the fatty infiltration of the FNH lesions, a detail that is rarely mentioned in literature [4,17,18]. Usually these aspects are found in generalized hepatic steatosis and in very rare cases the exclusive fatty infiltration of the FNH lesions is described. In the presented case obesity and dyslipidemia are the most probable cause of hepatic steatosis. The presence of fatty liver infiltration in the FNH nodules – confirmed by histology – may explain the contrast enhanced ultrasound findings.

The presence of multiple nodules and the absence of the central scar made it difficult for the CT scan to exclude hypervascular hepatic metastasis. MRI, by providing information about tissue characteristics of the lesions, is superior to other imaging methods (ultrasonography, CT scan) in the diagnosis of FNH. In the study of Shen *et al* [19] on 86 patients with FNH, confirmed through histological exam, the CT scan was able to accurately define the lesions in 60.3% of the cases and MRI in 77.4%. Magnetic resonance imaging has 70% sensitivity and 98 % specificity [4], but it was not available in this case.

The final diagnosis in this case was histological and it was concordant with the clinical and biochemical data of the patient. None of the performed imaging techniques was able to show a typical aspect of focal nodular hyperplasia.

Conclusions

Focal nodular hyperplasia may represent a difficult diagnostic challenge, especially in situations with multiple lesions or association with hepatic steatosis. Standard and Doppler ultrasonography have a relatively small role in establishing the diagnosis. Contrast enhanced ultrasonography, computed tomography and magnetic resonance imaging – considered trustworthy diagnosis methods for FNH – may sometimes provide discordant findings, making histological confirmation necessary. Imaging investigation data must always be correlated with the clinical and biological aspects.

References

- Craig JR, Peters RL, Edmondson HA. Tumors of the liver and intrahepatic bile ducts, Fasc 26, 2nd serv Washington DC: Armed Forces Institute of Pathology 1989.
- Colle I, de Beek BO, Hoorens A, et al. Multiple focal nodular hyperplasia. *J Gastroenterol* 1998; 33: 904-908.
- Ssalamah A, Schima W, Schmook M, et al. Atypical focal nodular hyperplasia of the liver: imaging features of non-specific and liver-specific MR contrast agents. *AJR Am J Roentgenol* 2002; 179: 1447-1456.
- Mortele KJ, Praet M, Vlierberghe H, Kunnen M, Ros PR. CT and MR imaging findings in focal nodular hyperplasia of the liver: radiologic – pathologic correlation. *Am J Roentgenol* 2000; 175: 687-692.
- Badea R. Ficatul In: Badea R, Dudea SM, Mircea P, Stamtian F (eds). *Tratat de ultrasonografie clinică*. Editura Medicală, București 2009: 105-175
- Sporea I. Ecografia cu substanta de contrast (CEUS) în evaluarea leziunilor hepatice circumscrise. In: Sporea I, Dănilă M, Popescu A, Șirli R. *Ecografia cu substanță de contrast în patologia abdominală*. Editura Mirton, Timișoara 2009: 27-29.
- Nguyen BN, Flejou JF, Terris B et al. Focal nodular hyperplasia of the liver: a comprehensive pathologic study of 305 lesions and recognition of new histologic forms. *Am J Surg Pathol* 1999; 23: 1441-1454.
- Lin LW, Yang JJ, Lin XY et al. Effect of fatty liver background on contrast enhanced ultrasonographic appearance of focal nodular hyperplasia. *Hepatobiliary Pancreat Dis Int* 2007; 6: 610-615.
- Piscaglia F, Venturi A, Mancini M et al. Diagnostic features of real time contrast enhanced ultrasound in focal nodular hyperplasia of the liver. *Ultraschall Med* 2010; 31: 276-282.
- Lencioni R, Della Pina C, Crocetti L. Impact of EFSUMB Guidelines on the use of contrast agents in liver ultrasound. In: Bolondi L (ed). *Advances in diagnostic imaging*. Springer 2006: 3-14.
- Kim MJ, Lim HK, Kim SH et al. Evaluation of hepatic focal nodular hyperplasia with contrast – enhanced gray scale harmonic sonography: initial experience. *J Ultrasound Med* 2004; 23: 297-305.
- Carlson S, Johnson CD, Bender CE, Welch T. CT of focal nodular hyperplasia of the liver. *AJR Am J Roentgenol* 2000; 174: 705-712.
- Vilgrain V. Focal nodular hyperplasia. *Eur J Radiol* 2006; 58: 236-245.
- Parsons L, Winter T. Right upper quadrant mass: possible metastasis. In: Sanders R, Winter T (eds). *Clinical Sonography – a practical guide*, Lippincott Williams & Wilkins 2007: 68-79.
- Bartolotta TV, Taibbi A, Matranga D, Malizia G, Lagalla R, Midiri M. Hepatic focal nodular hyperplasia: contrast-enhanced ultrasound findings with emphasis on lesion size, depth and liver ecogenity. *Eur Radiol* 2010; 20: 2248-2256.
- Strobel D, Seitz K, Blank W, et al. Tumor specific vascularization pattern of liver metastasis, hepatocellular carcinoma, hemangioma and focal nodular hyperplasia in the differential diagnosis of 1349 liver lesions in CEUS. *Ultraschall Med* 2009; 30: 376-382.
- Mortelé KJ, Stubbe J, Praet M, Van Langenhove P, De Bock G, Kunnen M. Intratumoral steatosis in focal nodular hyperplasia coinciding with diffuse hepatic steatosis: CT and MRI findings with histologic correlation. *Abdom Imaging* 2000; 25: 179-181.
- Chaoui A, Mergo PJ, Lauwers GY. Unusual appearance of focal nodular hyperplasia with fatty change. *AJR Am J Roentgenol* 1998; 171: 1433-1434.
- Shen YH, Fan J, Wu ZQ, Ma ZC, Zhou XD, Zhou J. Focal nodular hyperplasia of the liver in 86 patients. *Hepatobiliary Pancreat Dis Int* 2007; 6: 52-57.