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Contrast-enhanced Ultrasonography in Hepatosplenic Sarcoidosis

Authors

Dr M. Stryckers, Dienst Inwendige Geneeskunde, UZ Gent, De Pintelaan 185, 9000 Gent

Prof Dr D. Voet, Dienst Ultrasonografie, UZ Gent, De Pintelaan 185, 9000 Gent

Prof Dr D. Vogelaers, Dienst Inwendige Geneeskunde en Infectieziekten, UZ Gent, De Pintelaan 185, 9000 Gent

Prof Dr M. Afschrift, Dienst Ultrasonografie, UZ Gent, De Pintelaan 185, 9000 Gent
Prof Dr K. Verstraete, Dienst Radiologie, UZ Gent, De Pintelaan 185, 9000 Gent

Prof Dr S. Van Belle, Dienst Medische Oncologie, UZ Gent, De Pintelaan 185, 9000 Gent

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Abstract

We report a case of a 38-year old woman with atypical pain in the left lower hemi-abdomen. On abdominal B-mode ultrasonography the liver was normal; the spleen showed multiple subcentimetric hypoechoic nodules. A multidetector CT-examination revealed multiple small low-attenuation nodules in the liver and the spleen, suggestive for metastatic disease. Contrast-enhanced ultrasound (CEUS) revealed two hypoechoic nodules in the liver that were visible in the portal phase and disappeared in the late phase. The focal splenic lesions were visible as irregular hypo-enhancing nodules. An MRI examination, including T1, T2 and contrast-enhanced images, could not confirm the exact nature of the lesions. A core biopsy of a splenic nodule yielded noncaseating epitheloid cell granulomas. Different complementary examinations were normal and hepatosplenic sarcoidosis was diagnosed. The pain in the left lower hemi-abdomen was ascribed to irritable bowel syndrome.

Introduction

Sarcoidosis is usually a benign multisystem granulomatous disease of unknown origin. The lungs are affected in more than 90% of the cases. Splenic nodules are detected in approximately 15% and hepatic nodules in about 5% of the cases. Although hepatosplenic sarcoidosis is rare, it should be included in the differential diagnosis of focal hepatic and splenic lesions. The non-histologic differential diagnosis of hepatosplenic lesions is mainly based on imaging techniques. The first intention is to make the difference between malignant and benign disease. Contrast-enhanced ultrasonography (CEUS) is a new ultrasonographic tool and has a lot of possibilities if properly used. It has a diagnostic accuracy comparable to that of CT or MRI for the evaluation of focal liver lesions, and is more economic: the cost in Belgium of CT or MR is almost three times that of CEUS. However, little is known about the characteristics of hepatosplenic sarcoidosis on CEUS. We report a case of a woman with hepatosplenic sarcoidosis who underwent CEUS [1, 2].

Case report

A 38-year old woman was referred by her general practitioner because of atypical pain in the left lower hemi-abdomen. A physical examination of the abdomen revealed pain on palpation in the left lower hemi-abdomen without rebound tenderness. There was no palpable hepatosplenomegaly. An abdominal B-mode ultrasonography revealed a homogeneous parenchyma of the liver and multiple subcentimetric hypoechoic nodules in the spleen. A double contrast multidetector CT-examination with a 5 mm slice thickness revealed multiple small low-attenuation nodules (+/- 60 UH at the venous phase) in the liver and the spleen, suggestive for metastatic lesions and the patient was referred to the department of medical oncology. Because of the disagreement between the US and the CT examination of the liver,

CEUS of the liver was performed. Sulfur hexafluoride (SonoVue®, Bracco, Milano, Italy), a second generation ultrasound contrast medium was administered intravenously (1,4 mL) and the liver was scanned from 60 sec. on. Two hypoechoic hepatic nodules were detected in the portal phase which disappeared in the late phase. Otherwise, the liver parenchyma showed a homogeneous enhancement, without any argument for metastatic disease. Four minutes after injection, the spleen was examined. Multiple focal splenic lesions were visible as irregular nodules with low enhancement relative to the parenchyma. Because of the non-specific nature of the lesions on CEUS, a complete MR examination, including T1, T2 and contrast-enhanced images with gadolinium, was performed. On MRI, the hepatic lesions were too small for a proper evaluation, but the splenic lesions were very suggestive for malignant disease (figure 1). An ultrasound-guided core biopsy of a splenic lesion was performed with a 18-gauge needle, revealing noncaseating epitheloid granulomas. The differential diagnosis was directed to tuberculosis and sarcoidosis. A high resolution CT-scanning of the lungs revealed multiple micronodular lesions without hilar adenopathies. A tuberculin skin test was negative. Liver enzymes, inflammatory parameters (BSE, CRP, lymphocyte count), renal function parameters and serum calcium level were within normal limits. Angiotensin converting enzyme level was slightly elevated (36U/l). Serologic tests for other causes of granulomatous disease including Chlamydia, Brucella, Yersinia enterocolitica (type 3, 9) and Coxiella burnettii were negative. The patient was finally diagnosed with systemic sarcoidosis. Because of the lack of symptoms and a normal lung function test, no systemic therapy was initiated. The pain in the left lower hemi-abdomen was ascribed to ‘irritable bowel syndrome’.

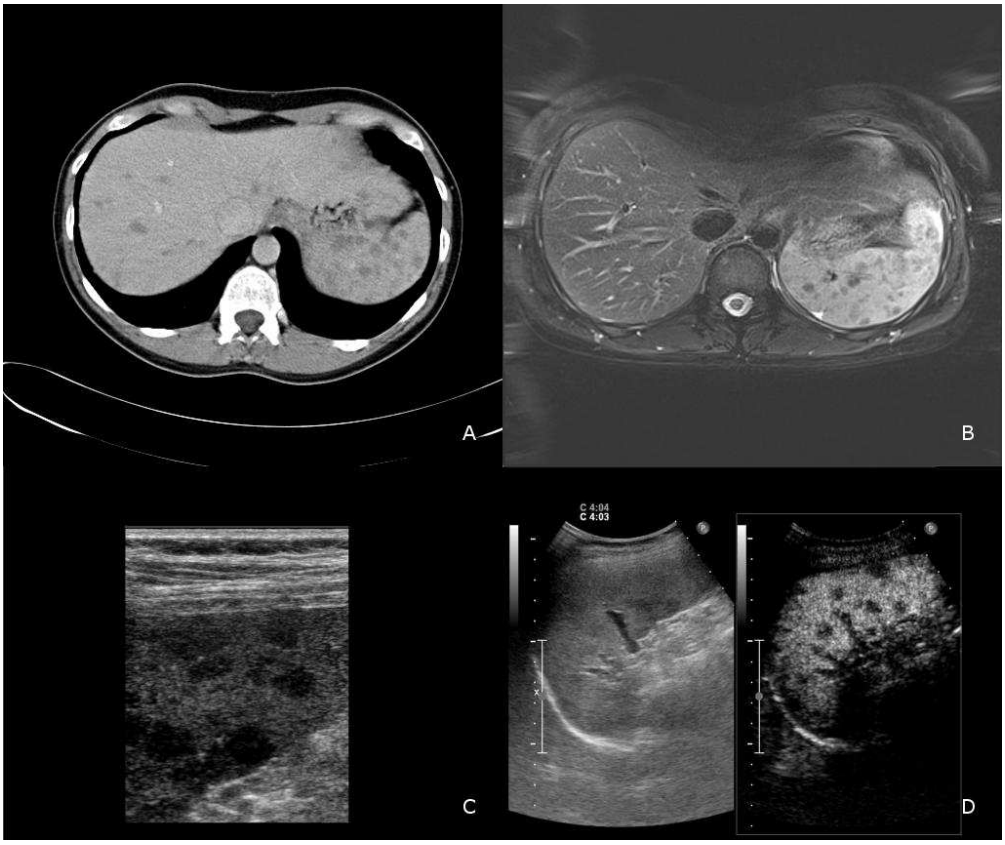

Figure 1:

A: A double-contrast multidetector CT examination of the abdomen demonstrates multiple irregular hypo-intense nodules (+/- 60 UH at the venous phase) in the liver and the spleen, suggestive for metastatic lesions. B: An abdominal MRI examination (T2 fatsat) demonstrates multiple hypo-intense nodules in the spleen with a diameter between 1 and 6 mm. The lesions in the liver were too small for a proper evaluation on MRI. C: On a high resolution US examination of the spleen, multiple poorly defined hypoechoic lesions are visible. D: Contrast-enhanced ultrasound of the spleen, late phase, demonstrates multiple hypoenhancing nodules.

Discussion

Sulfur hexafluoride (SF_6, SonoVue®) is a second generation US contrast agent consisting of phospholipid-stabilized microbubbles, smaller than 8 micrometers. Because of its small size, it can penetrate in the very small parenchymal vessels of the reticulo-endothelial system of the

liver and the spleen. In the liver an arterial phase can be distinguished from a portal venous phase (30 to 120 seconds after contrast injection) and a late parenchymal phase (> 120 seconds after contrast injection). The differentiation between benign and malignant hepatic lesions mainly depends on the characteristics in the late parenchymal phase. Hypoenhancement or no enhancement in the late parenchymal phase is suspicious for malignancy. According to the study by von Herbay et al. (2010) CEUS of the liver has a 90% sensitivity, 90% specificity and 89% accuracy for the diagnosis of malignancy [3]. According to the EFSUMB-guidelines, contrast-enhanced ultrasonography could replace MRI and CT in the near future for the investigation of focal hepatic lesions. The diagnostic accuracy of CEUS is higher than that of B-mode US and comparable to that of CT and MRI for the evaluation of focal liver lesions [1,4]. In our case, two hypoenhancing hepatic lesions were visualized in the portal venous phase. As the liver parenchyma was homogeneous on conventional US, and as the arterial phase of CEUS hardly contributes to the differentiation of benign from malignant focal lesions, we started CEUS in the portal phase. Because the hepatic nodules showed isoenhancement in the late parenchymal phase we could classify them as 'probably benign' but we were not able to characterize them.

Studies referring to the diagnostic investigation of splenic lesions with CEUS are rare. Pérez-Grueso et al. (2006) reported a case of splenic sarcoidosis assessed by CEUS. The splenic lesions were hypoechoic with respect to the parenchyma on B-mode US and remained hypoechoic with no enhancement after the injection of SF_6 [5]. In a study by Stang et al. (2009), 147 splenic lesions in 147 patients were investigated with B-mode US and CEUS. Iso-enhancement relative to splenic parenchyma or constantly no enhancement was suggestive for benign disease whereas progressive hypoenhancement (defined as 'increasing lesion-to-parenchyma-contrast'), was suspicious for malignancy with a 100% sensitivity (CI 95% [95-

100]) and a 83.3% specificity (CI 95% [73-92]) for the latter pattern. Progressive hypoenhancement had a positive predictive value of 87.8 % (CI 95% [79-94]), and a negative predictive value of 100% (CI 95% [94-100]) for malignancy. In this study by Stang et al. (2009), 4 patients with splenic sarcoidosis were included. The lesions of all four patients showed progressive hypo-enhancement on CEUS, which suggested malignancy. The enhancement pattern of nodular sarcoidosis was similar to that of lymphoma. Both, lymphoma and nodular sarcoidosis can give rise to multiple nodules that are seen as progressively hypo-enhancing lesions on CEUS with SF_6. Lymphoid lesions are mostly larger in size than sarcoid lesions, which are mostly less than 1cm in diameter [6] In our case we had focused on the liver, and only the late phase of the splenic perfusion was evaluated on CEUS. The enhancement pattern of the splenic nodules was more suggestive of a malignant disease. As the spleen, as opposed to the liver, was clearly diffusely affected, a splenic biopsy was performed. Neither CEUS nor double-contrast multidetector CT-scan or MRI with gadolinium contrast could clarify the exact nature of the hepatosplenic lesions. As far as the spleen is concerned, CEUS findings were in agreement with CT-scan and MRI. However, for the examination of the liver, CT-scan was in discordance with CEUS. While CT-scan suggested diffuse metastatic disease, CEUS could only visualize a few nodules which could be characterized as benign. In the abscence of a histopathological proof, no definite diagnosis of the hepatic nodules can be made. We can only assume that in this patient with proven splenic sarcoid involvement, the hepatic nodules most probably were signs of sarcoid involvement of the liver. Whether the difference between the CEUS perfusion patterns of the splenic and the hepatic nodules can contribute to the diagnosis of hepatosplenic sarcoidosis, should be proved by further observations in patients with proven hepatosplenic sarcoid involvement.

Conclusion

The enhancement of splenic sarcoid nodules described in literature is atypical and cannot be differentiated from splenic lymphoma or malignancy. In our case, we focused on the liver and only the late phase of the spleen was evaluated. A few concomitant hepatic nodules in the same patient most probably resided on an hepatic localisation of the sarcoid process. On CEUS they behaved as benign nodular lesions. Neither CEUS nor double-contrast multidetector CT-scan or MRI with gadolinium contrast could clarify the exact nature of the lesions. So far, the diagnosis of hepatosplenic sarcoidosis has to be confirmed by histology.

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