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Roberto Chiavaroli, Pierfrancesco Grima. Characterization of non traumatic focal splenic lesions using Contrast Enhanced Sonography. Journal of Clinical Ultrasound, 2011, 39 (6), pp.310. 10.1002/jcu.20831. hal-00638140

HAL Id: hal-00638140 https://hal.science/hal-00638140

Submitted on 4 Nov 2011

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Journal of Clinical Ultrasound

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Journal:	Journal of Clinical Ultrasound
Manuscript ID:	JCU-10-035.R2
Wiley - Manuscript type:	Research Article
Keywords:	ultrasonography, contrast agent, spleen, cyst, neoplasms



 Characterization of non traumatic focal splenic lesions using Contrast Enhanced Sonography

CEUS of the spleen in non traumatic focal lesions

Purpose. To compare the usefulness of contrast enhanced ultrasound (CEUS) with contrast enhanced computed tomography (CT) for assessing non-traumatic focal lesions of the spleen.

Methods. CEUS and CT findings in 22 patients with fever of unknown origin and ultrasound detected splenic focal lesions were analyzed retrospectively. CEUS was performed using an ultrasound unit equipped with a 3.6-Mhz probe and contrast media-analyzing software. A 4-ml bolus of second-generation contrast medium was used. The CEUS examinations comprised a 4-minute recording following injection of the contrast medium. Magnetic resonance imaging, splenic biopsy, or ultrasound follow-up were used to facilitate diagnosis if findings from CT were inconclusive.

Results. The final diagnoses were: 7 splenic infarcts, 5 hemangiomas, 3 lacerations, 2 benign cysts, 1 lymphoma, 1 granuloma, 1 abscess, and 2 lesions of unknown etiology. CEUS and CT had the same specificity (77.2%). Both CEUS and CT failed to characterize nodular hypovascular lesions with a hypoenhancing pattern.

Conclusions. CEUS is as effective as CT for assessing non-traumatic focal lesions of the spleen. If CEUS findings are consistent with benign splenic lesions, CT seems to be of limited additional value.

Keywords. ultrasonography, contrast agent, spleen, cysts, neoplasms.

Introduction

Focal lesions of the spleen incidentally detected by ultrasound (US) in a non-traumatic clinical scenario are not uncommon and may complicate a differential diagnosis. Contrast enhanced computed tomography (CT) is considered the primary tool of choice for assessing splenic abnormalities and sonography is generally not considered useful for determining the specific cause of these lesions.¹ The usefulness of contrast-enhanced ultrasound (CEUS) with a second generation sonographic contrast agent for differential diagnosis of benign and malignant focal abnormalities of the splenic parenchyma was recently described, but the actual utility of CEUS in a non-traumatic clinical setting remains controversial ¹⁻⁸. In the present study, we performed a retrospective comparison of CEUS and CT findings of non traumatic focal lesions incidentally detected by routine upper abdomen US examination in 22 patients admitted to the Infectious Diseases unit for fever of unknown etiology.

Materials and Methods

Patients

This study was approved by the local institutional ethics committee and written informed consent, according to legislative requirements, was obtained from each patient for CEUS and spleen biopsy.

Between February 2006 and September 2008 we investigated by CEUS of the spleen twenty-two patients (10 female and 12 males, median age 50 years, range 24 - 77) admitted to our unit because of fever of unknown origin and with US detected focal lesions of the spleen.

Ultrasound examination

A GE Logic 5 ultrasound unit (General Electric-Connecticut USA) equipped with a contrast specific , continuous-mode software and a 3,6 Mhz transducer was used both for ultrasound standard examination and CEUS of the spleen.

Contrast Enhanced Ultrasound examination

CEUS procedures and lesion diagnostic criteria

CEUS was performed in harmonic mode with a mechanical index of 0.08 to 0.09. A 4ml bolus of second-generation contrast medium (Sonovue-Bracco, Milan) was used and injected in the antecubital vein. CEUS studies were analyzed on the basis of a review of reference clips stored in the sonographic unit. We identified three CEUS patterns using the surrounding splenic parenchyma as an in vivo reference: hypoenhancement, isoenhancement, and hyperenhancement, by scanning from 0 to 50 seconds during the early phase after injection, between 50 seconds and 120 during the parenchymal phase and between 120 seconds and 4 minutes after injection during the late phase. According to previous reports, ¹⁻⁸ cystic lesions were considered to be malignant if enhancement of the cyst wall or septa was noted. Focal solid lesions were considered to be hemangiomas or hamartomas if we detected isoenhancement in all phases or if we detected hyperenhancement during the early phase (from 0-50 seconds) and isoenhancement during the late phase. A focal, nodular-shaped lack of enhancement in the late phase (hypoechoic lesions) after early enhancement was considered to suggest malignancy while absence of enhancement in all phases was considered to be due also to splenic granuloma or abscess¹. Segmental subcapsular lesions of the spleen pointing toward the hilum with a hypoechoic pattern in all the phases were considered to be splenic infarcts, while irregular or branching parenchymal stripes constantly hypoechoic after contrast medium injection were considered to be spontaneous parenchymal lacerations (Fig.1).⁹⁻

Clinical and radiological examination

All patients underwent microbiological laboratory tests and abdominal and chest CT after CEUS examination for disease staging. Magnetic resonance imaging (MRI), US follow-up, or echo-guided spleen aspiration biopsy using a 22-gauge Chiba needle was performed if CT findings were inconclusive.¹²

Statistical Analysis

Continuous variables are reported as the mean \pm standard deviation. Categorical factors are reported as percentages. Statistical calculations were performed with MedCalc software, version 9.6.0.0. (bvba, Mariakerke, Belgium)

Results

The final diagnoses are summarized in Table 1. None of the patients had symptoms other than fever. US detected multiple focal lesions of the spleen (median size 4.7 cm, range 0.4-9 cm) in 4 patients. Baseline ultrasound showed no isoechoic lesions, hypoechoic lesions in 16 patients, hyperechoic lesions in 4 patients and anechoic lesions in 2 patients. CEUS showed anechoic nodular lesions without enhancement of the cyst wall or septa in 2 patients (Fig. 2a-2c) In 3 patients with nodular lesions, a persistent isoenhancement was noted in all phases, showing an enhancement pattern similar to that of the adjacent splenic tissue. In 2 patients hyperenancing nodular lesions were detected only during the early arterial phase with rapid centripetal filling in and they became undetectable in the late phase.

Hypoechoic nodular lesions with an absence of enhancement in all phases was observed in 5 patients (Fig.3a-3c). Splenic CEUS showed persistent delayed hypoenhancement of segmental subcapsular lesions in 7 patients (Fig. 4a-4c) and of irregular parenchymal stripes in 3 patients. CEUS findings in lesions of all etiology are summarized in Table 2. According to these results, CEUS supported a diagnosis of benign cystic lesions in 2 patients, hemangioma in 5 patients, splenic infarct in 7 patients, and splenic lacerations in 3 patients. CEUS findings were confirmed by CT abdominal examination in all cases. Both CEUS and CT supported a final diagnosis in 17 of 22 patients (77.2%), and failed to characterize nodular splenic lesions in 5 patients with persistent hypoenhancing pattern. MRI was performed in one of these patients with inconclusive findings. Splenic aspiration biopsy was performed in 2 of these patients. The final diagnosis was splenic lymphoma infiltration and sarcoid granuloma. In 3 patients, US follow-up of monthly examinations for at least 1 year showed that the splenic lesions were benign.

In two of these patients the diagnosis of a benign splenic tumor was most likely because metastasised malignant diseases or extrasplenic pathology were ruled out by abdominal CT, fever disappeared after few days of antibiotics therapy and monthly clinical and ultrasound follow up during the first year showed no clinical symptoms and absence of increase in size of the lesion. In one of these patients with a nodular splenic lesion of unknown origin, blood culture and clinical follow-up allowed us to reach a diagnosis of a small splenic abscess due to left heart endocarditis (Table 1).

Discussion

The spleen is particularly suitable for CEUS studies because of its topography, small size, homogeneous parenchyma, high vascularization, and intense and long-lasting contrast enhancement.¹⁻¹³ Several reports demonstrated that CEUS of the spleen significantly improves the diagnosis of parenchymal lacerations by enhancing the detection of avascular areas during the late phase of the examination.⁹⁻¹¹ At the present time, however, European CEUS guidelines warrant the use of this tool for only blunt abdominal trauma and, in particular, to avoid CT or MRI during follow-up.¹⁴ Reports of the use of splenic CEUS to characterize non-traumatic focal lesions remain scarce. Some authors have described a microbubble wash-out in the late-phase for a differential diagnosis of malignant lesions, but the reliability of this diagnostic tool in clinical practice is not yet confirmed. To date, however, there have been no studies to compare CEUS with CT features in the assessment of focal lesions of the spleen. Three of 5 hemangiomas showed an enhancement pattern similar to splenic tissue, while 2 of 5 lesions showed a rapid and hyperechoic enhancement in the early-phase with centripetal filling in. The splenic lymphoma we described appeared as a constantly hypoechoic lesion, more easily defined during the late phase but without clear intralesional

microcirculation or rim enhancement in the early phase. Our findings indicated that a

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persistent hypoenhancing CEUS pattern of nodular splenic lesions may also be common to benign lesions such as small abscesses or granulomas, so that differentiation of these lesions from malignant diseases is often not possible.⁸ On the other hand, our data showed that CT has the same specificity as CEUS for the diagnosis of hypovascular solid lesions of the spleen because of the inability to characterize hypodense splenic nodules. The difficulty in making a differential diagnosis using CT and CEUS is probably due to the lack of a dual splenic vascular supply because double vascularization is useful for characterizing focal hepatic lesions using contrast-enhanced media.¹⁴ Asymptomatic segmental-shaped hypovascular lesions of the spleen are often due to splenic infarcts. In patients with no history of abdominal trauma, irregular-shaped hypoenhancing parenchymal lesions may be due to spontaneous rupture of an enlarged spleen, which sometimes occurs as a complication of infectious diseases characterized by splenomegaly, such as mononucleosis and malaria, or during myeloproliferative diseases.¹⁵ The unenhanced US patterns of mild spontaneous splenic lacerations in the absence of acute bleeding and perisplenic effusion do not differ from those of ischemic lesions and both these lesions may be difficult to distinguish from the surrounding splenic parenchyma. After contrast media injection, splenic infarct shows as a clear wedge-shaped lack of enhancement relative to the spleen capsule; while splenic lacerations appear as typical unenhanced branching stripes, usually perpendicular to the spleen surface. In our experience, CEUS of the spleen is as effective as CT for diagnosing these lesions in non-traumatic splenic pathology. Although abdominal CT is commonly used to rule out extrasplenic malignancy, most nodular lesions of the spleen are hypovascular and CT study seems to be of limited additional value to characterize focal lesions that have a benign pattern on CEUS. Finally CEUS might facilitate a rapid diagnosis and eliminate the need for CT contrast media and ionizing radiation during follow-up. CEUS of the spleen is simple, rapid, and safer and less expensive than CT and MRI. Based on the present findings, CEUS might be a useful first tool to

characterize lesions of the spleen detected incidentally by US and CEUS is as effective as CT for assessing this kind of lesion.

Conflict of interest statement

All authors have no conflict of interest with regard to publication of this article.

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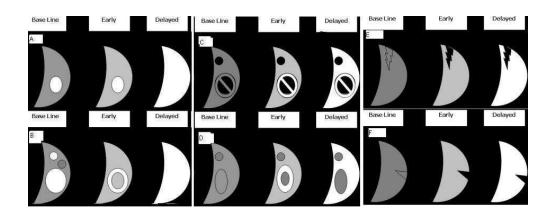


Figure 1.

Schematic display of the dynamic ultrasound contrast enhancement of splenic Hamartoma (A), Hemangioma (B), benign (upper) and malignant Cysts (C), Lymphoma (upper) and Metastasis (D),Laceration (E) and Ischemic lesion (F),during the base line, early and delayed phase.

249x96mm (96 x 96 DPI)

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FINAL	CEUS	Abdominal	Abdominal	Splenic	Follow UP	
DIAGNOSIS		СТ	MRI	Biopsy		Cases
Benign cists	diagnostic	diagnostic				2
Haemangioma	diagnostic	diagnostic				5
Splenic Infarct	diagnostic	diagnostic				7
Lacerations	diagnostic	diagnostic				3
Lymphoma	inconclusive	inconclusive	inconclusive	diagnostic		1
Sarcoid	inconclusive	inconclusive		diagnostic		1
Granuloma						
Splenic abscess	inconclusive	inconclusive			diagnostic	1
Unknown cause	inconclusive	inconclusive			diagnostic	2
(benign lesions)					_	
Total						22

Tab.1 Ceus and CT diagnostic value for final diagnosis in all patients

	Haemangiomas	Lymphoma	Granuloma	Abscesses	Infarcts	Lacerations	Benign nodular lesions	Cysts
n	5	1	1	1	7	3	2	2
Early phase (0-50 s)								
homogeneous	3	0	0	0	0	0	0	0
hyperechoic	2	0	0	0	0	0	0	0
hypoechoic	0	1	1	1	7	3	2	2
Enhancement pattern	Centripetal filling-in(n =2)	None	None	None	Wedge shaped	Branching stripes	None	Round margin
Parenchymal phase (50-120 s)								
homogeneous	5	0	0	0	0	0	0	0
hyperechoic	0	0	0	0	0	0	0	0
hypoechoic	0	1	1	1	7	3	2	2
Enhancement pattern	None	None	None	None	Wedge shaped	Wedge shaped	None	Round margin
Late phase (120-240 s)								
homogeneous	5	0	0	0	0	0	0	0
hyperechoic	0	0	0	0	0	0	0	0
hypoechoic	0	1	1	1	7	3	2	2
Enhancement pattern	None	None	None	None	Wedge shaped	Wedge shaped	None	Round margin

Table 2Contrast Enhanced Ultrasound findings in lesions of all etiologies

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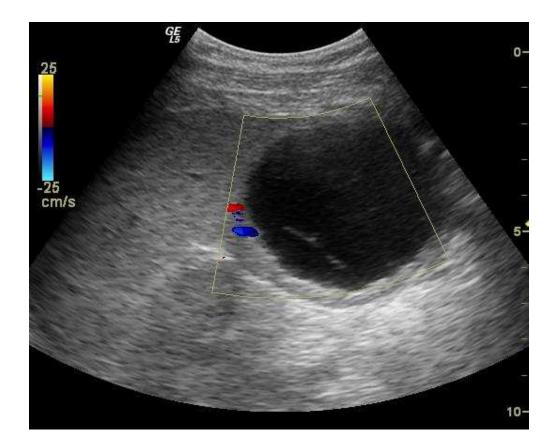


Figure 2a. Benign splenic cyst: Large avascular cystic lesion of the spleen with thick wall and fine septa by US color-doppler. 140x114mm (96 x 96 DPI)



Figure 2b. Benign splenic cyst : CEUS shows no enhancement of wall and septa. 138x110mm (96 x 96 DPI)

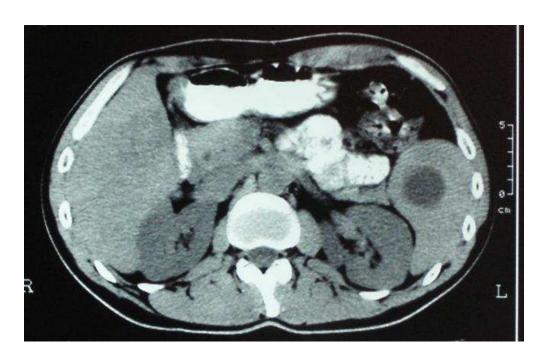


Figure 2c. Homogeneous hypodendse cystic lesion by abdominal CT. study. 173x109mm (96 x 96 DPI)

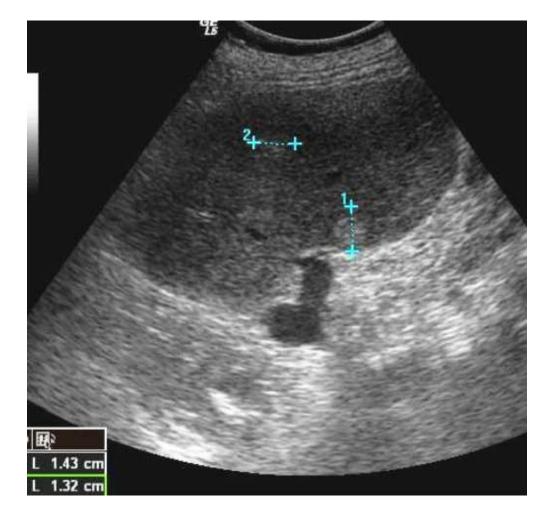


Figure 3a. Sarcoid granulomata of the spleen: Hyperechoic nodular lesions by US base line examination. 134x127mm (96 x 96 DPI)



Figure 3b. Splenic nodular lesions are hypoechoic during all the phases of CEUS study. 142x120mm (96 x 96 DPI)



Figure 3c. Hypovascular nodular lesions by Abdominal CT. 127x138mm (96 x 96 DPI)

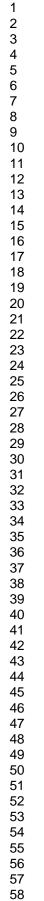






Figure 4a. Splenic infarct; US shows a segmental shaped hypoechoic lesion of the spleen. 140x114mm (96 x 96 DPI)



Figure 4b. CEUS shows two hypoenhancing subcapsular lesion. 140x114mm (96 x 96 DPI)

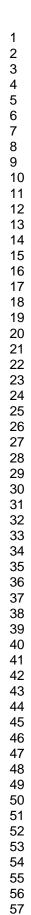




Figure 4c. Abdominal CT shows multiple hypodense subcapsular lesions of the spleen 118x84mm (96 x 96 DPI) Response to Comments fom the Editor

MATERIALS and METHODS

1) I mentioned 3 CEUS patterns ; anechoic, isoechoic and hypoechoic, but i mean hypoenhancement, isoenhancement and hypernhancement. I have made the correction throughout the text.

2) The statement has been reworded "A focal, nodular-shaped lack of enhancement in the late phase (hypoechoic lesions) after early enhancement was considered to suggest malignancy while absence of enhancement in all phases was considered to be due also to splenic granuloma or abscess."

3) The statement in the abstract has been corrected "*Magnetic resonance imaging, splenic biopsy, or ultrasound follow-up were used to facilitate diagnosis if findings from CT were inconclusive.*"

4)The statistical software i used is not from USA. The maker of the software is fro Europe "MedCalc software, version 9.6.0.0. (bvba, Mariakerke, Belgium)"

RESULTS:

5) I mean isoenhancement

6 I mean hyperenhancement of nodular lesion

7 I mean that all hyperenhancing nodular lesions with centripetal filling in in the early phase became undetectable in the late phase

The statements have been rewrote: "in 3 patients with nodular lesions, a persistent isoenhancement was noted in all phases, showing an enhancement pattern similar to that of the adjacent splenic tissue . In 2 patients hyperenancing nodular lesions were detected only during the early arterial phase with rapid centripetal filling in and they became undetectable in the late phase."

8) The statements "Further studies are warranted to assess the reliability of CEUS in routine clinical practice. The present findings suggest that when CEUS features are consistent with benign splenic lesions, abdominal CT may be avoided, and CT studies and more expensive and invasive tools such as MRI and needle biopsy can be saved for

patients with solid nodular hypovascular lesions. " have been deleted.

Characterization of non traumatic focal splenic lesions using Contrast Enhanced Sonography

Keywords:

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considered to be splenic infarcts, while irregular or branching parenchymal stripes constantly hypoechoic after contrast medium injection were considered to be spontaneous parenchymal lacerations (Fig.1).⁹⁻¹¹

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All patients underwent microbiological laboratory tests and abdominal and chest CT after CEUS examination for disease staging. Magnetic resonance imaging (MRI), US follow-up, or echo-guided spleen aspiration biopsy using a 22-gauge Chiba needle was performed if CT findings were inconclusive¹².

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lasting contrast enhancement.¹⁻¹³ Several reports demonstrated that CEUS of the spleen significantly improves the diagnosis of parenchymal lacerations by enhancing the detection of avascular areas during the late phase of the examination.⁹⁻¹¹ At the present time, however, European CEUS guidelines

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but without clear intralesional microcirculation or rim enhancement in the early phase. Our findings indicated that a persistent hypoenhancing CEUS pattern of nodular splenic lesions may also be common to benign lesions such as small abscesses or granulomas, so that differentiation of these lesions from malignant diseases is often not possible.⁸ On the other hand, our data showed that CT has the same specificity as CEUS for the diagnosis of hypovascular solid lesions

of the spleen because of the inability to characterize hypodense splenic nodules. The difficulty in making a differential diagnosis using CT and US is probably due to the lack of a dual splenic vascular supply because double vascularization is useful for characterizing focal hepatic lesions using contrast-enhanced media.¹⁴

Asymptomatic segmental-shaped hypovascular lesions of the spleen are often due to splenic infarcts. In patients with no history of abdominal trauma, irregularshaped hypoenhancing parenchymal lesions may be due to spontaneous rupture of an enlarged spleen, which sometimes occurs as a complication of infectious

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diseases characterized by splenomegaly, such as mononucleosis and malaria, or during myeloproliferative diseases.¹⁵ The unenhanced US patterns of mild spontaneous splenic lacerations in the absence of acute bleeding and perisplenic effusion do not differ from those of ischemic lesions and both these lesions may be difficult to distinguish from the surrounding splenic parenchyma. After contrast media injection, splenic infarct shows as a clear wedge-shaped lack of enhancement relative to the spleen capsule; while splenic lacerations appear as typical unenhanced branching stripes, usually perpendicular to the spleen surface. In our experience, CEUS of the spleen is as effective as CT for diagnosing these lesions in non-traumatic splenic pathology. Although abdominal CT is commonly used to rule out extrasplenic malignancy, most nodular lesions of the spleen are hypovascular and CT study seems to be of limited additional value to characterize focal lesions that have a benign pattern on CEUS. Finally CEUS might facilitate a rapid diagnosis and eliminate the need for CT contrast media and ionizing radiation during follow-up. CEUS of the spleen is simple, rapid, and safer and less expensive than CT and MRI. Based on the present findings, CEUS might be a useful first tool to characterize lesions of the spleen detected incidentally by US, and CEUS is as effective as CT for assessing this kind of lesion.

Conflict of interest statement

All authors have no conflict of interest with regard to publication of this article.

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Deleted: Further studies are warranted to assess the reliability of CEUS in routine clinical practice. The present findings suggest that when CEUS features are consistent with benign splenic lesions, abdominal CT may be avoided, and CT studies and more expensive and invasive tools such as MRI and needle biopsy can be saved for ¶ patients with solid nodular hypovascular lesions.

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