Various aspects of Contrast-enhanced Ultrasonography in splenic lesions – a pictorial essay

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Abstract
Spleen pathology is rare in comparison with other abdominal organs, but often its lesions occur in complex pathological contexts, with systemic involvement. Although the lesions could be discretely symptomatic, their evolutionary potential might be severe. Conventional B-mode and Doppler ultrasound are the first-line imaging methods in spleen assessment, but frequently they do not allow the characterization of focal splenic abnormalities. Contrast-enhanced ultrasound (CEUS) is fast, safe, easy to perform, non-irradiating and can be used in patients with renal failure. By highlighting splenic macro and micro-vascularization, CEUS significantly increases the detection rate and allows the characterization of vascular (infarction, ischemia, thrombosis) and traumatic lesions, with high diagnostic accuracy. Additionally, ectopic splenic tissue can be identified with high accuracy. The method improves both the detection and characterization of splenic nodules, but some limitations still remain, especially in the differential diagnosis between malignant and some benign lesions. This article aims to portray aspects of CEUS imaging in various splenic pathologies using clinical examples from our experience and to review the CEUS contribution in the diagnosis of splenic lesions.

Keywords: ultrasound; contrast enhanced ultrasound (CEUS); spleen

Introduction
Spleen pathology is rare compared to other abdominal organs, but, far from being the “silent and forgotten” organ of the abdomen, the spleen is affected by various systemic disorders [1].

Ultrasonography (US) is the first-line imaging method for evaluation of the splenic parenchyma. However, the focal splenic lesions (FSL) are frequently difficult to characterise only by B-mode and Doppler US. Contrast-enhanced ultrasound (CEUS) offers several undeniable advantages, by being a fast, portable, non-irradiating method, without nephrotoxicity and relatively cheap when compared to computed tomography (CT) scan and magnetic resonance imaging (MRI).

The aim of this pictorial essay is to describe CEUS particularities in different splenic lesions, with illustrative examples from our experience.

Examination technique
CEUS should be performed only after complete B-mode and Doppler ultrasound examination, when baseline examination is inconclusive, in order to establish a definitive diagnosis [2,3]. In order to obtain the best image, it is recommended to use the highest frequency available probe, tailored to the depth of the targeted area.
Usually, a convex 3-5 MHz probe is used. In children or slim patients, a 7.5-12 MHz linear probe can be used.

As contrast agent (CA), SonoVue (Bracco, Italy) in a volume of 1-1.2 ml for convex probe and 2-2.4 ml for a linear probe is used in our department.

**Ectopic spleen tissue**

An accessory spleen (splenunculus) is usually located near the spleen and can be easily diagnosed by conventional US. Difficulties occur in ectopic spleen diagnosis, which can be easily confused with tumors or pathological adenopathies. On CEUS, splenosis shows vascular dynamics similar to that of the normal spleen [4]. Small nodules may also show homogeneous arterial enhancement. The CEUS diagnosis is based on the persistence of enhancement in the late-phase for more than 5 minutes. A particular situation we encountered was splenosis located in contact with liver capsule, mimicking a liver tumor. The three phases contrast dynamics both in liver and spleen and the enhancement more intense in spleen tissue could have supported misdiagnosis, but the correlation of CEUS data with patient’s medical history and normal biological tests suggested splenosis (fig 1).

**Splenic infarction**

Splenic infarctions are some of the most common FSL, caused by different hematologic (sickle-cell anemia, thrombophilia, hematologic malignancies) or immunological disorders [5,6]. CEUS allows the diagnosis in the acute phase showing a non-enhancing area during the entire exploration and enables the correct assessment of its shape and extent with a very high diagnostic accuracy. The lesion is clearly visible during venous and late phase. One particular etiology we must keep in mind is endocarditis. Small infarctions due to septic emboli from infectious endocarditis can be accurately detected by CEUS.

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**Fig 1.** Ectopic spleen tissue after posttraumatic splenectomy, located in contact with liver capsule, case with histologic confirmation: a) B-mode appearance. Homogeneous round nodule, isoechoic with the liver, with its own capsule; b) CEUS examination. Homogeneous intense arterial hyperenhancement, c) venous and late phase. Homogeneous isoenhancement, no late wash-out at 4 minutes after contrast injection.

**Fig 2.** Splenic infarction in a 63 years old male, with recurrent fever, dyspnea and abdominal pain, diagnosed with endocarditis: a) hypoechoic area on B-mode examination, without Doppler signal inside; b) venous phase. On CEUS examination no contrast enhancement can be seen inside the infarction area.
Splenic infarctions may also appear as complications of chemoembolization for hepatocellular carcinoma (HCC) [6]. Other successful applications of CEUS also used in our department are to evaluate the necrotic area and arterial permeability after therapeutic partial embolization of the splenic artery branch in cirrhotic patients (fig 3) or to confirm splenic vein permeability (fig 4).

**Splenic trauma**

Although contrast-enhanced CT remains the prime-line investigation in polytrauma patients, studies proved the utility of CEUS in the diagnosis, minimally invasive therapy, and follow-up of minor, blunt trauma, especially in children and young women [8-10]. Due to its arterial inhomogeneity and long-lasting contrast enhancement, the spleen is examined after the kidneys and liver, the lesions being clearly visible in the venous and late phase. The US appearance varies depending on the time between trauma and examination and lesions can be missed in the first 24 hours. CEUS significantly improves diagnosis showing hematomas and lacerations appearing as non-enhanced areas and contusions as ill-defined, hypoenhancing areas (fig 5) [3]. Sometimes, contrast extravasation as a sign of active bleeding can be seen within the splenic parenchyma or perisplenic hematomas [3].

**Splenic abscess**

Splenic abscesses are very rare and generally occur by hematologic dissemination from a primary infection site [11]. Bacterial abscesses are usually solitary, larger
than 2 cm, with B-mode and CEUS appearance similar to those from liver. Fungal abscesses are small, multiple, hypoechoic or target-like lesions and usually appear in immune compromised patients. On CEUS they appear non-enhancing or with a thin arterial hyperenhancing rim, that washes out in the venous and late phase.

**Splenic hemangiomas**

Splenic hemangiomas are the most common incidentally found benign splenic focal nodules (SFN) and their contrast enhancement is different from liver hemangiomas [6]. Typical nodular hyper-enhancement seen in liver hemangiomas is found in only 7% of splenic hemangiomas [12]. Capillary hemangioma appears as small hyperechoic round, well delineated SFN that enhances on CEUS as a normal spleen and becomes undetectable, without late wash out [4]. On CEUS, arterial enhancement of the cavernous hemangioma may be centripetal or diffuse, faster or slower, complete or incomplete due to fibrosis or thrombosis [6]. In the late phase no wash out is typical, but studies reported discrete late wash out in up 2/3 of cases (fig 6, fig 7) [12,13].

**Splenic hamartomas**

Splenic hamartomas are rare benign SFN originating from the red pulp, often less than 3 cm. They are composed of normal spleen tissue and dilated splenic sinusoids [6]. On B-mode US they may appear as cystic lesions with septa or as hypoechoic inhomogeneous nodules. Doppler examination shows hypervascular lesions, some of them having a wheel distribution of vessels. CEUS examination shows an intense and homogeneous, centripetal or centrifugal arterial hyper-enhancement and moderate late wash out [6].

It must be outlined that the differential diagnosis between splenic hemangiomas, hamartomas or lymphangioma is often difficult to perform, frequently the final diagnosis suggesting a benign angiomatous lesion, as hemangioma or hamartoma [6].

**Splenic cysts**

Usually, cysts are easily diagnosed on US, no other investigations being necessary. CEUS is recommended only for complicated cysts if diagnosis on B-mode US is unclear. At CEUS they are non-enhancing during the en-
tire exploration. But CEUS alone might be inconclusive in differential diagnosis between small cysts and fungal abscesses, granulomas or necrotic metastases and complementary investigations are necessary.

**Lymphangioma**

Lymphangioma is a rare congenital malformation of the lymphatic duct, usually associated with capillary, cavernous or cystic splenic lymphangiomas. They are usually located in the subcapsular area. The cystic form is the most common. B-mode US usually shows a solitary lesion containing multiple hypoechoic cysts of various sizes, with internal debris or septa [6]. On Doppler exam, the walls and septa may show vascular signal. On CEUS, they present arterial enhancement at the capsule and septum level, with or without discrete late wash-out (fig 8, fig 9) [2].
Splenic granulomatous lesions

Splenic involvement is commonly seen in tuberculosis or sarcoidosis. Usually, on B-mode US, granulomas are multiple, small, hypoechoic, well delineated lesions. They may be associated with microcalcifications, especially tuberculosis granuloma. On CEUS, they are usually hypoenhancing in the arterial phase, less frequently isoenhancing, with rapid and pronounced wash out, which makes them difficult to differentiate from malignant nodules. Difficulties also arise in differential diagnosis between granulomas and miliary abscesses, since both types of lesions are found in immune compromised patients (fig 10).

Lymphoma

Lymphoma is the most common splenic malignancy [2], splenic involvement being found at diagnosis in up to 30% of patients, more frequently in non-Hodgkin’s lymphoma. The US findings vary: homogeneous splenomegaly, miliary nodules, multiple FSL or unique, macronodular, “bulky” lesion. On CEUS, the lymphoma lesions have, in most cases, iso- or discrete arterial hypoenhancing, with rapid, pronounced, and progressive wash out, starting less than 1 minute after infusion (fig 11) [12,14]. Studies show that the wash out in malignant SFN appears faster and is more pronounced than in benign lesions.

Fig 10. Multiple granulomatous lesions in a HIV and TBC infected patient: a) B-mode appearance – small hypoechoic lesions and small calcifications; CEUS examination. Small hypoenhancing lesions can be seen in arterial phase (b), pronounced wash-out in the venous phase (c), and in the late phase (d).

Fig 11. Splenic infiltration in 76 year old patient with hepatitis C virus infection who developed Non-Hodgkin lymphoma: a) splenomegaly with multiple hypoechoic, round, well delineated lesions, B-mode examination; CEUS examination. At the beginning of the arterial phase the lesions are slightly hypoechoic (b), with rapid wash out clearly visible at the end of the arterial phase (c); pronounced wash-out in the late phase (d).
On the other hand, CEUS proved to be very useful for detection of lymphomatous infiltration. Studies showed 90% sensitivity and 100% specificity compared to CT for detection of lymphoma nodules [15]. Other studies showed CEUS sensitivity higher than CE-CT or FDG PET in detecting splenic lymphoma lesions in patients with Hodgkin’s lymphoma [16].

**Splenic metastases**

Splenic metastases are very rare and occur late in the evolution of the disease. Most common, splenic metastasis occur from breast cancer, lung cancer, colorectal cancer, ovarian cancer, and malignant melanoma [17]. On CEUS, they usually present arterial enhancement similar to liver metastases, and rapid and pronounced wash out (fig 12).

Studies proved that CEUS increases the detection rate of splenic metastases by up to 40% compared to US [18]. CEUS is also useful in post-treatment follow-up after chemotherapy, avoiding multiple irradiations.

In conclusion, CEUS proves to be a very useful diagnostic method in daily practice, significantly increasing the detection rate of FSL. The method allows ectopic splenic tissue diagnosis with high accuracy. In case of infarction and traumatic lesions, CEUS allows a correct assessment of their extension and is very useful in the follow-up of those lesions conservatively managed. Regarding the characterization of SFN, CEUS still has a limited role, allowing the selection of splenic nodules with certain benign features, for which only serial imaging is recommended for follow-up. We strongly believe that current use of CEUS in clinical practice paralleling with CT and MRI increases the diagnostic accuracy of splenic lesions and significantly shortens the time to diagnosis.

**Conflict of interest:** none

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