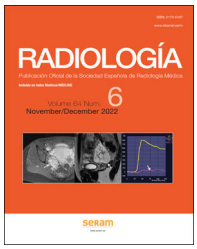
Radiología 67 (2025) 61–73

RADIOLOGÍA

www.elsevier.es/rx



RADIOLOGY THROUGH IMAGES

The role of contrast-enhanced ultrasound in the evaluation of focal splenic lesions

P. García Barquín[a,*], E. Lángara García-Echave[a], I. Pérez Arroyuelos[a], E. Ingunza Loizaga[a], C. Berastegi Santamaría[a], G. Irigoyen[b]

[a] *Departamento de Radiología, Hospital Galdakao Usansolo, Galdakao, Bizkaia, Spain*
[b] *Departamento de Anatomía Patológica, Hospital Galdakao-Usansolo, Galdakao, Bizkaia, Spain*

Received 29 April 2023; accepted 2 July 2023
Available online 24 January 2025

KEYWORDS
Spleen;
Ultrasound;
Microbubbles;
Diagnosis;
Pathology;
Neoplasms

Abstract The purpose of this article is to evaluate the role of contrast-enhanced ultrasound in the characterization of non-traumatic focal splenic lesions.

Focal splenic lesions are less common than in other abdominal organs like the liver. Conventional ultrasound and Doppler ultrasound have a limited role in the characterization of splenic lesions, resulting in many of them unspecified.

Contrast ultrasound is an accessible, cheap, and safe technique which can help in the immediate characterization of lesions incidentally detected in the ultrasound examination, being a good alternative to others imaging techniques.

We review in detail the technique and the main indications. We also analyze imaging findings and enhancement pattern by using representative case of the main splenic lesions for both benign (epithelial cyst, cystic lymphangioma, hemangioma, hamartoma, infarction, sclerosing angiomatous nodular transformation, abscesses, sarcoidosis), and malignant (lymphoma, metastasis) and its pathological correlation in some cases.

PALABRAS CLAVE
Bazo;
Ecografía;
Microburbujas;
Diagnóstico;
Anatomía patológica;
Neoplasias

Papel de la ecografía con contraste en la evaluación de lesiones focales esplénicas

Resumen El objetivo del artículo es evaluar el papel de la ecografía con contraste en la caracterización de las lesiones focales esplénicas no traumáticas.

Las lesiones focales esplénicas son poco frecuentes en comparación con las hepáticas. La ecografía convencional y la ecografía doppler tienen un papel limitado en la caracterización de las lesiones esplénicas, resultando muchas de ellas inespecíficas. La ecografía con contraste es

* Corresponding author.
E-mail address: paulagarciabarquin@gmail.com (P. García Barquín).

una técnica accesible, barata y segura que puede ayudar en la caracterización inmediata de las lesiones detectadas incidentalmente en el examen ecográfico, siendo una buena alternativa a otras técnicas de imagen.

Revisamos en detalle la técnica empleada, los fundamentos y principales indicaciones. También analizamos los hallazgos de imagen y el patrón de realce mediante casos representativos de las principales lesiones esplénicas tanto benignas (quiste epitelial, linfangioma quístico, hemangioma, hamartoma, infarto, transformación angiomatosa nodular esclerosante, abscesos, sarcoidosis), como malignas (linfoma, metástasis) y su correlación anatomopatológica en algunos casos.

Introduction

Focal splenic lesions are less common than liver lesions and are often detected incidentally.[1,2] In addition, most splenic lesions are benign and silent and radiological findings can be superimposed on each other, at times appearing non-specific.[2] Moreover, histological diagnosis is not always possible, as neither biopsy nor splenectomy are free of complications. Some authors have reported overall complication rates of around 8%.[3] It is therefore important to find an alternative technique to avoid invasive procedures or unnecessary splenectomies.

The aim of this article is to evaluate the role of contrast-enhanced ultrasound (CEUS) in the characterisation of major non-traumatic splenic focal lesions.

We provide a detailed review of the technique used and the fundamentals of CEUS. We have also analysed the main imaging findings and the pattern of enhancement using representative cases of both benign (epithelial cyst, cystic lymphangioma, haemangioma, hamartoma, infarction, sclerosing angiomatoid nodular transformation, abscesses and sarcoidosis) and malignant (lymphoma and metastases) lesions and their correlation from a pathology point of view in some cases.

Reminder of the anatomy and histology of the spleen and splenic vasculature

The spleen is an intraperitoneal organ located in the left hypochondrium, measuring 9 to 12 cm. Anatomically, it consists of a peripheral capsule with a series of internal projections called trabeculae. Histologically, it is composed of two main regions: the red pulp and the white pulp. The red pulp is composed of small cavities of venous sinusoids and splenic cords (cords of Billroth) consisting of macrophages, lymphocytes, reticular cells, dendritic cells, plasmocytes and meshwork of reticular fibres. The white pulp consists of lymph-related nodules called Malpighian corpuscles[4] (Fig. 1A).

The splenic circulation consists of two different circuits: most of the splenic circulation is the open circulation, where blood enters the red pulp and then drains into the venous sinuses through the splenic cords, while a proportion of the blood passes directly into the venous sinuses and constitutes the so-called closed circulation[4] (Fig. 1B).

General considerations of contrast-enhanced ultrasound

Ultrasound contrast (second generation) consists of gas microbubbles (sulfur hexafluoride) of a few microns in size (2–5 μm) coated with a phospholipid shell, lipid on the inside and hydrophilic on the outside, which makes them poorly soluble in blood. Contrast bubbles are administered with a rapid bolus (1.2–2.4 ml) followed by 10 ml of normal saline.[5] Circulating microbubbles are purely intravascular (they do not cross the endothelium and therefore do not pass into the interstitium) and oscillate irregularly in low mechanical index configurations (0.1), creating non-linear reflections which resonate at diagnostic ultrasound frequencies (3–5 MHz).[6] The mechanical index is a measure of the power of the ultrasound beam.

Using specific pre-designed software, the baseline image, the background echoes, are suppressed. We obtain a virtual image in real time that allows us to evaluate the enhancement of the lesions in the different phases and the washout. It is recommended to perform a continuous study in the arterial phase and then intermittently to ensure preservation of the bubbles. The enhancement of the lesions is compared to the adjacent parenchyma.[6]

The main advantages of the technique include, firstly, its great accessibility, which enables immediate characterisation of a spleen lesion detected incidentally during an ultrasound examination, with real-time evaluation. It is also a safe technique, with a low rate of adverse effects and allergic reactions, and can be used in patients with liver and/or kidney dysfunction.[6] Ultrasound contrast is not nephrotoxic, as the gaseous component is eliminated via the respiratory tract, while the phospholipid component is metabolised by the liver.[6] CEUS can also play an important role in guiding biopsy of lesions not identified by conventional ultrasound[7] (Table 1).

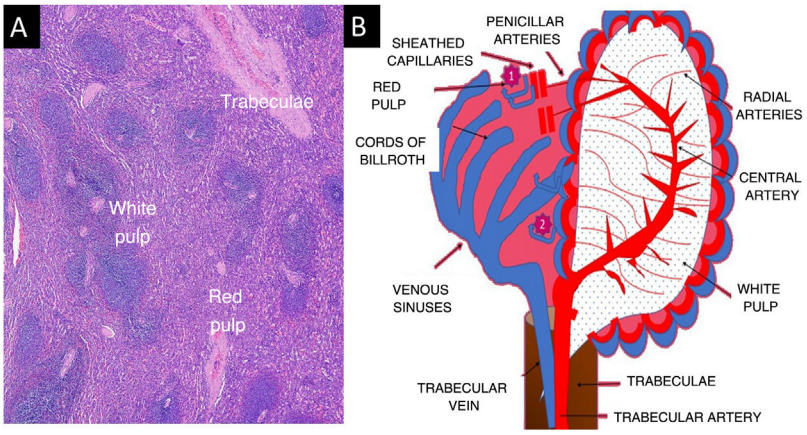


Figure 1 Diagram of the histology and basic vascularisation of the spleen. (A) Splenic parenchyma slices showing white pulp and red pulp. (B) Representative diagram of the two vascular circuits in the spleen. Diagram adapted from Stevens and Lowe. Human histology. Vascular anatomy of the spleen. 5th ed. 2020, pp 120–139. Circulation in the spleen begins in the splenic artery, which branches into trabecular arteries that give off a series of central arteries (surrounded by white pulp). The blood then enters the red pulp through specialised vessels (penicillar arteries and sheathed capillaries), draining into the cords of Billroth (splenic cords) (leaving the vascular system). The blood then seeps through the spaces between the reticular cells, which form the splenic cords, and enters the splenic venous sinuses. The blood leaves the system through the trabecular veins and enters the splenic vein. This route is the open circulation (number 1 in the diagram). A small proportion passes directly into the venous sinuses and constitutes the so-called closed circulation (number 2 in the diagram).

Table 1 Advantages and disadvantages of contrast-enhanced ultrasound.

Advantages	Disadvantages
Accessible and cheap	Poor assessment of the subcapsular region and possibility of areas obscured by lung bases
It does not emit ionising radiation.	It is operator dependent
Possibility of completing the B-mode ultrasound study at the same time	Small lesions can be difficult to characterise
Safe, with a low rate of adverse effects	As a purely intravascular contrast, the information provided by other contrast media when they enter the interstitium is lost
Can be used as an alternative in patients with contraindication for iodinated contrast	Contraindicated in patients with severe pulmonary hypertension, recent myocardial infarction, severe heart, lung, liver or kidney disease
Optimum time resolution, with real-time evaluation	Deep lesions can be masked with contrast dye at high doses
Contrast administration can be repeated if necessary	The examiner has to focus on a single plane, so several lesions cannot be studied at the same time
Can serve as a biopsy guide for lesions poorly identified in B-mode	

Splenic ultrasound and contrast-enhanced ultrasound of the spleen

Ultrasound is usually the first diagnostic technique for the spleen. It is usually easily assessed via the intercostal route and in maximal inspiration, although it can also be assessed with the patient in the right lateral decubitus position.

However, characterisation of lesions by greyscale and Doppler ultrasound is limited due to the low contrast between the lesion and the parenchyma. Depending on their nature, splenic lesions can be classified into four categories: cystic; solid-cystic; solid; and infectious or granulomatous.[8]

Studies have shown that on conventional ultrasound, most malignant lesions are hypoechoic, while most benign lesions are hyperechoic. Unlike benign lesions, malignant lesions usually cause splenomegaly.[9]

Previous studies have demonstrated the utility of CEUS for the assessment of congenital (asplenia or accessory spleens) or vascular (infarction and splenic trauma) disease.[10,11] The use of CEUS in the assessment of focal splenic lesions, however, is not widespread in routine clinical practice. According to the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB), which made its latest recommendations in 2017, the use of CEUS can provide additional information to narrow down the diagnosis. CEUS differentiates lesions that are likely to be benign from malignant lesions, increasing sensitivity and specificity compared to conventional ultrasound, especially when combined with adequate clinical information.[10,12] Some studies suggest that even lower doses can be administered in the spleen because of the organ's high avidity for microbubbles.[5,6] It should also be borne in mind that in the assessment of small, deep lesions it is best to inject

small volumes of contrast to minimise attenuation that may obscure the region of interest.

The characteristics of the spleen in terms of histology and vascularisation lead to two specific imaging findings in CEUS:

- *''Zebra'' enhancement pattern,* due to two different vascular circuits with different flow rates, through the red pulp (which enhances earlier) and the white pulp (which enhances later), resulting in characteristic heterogeneous uptake in the arterial phase, as in computed tomography (CT) and magnetic resonance imaging (MRI) scans.[13]
- *Long enhancement profile*. Spleen enhancement becomes homogeneous after 60 seconds. The ultrasound contrast is purely intravascular, it is sequestered in the macrophages in the splenic cords and does not pass into the interstitium; this will result in a longer-lasting enhancement than in the liver of 5–7 minutes.[14,15]

Important reminder: the spleen is ideally suited for contrast-enhanced ultrasound because of its superficial location, homogeneous parenchyma, high vascularity and long uptake profile.

Enhancement features of focal splenic lesions

Depending on the pattern of enhancement, lesions can be divided into four categories: lesions with no enhancement (no uptake in either the arterial or parenchymal phases); lesions with hyperenhancement in the arterial phase and persistent enhancement in the late phase; lesions with variable arterial enhancement with slight washout; and lesions with variable enhancement in the arterial phase with rapid washout[14,16] (Fig. 2).

Absence of enhancement at any stage or persistent late-stage enhancement are characteristic findings of benign lesions.[10] Late stage washout is typical of malignant lesions due to the absence of sinusoidal spaces and cells of the reticuloendothelial system (Fig. 2).

In addition, we need to know the patient's clinical history, previous medical history and blood test results, and correlate with previous imaging studies.[8]

Important reminder: the nature of the lesion and the temporal pattern of contrast enhancement and washout are key elements in narrowing the range of differential diagnosis of focal splenic lesions.

Benign lesions

Epithelial cyst

Splenic cystic lesions are rare (0.07%). Congenital or primary cysts occur in children or adolescents.[16] They are usually simple cysts (anechoic, with posterior acoustic enhancement, unilocular, well-defined and with cellular cover) and do not show enhancement on CEUS.

Pseudocyst

Asymptomatic splenic cysts are usually pseudocysts secondary to trauma without cellular covering or false cysts (75–80%). They may have internal echoes, a septum and parietal calcifications and do not show enhancement on CEUS[13] (Fig. 3).

Cystic lymphangioma

This is a rare benign tumour of unknown origin, most common in children and young adults. It tends to be an incidental finding and asymptomatic in most cases. It is characterised by cystic dilations of the lymphatic vessels and has a subcapsular location. These are multilocular cystic lesions with internal echoes or septa. Colour Doppler ultrasound can demonstrate vascularisation of the cyst wall. A characteristic ''Gruyère cheese'' appearance with enhancement of the septa and capsule has been described in CEUS images[6] (Fig. 4).

Haemangioma

This is a congenital lesion arising from the sinusoidal epithelium, vascular channels and cells of the reticuloendothelial system. It is the most common benign tumour of the spleen and is classified as a benign vascular lesion. The prevalence is 0.3–14% in post-mortem examinations and it occurs in young adults.[17] There may be multiple haemangiomas, as in Klippel-Trenaunay-Weber syndrome or Kasabach Merritt syndrome. Two types are described: capillary (solid) and cavernous (solid-cystic).

The appearance of haemangiomas on baseline ultrasound is variable, they can be solid (usually hyperechogenic) or solid-cystic. After contrast, haemangiomas may show peripheral enhancement in the arterial phase and persistent late enhancement (capillaries). In the spleen it is less common to identify the characteristic enhancement pattern of cavernous haemangiomas (peripheral arterial nodular uptake and centripetal filling).[18] They usually refill in the late phase due to the high avidity of macrophages and cells of the reticuloendothelial system for microbubbles (Fig. 5). Some haemangiomas with slow late washout have been described.[12] In these cases, MRI may be useful as an alternative method due to its higher specificity.[19]

Infarction

Splenic infarction occurs when the splenic artery or one or more of its branches are occluded by an embolus (infectious or otherwise) or by a clot. It may be complete or affect one segment of the spleen.

The infarction can be difficult to identify on conventional ultrasound, particularly in the acute phase, when it often

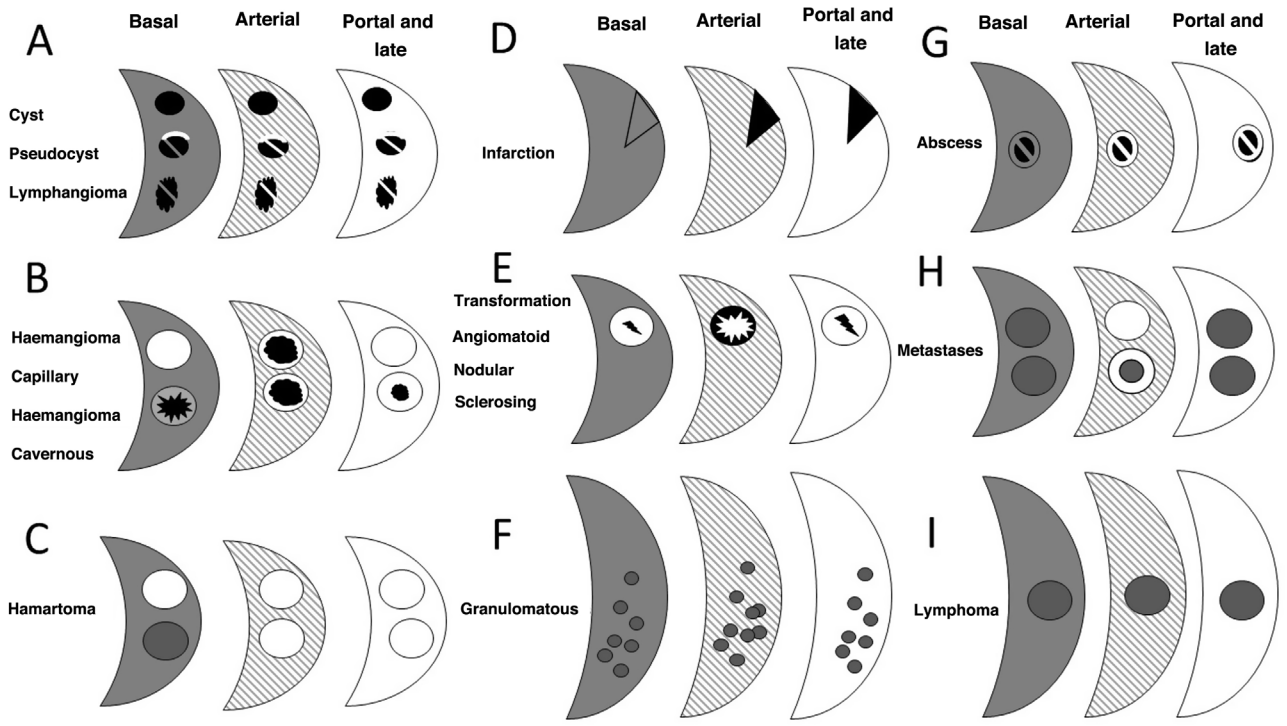


Figure 2 Representative diagram of the main splenic focal lesions and their appearance on baseline ultrasound and after administration of ultrasound contrast. (A) Cysts are anechoic, unilocular, well-defined and show no enhancement after contrast administration. Pseudocysts may have internal echoes, septa and parietal calcifications. Cystic lymphangioma is a multilocular cystic lesion with echoes or internal septa which may show enhancement after contrast administration. (B) Haemangiomas have a variable appearance on baseline ultrasound. Capillary haemangiomas are usually solid and hyperechogenic. After contrast administration, haemangiomas may show peripheral enhancement in the arterial phase and persistent late enhancement. Cavernous haemangiomas have peripheral arterial nodular uptake and centripetal filling. (C) Hamartomas are usually well-defined solid nodular lesions (hyper- or hypoechoic). After contrast administration, they show homogeneous and early uptake in the arterial phase and homogeneous and persistent enhancement in the venous and late phases. (D) An infarction usually appears isoechoic with respect to the parenchyma in the acute phase. After contrast administration, a complete absence of enhancement with a well-defined wedge-shaped morphology can be identified. (E) On baseline ultrasound, sclerosing angiomatoid nodular transformation of the spleen appears as a single, hyperechoic lesion. It has a characteristic dynamic behaviour, with a ring-like enhancement in the arterial phase, gradual centripetal uptake through the fibrous septa, giving it a ''cartwheel'' appearance, and persistent enhancement in the late phases with a central scar with poor uptake. (F) Granulomatous disease appears as multiple hypoechoic nodules and splenomegaly. (G) Splenic abscesses are typically cystic, with a thick, irregular wall and may contain septa. Contrast-enhanced ultrasound may show enhancement of the wall and septa, with no uptake by the necrotic component. (H) Metastases have a variable ultrasound appearance depending on the primary cancer. After contrast administration they show variable ring enhancement and washout in the late phases. (I) Lymphoma has different forms of presentation; it usually appears as an enlarged spleen without a demarcated mass, as a solitary mass, as multiple masses or as miliary nodules. They are usually hypoechoic lesions on ultrasound, although sometimes only diffuse heterogeneity of their echostructure is seen. After contrast administration, the lesions show poor uptake in the arterial phase with gradual and intense washout.

appears isoechoic with respect to the parenchyma. In the subacute phase a hypoechoic and heterogeneous solid-cystic area with no Doppler signal can be identified.[20] After contrast administration, a complete absence of enhancement with a well-defined wedge-shaped morphology can be identified and the edges and extent of the infarct can be better delineated in the late phase[21] (Fig. 6).

Hamartoma

This is a benign lesion considered to be a developmental abnormality and it can occur at any age. It is associated with other hamartomas in other locations and, with haemangiomas, is included in the category of benign vascular lesions.[22]

On ultrasound hamartomas are usually well-defined solid nodular lesions (hyper- or hypoechoic), which may have vascularisation on colour Doppler. After contrast administration, they show homogeneous early enhancement in the arterial phase and persistent, late, homogeneous enhancement in the venous and late phases[23] (Fig. 7).

Sclerosing angiomatoid nodular transformation of the spleen

Sclerosing angiomatoid nodular transformation (SANT) of the spleen is a non-cancerous vascular lesion recognised in

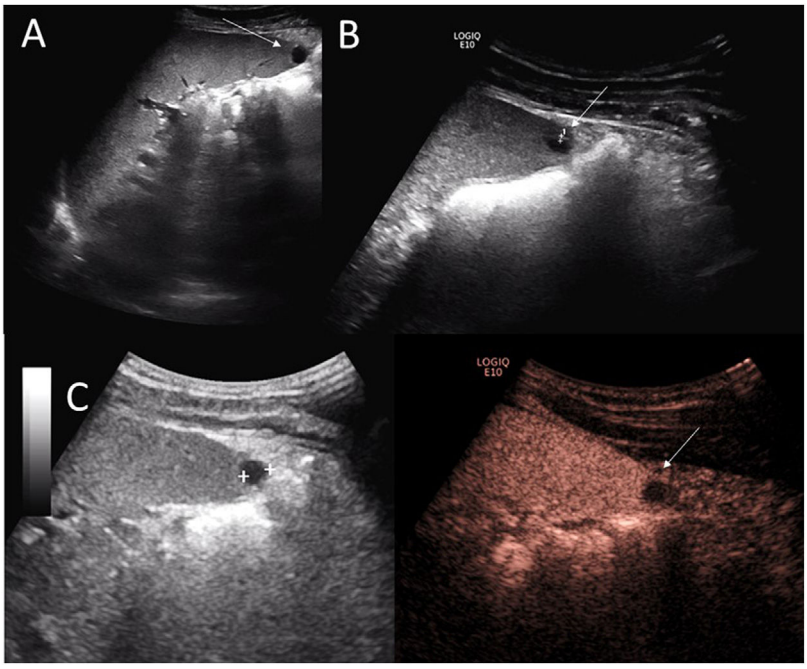


Figure 3 50-year-old male who attended for routine ultrasound. (A and B) Baseline ultrasound demonstrating a well-demarcated unilocular anechoic millimetre-sized lesion with minimal internal septation (white arrows) and septum (between cursors in B). (C) Contrast-enhanced ultrasound with complete absence of uptake by the lesion and septum (white arrow). Findings compatible with a pseudocyst.

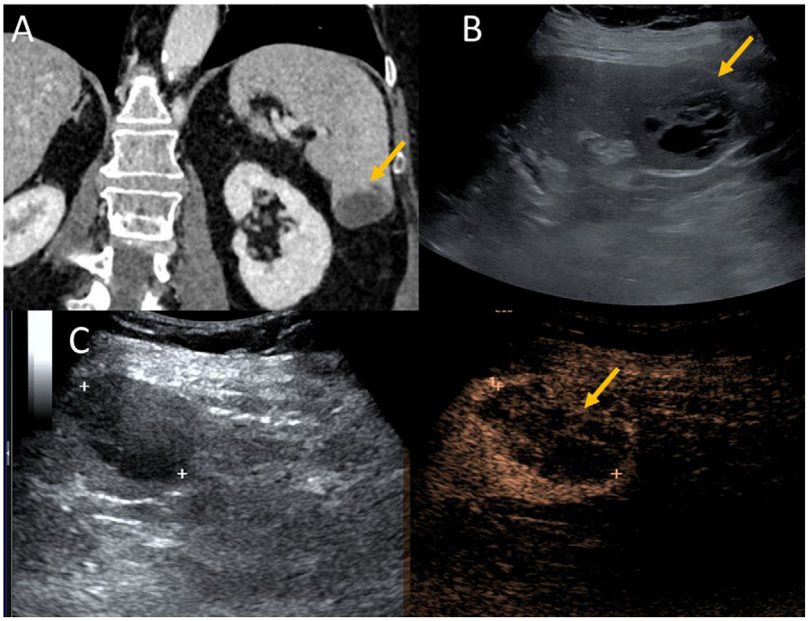


Figure 4 60-year-old woman attending a routine check-up. (A) Coronal computed tomography with incidental finding of a focal hypodense splenic lesion (yellow arrow). (B) Baseline ultrasound demonstrating a multilocular lobulated cystic lesion with multiple internal septa (yellow arrow). (C) Contrast-enhanced ultrasound demonstrating a cystic lesion (between cursors) with mild septal uptake (yellow arrow). The suggested diagnosis was cystic lymphangioma.

2004, with few cases having been reported.[24] The diagnostic suspicion is established by imaging tests and confirmed by pathology examination and immunohistochemistry.

It consists of multiple small tortuous vessels (capillaries, sinusoids and small veins) forming nodules, immersed in a radially arranged fibrosclerotic stroma containing macrophages, myofibroblasts, lymphocytes and plasma cells.[24]

The appearance of SANT on baseline ultrasound is variable, and they are usually single, large, hypo- or hyperechoic

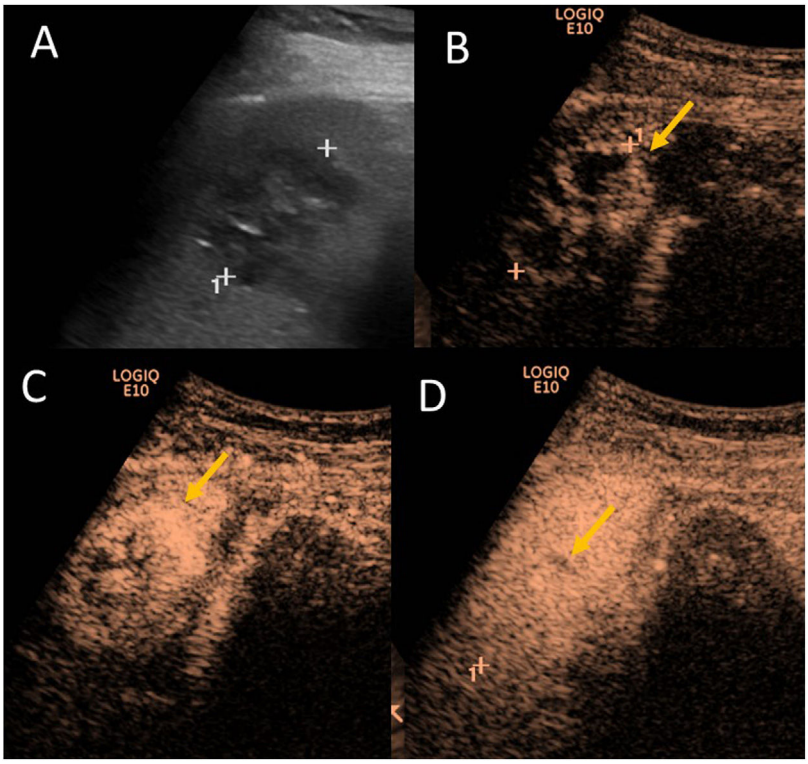


Figure 5 48-year-old woman attending for routine ultrasound. (A) Baseline grey scale ultrasound showing several lesions with hyper- and hypoechogenic areas within them (one of which is marked between cursors). (B–D) Contrast-enhanced ultrasound scans in arterial (12 seconds) (B), parenchymal (60 seconds) (C) and late (120 seconds) (D) phases, demonstrating nodular peripheral enhancement in the arterial phase, gradual centripetal uptake with complete filling of the lesion and persistent enhancement in late phases (yellow arrows). The suggested diagnosis was a haemangioma.

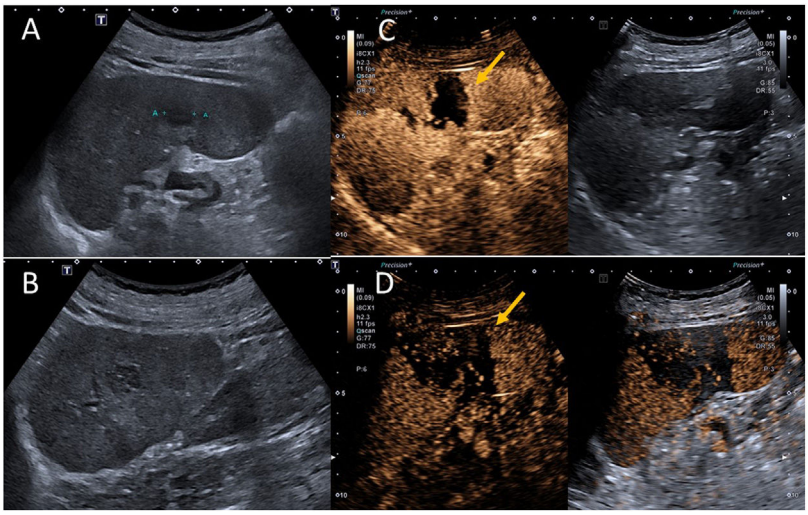


Figure 6 79-year-old male with vascular disease, with acute pain in the left hypochondrium. (A and B) Baseline greyscale ultrasound showing a 13-mm focal splenic lesion of heterogeneous appearance (between cursors in A). (C and D) Ultrasound after contrast at 60 seconds (C) and contrast-B-mode fusion images at 120 seconds (D) showing a large area of absence of contrast with wedge-shaped morphology (yellow arrows), compatible with a splenic infarction.

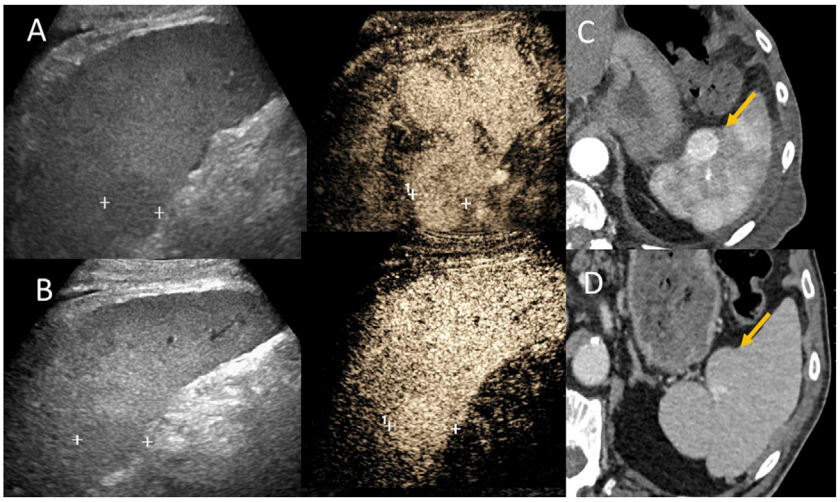


Figure 7 79-year-old male. (A) Baseline ultrasound with incidental finding of a solid focal splenic lesion (between cursors); hypoechoic, well-defined, with an appearance not typical of a haemangioma. (A and B) Contrast-enhanced ultrasound in arterial phase at 20 seconds (lesion between cursors) (A) and parenchymal phase at 70 seconds (lesion between cursors). (C and D) Correlation with computed tomography, showing early homogeneous enhancement of the lesion in the arterial phase (yellow arrow) (C) and maintained in the venous phase (yellow arrow) (D). Characteristic enhancement of a benign lesion. The suggested diagnosis was hamartoma.

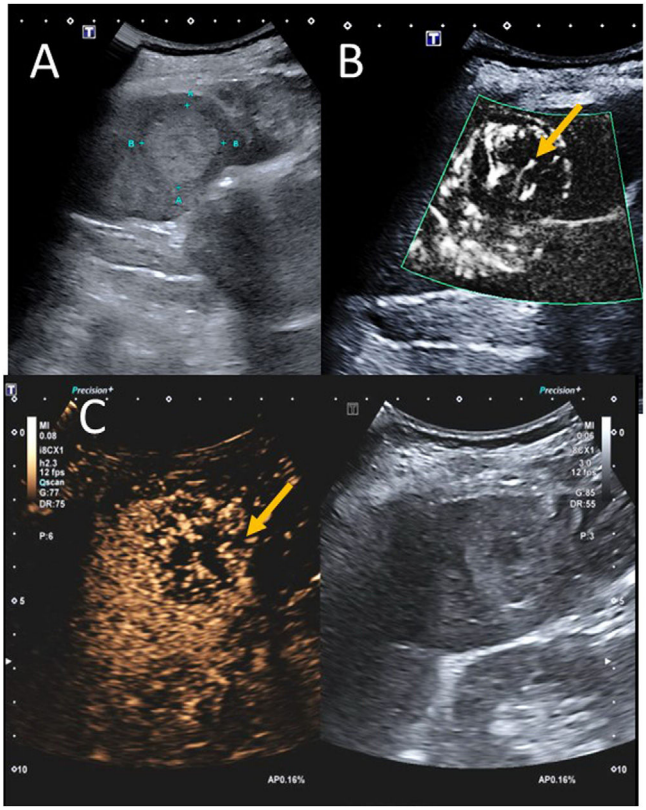


Figure 8 80-year-old male with advanced dementia. (A) Incidental finding of a solid, hyperechoic focal splenic lesion with a hypoechoic centre, well-defined on baseline ultrasound (marked between cursors). (B) SMI (superb micro-vascular imaging) Doppler ultrasound, showing a vascular structure in the centre of the lesion (yellow arrow). (C) Arterial phase contrast-enhanced ultrasound at 15 seconds showing cartwheel uptake with radial arrangement and a central vessel. In this case, a sclerosing angiomatoid nodular transformation of the spleen was suggested as the most likely diagnosis and confirmed by an MRI scan (which we do not have). Due to the patient's age and different comorbidities (advanced dementia), the decision was made to manage without splenectomy.

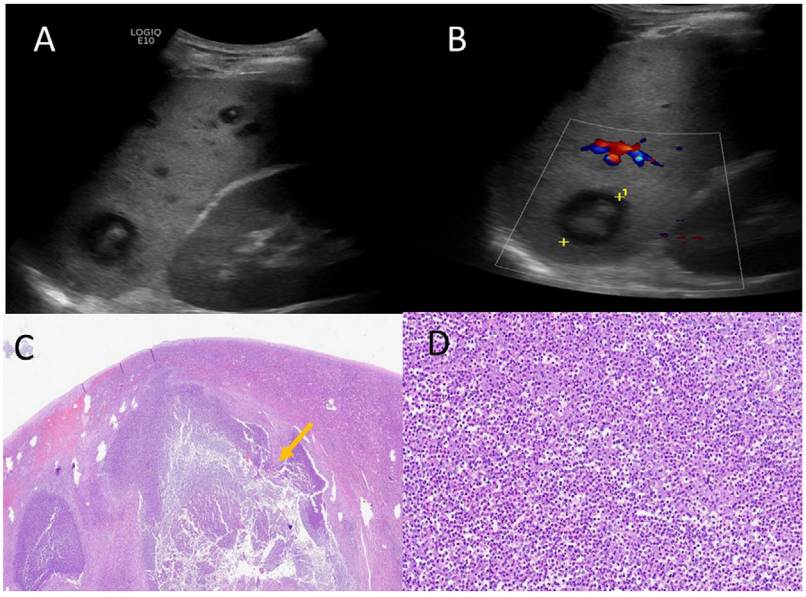


Figure 9 24-year-old male with acute leukaemia undergoing chemotherapy. Left hypochondrium pain and abdominal distension with fever despite full antibiotic coverage. (A and B) Baseline ultrasound and colour Doppler ultrasound with multiple lesions of ''bull's eye'' morphology with echogenic centre and hypoechoic periphery and no vascularisation in the colour Doppler study (marked between cursors in B). In this case, contrast-enhanced ultrasound was ruled out. The suggested diagnosis was multiple splenic abscesses of possible fungal origin. Due to the poor response to antibiotic therapy, it was decided to perform a splenectomy. (C and D) Splenectomy specimen. Splenic parenchymal slices showing diffuse effacement of the general architecture, identifying multiple foci of acute abscessing inflammation, with areas of fibrosis and necrosis (yellow arrow in C). High magnification reveals a mixed, predominantly acute inflammatory infiltrate consisting of numerous polymorphonuclear neutrophils and cellular debris, as well as occasional histiocytes and lymphocytes (D). No microorganisms were isolated in the microbiological culture.

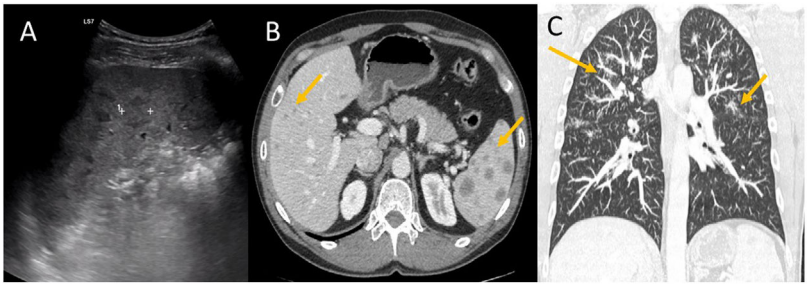


Figure 10 50-year-old male with left hypochondrium pain and anaemia. (A) Baseline ultrasound showing an enlarged spleen with multiple hypoechoic splenic lesions (between cursors) and liver lesions (not shown). In this case, contrast-enhanced ultrasound was not performed. (B) Abdominal computed tomography showing multiple splenic and hepatic hypodense lesions (yellow arrows). (C) Coronal slice of a chest CT scan showing ill-defined lung opacities and some nodules in a perilymphatic distribution (yellow arrows), findings suggestive of diffuse lung involvement due to sarcoidosis. Transbronchial biopsy confirmed the diagnosis of sarcoidosis.

lesions. Doppler study can demonstrate the presence of intralesional vessels. They have a characteristic dynamic behaviour, with ring-like enhancement in the arterial phase, gradual uptake through the fibrous septa, giving a cartwheel appearance, and persistent enhancement in the late phases with a central scar with poor uptake.[25] The treatment is splenectomy[24] (Fig. 8).

Splenic abscesses

Seventy per cent of splenic abscesses arise from haematogenous spread of an infectious source, with endocarditis, urinary tract infections, appendicitis and recent surgery being the most common.[6]

Splenic abscesses are typically cystic, with a thick, irregular wall, and may contain septa. In CEUS, abscesses may show enhancement of the wall and septa, with no uptake by the necrotic component, which helps to differentiate them from simple cysts.[16] Correlation of imaging findings with clinical and laboratory findings is essential in these cases (Fig. 9).

Granulomatous diseases

Granulomatous diseases, such as tuberculosis and sarcoidosis, can affect the spleen; for example, 60% of patients with sarcoidosis have splenic involvement.[26] The classic presentation is splenomegaly with multiple focal lesions

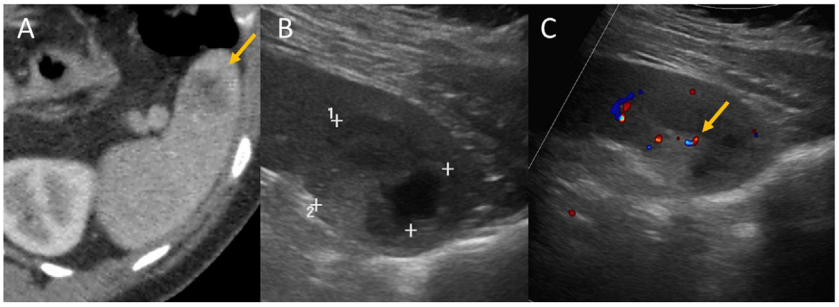


Figure 11 66-year-old woman. History of operated-on ovarian serous carcinoma under follow-up. Patient has a pacemaker, so magnetic resonance imaging contraindicated. (A) Axial computed tomography with contrast with finding of a splenic lesion showing a slight increase in size with respect to previous scans (yellow arrow). (B) Baseline grey scale ultrasound showing a mixed solid-cystic lesion (shown between cursors) (C) Colour Doppler ultrasound showing vascularisation within the lesion with presence of chaotic vessels (yellow arrow).

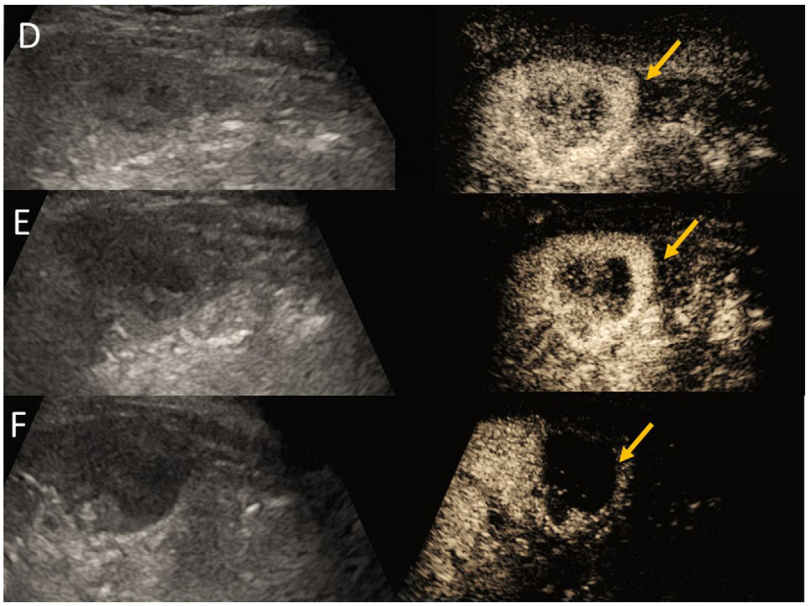


Figure 12 Same patient as Fig. 11. History of operated-on ovarian serous carcinoma under follow-up. Patient has a pacemaker, so magnetic resonance imaging contraindicated. (D–F) Contrast-enhanced ultrasound at 16 seconds (D), 40 seconds (E) and 3 min (F). Heterogeneous enhancement of the lesion with rapid and continuous washout identified in the late phases (yellow arrows), suggestive of a malignant lesion; in this case metastasis was suggested as a first option.

and evidence of sarcoidosis at another site.[26] On ultrasound, splenic lesions in sarcoidosis can be detected as small nodules, with hypoechoic attenuation compared to the surrounding parenchyma[26] (Fig. 10).

Malignant lesions

Metastases

Splenic metastases are rare (7% of cancer patients). The most common primary cancers to metastasise to the spleen are breast, lung, colorectal, ovarian and melanoma.[27]

The ultrasound appearance is variable (they may look like solid-cystic or solid lesions), depending on the primary cancer. After contrast administration, metastases show variable enhancement and rapid washout due to the lack of sinusoidal spaces and cells of the reticuloendothelial system[22] (Figs. 11, 12 and 13). Sometimes they may have chaotic vessels and necrotic areas in their interior.

Lymphoma

This is the most common malignant tumour of the spleen. It is usually the first manifestation of a systemic lymphoma and the spleen is usually affected secondarily in 10–30% at diagnosis, with non-Hodgkin's lymphomas being the most common.[28]

Primary splenic lymphoma is very rare, with and incidence of less than 1%; in these cases it is usually due to diffuse large B-cell lymphoma or mantle cell lymphomas.

As in other organs, the imaging findings of lymphoma in the spleen can be very different. Lymphoma may appear

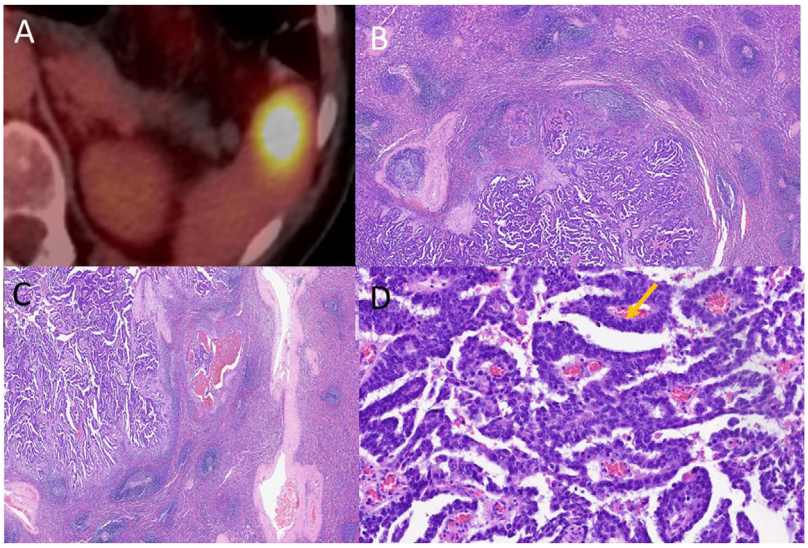


Figure 13 Same patient as Fig. 11. History of operated-on ovarian serous carcinoma under follow-up. (A) Fluorodeoxyglucose positron emission tomography showing lesion with high avidity for the radiopharmaceutical. Splenectomy was performed with a diagnosis of infiltration by high-grade serous carcinoma. (B–D) Slices corresponding to the splenectomy specimen showing invasion of the splenic parenchyma by an epithelial cancer with papillary and glandular pattern, consisting of fibrovascular axes (arrow) lined by atypical polygonal cells with eosinophilic cytoplasm and hyperchromatic nucleus, with prominent nucleolus and pleomorphism. Immunohistochemistry techniques showed positivity for PAX-8, WT1 and ER, with the tumour profile being compatible with serous adenocarcinoma of ovarian origin.

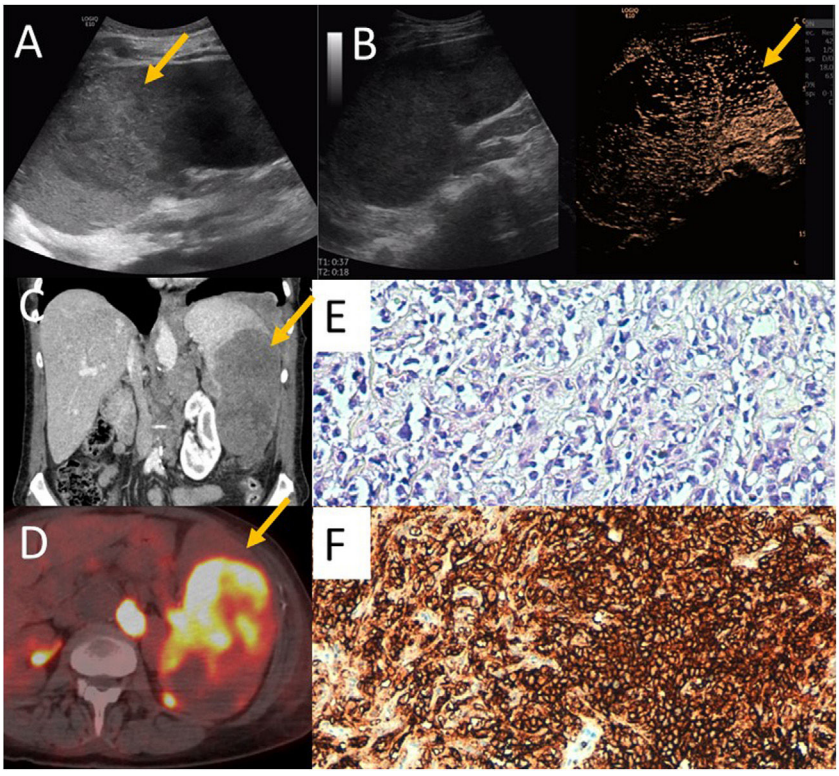


Figure 14 50-year-old patient with abdominal pain. (A) B-mode ultrasound: splenomegaly and heterogeneous appearance of the parenchyma with peri-splenic soft tissue and presence of a large splenic mass. (B) Contrast-enhanced ultrasound at 60 seconds shows a heterogeneous hypovascular lesion (yellow arrow). Computed tomography (C) and fluorodeoxyglucose positron emission tomography (D) were performed, confirming a splenic mass and peri-splenic tissue and multiple retroperitoneal lymphadenopathy (yellow arrows). (E) A biopsy was taken of the peri-splenic tissue. Pathology shows cylinders of fibroadipose tissue with extensive invasion by a lymphoid neoplasm with a diffuse pattern consisting of large cells of centroblastic morphology, with associated foci of sclerosis, necrosis and high mitotic activity. (F) Immunohistochemical study shows positivity for B-cell lymphoid lineage markers (CD20), with findings consistent with diffuse large B-cell lymphoma.

as a homogeneous enlargement of the spleen without a demarcated mass (infiltrative lesion), as a solitary mass, as multiple masses or as miliary nodules.

They are usually hypoechoic lesions on ultrasound, although sometimes only diffuse heterogeneity of their echostructure is seen. After contrast administration, the lesions show poor uptake in the arterial phase with gradual and intense washout[20,29] (Fig. 14).

Important reminder: lesions showing poor arterial enhancement and gradual washout in the late phase suggest malignancy and require further imaging studies or biopsy, particularly in high-risk groups.

Conclusions

CEUS, in addition to being a simple, safe and accessible technique, has an added role in the characterisation of focal splenic lesions and may be a good alternative to other imaging techniques in the characterisation of splenic lesions found incidentally on ultrasound examination. Absence of enhancement at any stage or persistent late-stage enhancement are characteristic findings of benign lesions. Late stage washout is typical of malignant lesions due to the absence of sinusoidal spaces and cells of the reticuloendothelial system.

CRediT authorship contribution statement

1 Responsible for the integrity of the study: PGB, ELG, IPA, EIL and CBS.
2 Study conception: PGB, ELG, IPA, EIL and GI.
3 Study design: PGB, ELG, IPA and EIL.
4 Data collection: PGB, GI, and CBS.
5 Data analysis and interpretation: PGB, ELG and IPA.
6 Statistical processing: PGB.
7 Literature search: PGB, CBS.
8 Drafting of the article: PGB, ELG, IPA and EIL.
9 Critical review of the manuscript with intellectually relevant contributions: PGB, ELG, IPA, GI and CBS.
10 Approval of the final version: PGB, ELG, IPA, EIL, GI and CBS.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

References

1. Catalano O, Lobianco R, Sandomenico F, D'Elia G, Siani A. Real-time contrast-enhanced ultrasound of the spleen: examination technique and preliminary clinical experience. Radiol Med. 2003;106:338–56.
2. Yu X, Yu J, Liang P, Liu F. Real-time contrast-enhanced ultrasound in diagnosing of focal spleen lesions. Eur J Radiol. 2012;81:430–6, http://dx.doi.org/10.1016/j.ejrad.2010.12.052.
3. Olson MC, Atwell TD, Harmsen WS, Konrad A, King RL, Lin Y, et al. Safety and accuracy of percutaneous image-guided core biopsy of the spleen. AJR Am J Roentgenol. 2016;206:655–9.
4. Lowe JS, Anderson PG, Anderson SI. Anatomía vascular del bazo. Histología humana. 5th ed; 2020. p. 120–39.
5. Wilson SR, Burns PN. Microbubble-enhanced US in body imaging: what role? Radiology. 2010;257:24–39, http://dx.doi.org/10.1148/radiol.10091210.
6. Zavariz JD, Konstantatou E, Deganello A, Bosanac D, Huang DY, Sellars ME, et al. Common and uncommon features of focal splenic lesions on contrast-enhanced ultrasound: a pictorial review. Radiol Bras. 2017;50:395–404, http://dx.doi.org/10.1590/0100-3984.2015.0209.
7. Lerchbaumer MH, Althoff CE, Fischer T. Real-time CEUS-guided biopsy revealing a littoral cell angioma of the spleen after inconclusive CT and MRI findings. J Ultrason. 2021;21:244–7.
8. Lee HJ, Kim JW, Hong JH, Kim GS, Shin SS, Heo SH, et al. Cross-sectional imaging of splenic lesions. Radiographics. 2018;38:435–6, http://dx.doi.org/10.1148/rg.2018170119.
9. Yang R, Lu Q, Xu J, Huang J, Gao B, Zhang H, et al. Value of contrast-enhanced ultrasound in the differential diagnosis of focal splenic lesions. Cancer Manag Res. 2021;13:2947–58, http://dx.doi.org/10.2147/CMAR.S300601.
10. Sidhu PS, Cantisani V, Dietrich CF, Gilja OH, Saftoiu A, Bartels E, et al. The EFSUMB guidelines and recommendations for the clinical practice of contrast-enhanced ultrasound (CEUS) in non-hepatic applications: update 2017 (long version). Ultraschall Med. 2018;39:2–44.
11. Catalano O, Cusati B, Nunziata A, Siani A, et al. Real-time, contrast-specific sonography imaging of acute splenic disorders: a pictorial review. Emerg Radiol. 2004;11:15–21, http://dx.doi.org/10.1007/s10140-004-0343-6.
12. Li XZ, Song J, Sun ZX, Yang YY, Lin YQ, Wang H. Conventional ultrasound and contrast-enhanced ultrasound in the diagnosis of splenic diseases: a systematic review and meta-analysis. J Ultrasound Med. 2020;39:1687–94, http://dx.doi.org/10.1002/jum.15291.
13. Omar A, Freeman S. Contrast-enhanced ultrasound of the spleen. Ultrasound. 2016;24:41–9, http://dx.doi.org/10.1177/1742271X15617214.
14. Gorg C, Graef C, Bert T. Contrast-enhanced sonography for differential diagnosis of an inhomogenous spleen of unknown cause in patients with pain in the left upper quadrant. J Ultrasound Med. 2006;25:729–34, http://dx.doi.org/10.7863/jum.2006.25.6.729.
15. Lim AK, Patel N, Eckersley RJ, Taylor-Robinson SD, Cosgrove DO, Blomley MJ. Evidence for spleen-specific uptake of a microbubble contrast agent: a quantitative study in healthy volunteers. Radiology. 2004;231:785–8, http://dx.doi.org/10.1148/radiol.2313030544.
16. Von Herbay A, Barreiros AP, Ignee A, Westendorff J, Gregor M, Galle PR, et al. Contrast-enhanced ultrasonography with SonoVue. Differentiation between benign and malignant lesions of the spleen. J Ultrasound Med. 2009;28:421–34, http://dx.doi.org/10.7863/jum.2009.28.4.421.
17. Abbott RM, Levy AD, Aguilera NS, Gorospe L, Thompson WM. From the archives of the AFIP: primary vascular neoplasms of the spleen: radiologic-pathologic correlation. Radiographics. 2004;24:1137–63, http://dx.doi.org/10.1148/rg.244045006.
18. Dietrich CF, Mertens JC, Braden B, Schuessler G, Ott M, Ignee A. Contrast-enhanced ultrasound of histologically proven liver hemangiomas. Hepatology. 2007;45:1139–45, http://dx.doi.org/10.1002/hep.21615.
19. Vilanova JC, Barceló J, Smirniotopoulos JG, Pérez-Andrés R, Villalón M, Miró J, et al. Hemangioma from head to toe: MR imaging with pathologic correlation. Radiographics. 2004;24:367–85, http://dx.doi.org/10.1148/rg.242035079.

20. Goerg C, Schwerk WB. Splenic infarction: sonographic patterns, diagnosis, follow-up, and complications. Radiology. 1990;174:803–7, http://dx.doi.org/10.1148/radiology.174.3.2406785.
21. Görg C, Zugmaier G. Chronic recurring infarction of the spleen: sonographic patterns and complications. Ultraschall Med. 2003;24:245–9, http://dx.doi.org/10.1055/s-2003-41712.
22. Stang A, Keles H, Hentschke S, von Seydewitz CU, Dahlke J, Malzfeldt E, et al. Differentiation of benign from malignant focal splenic lesions using sulfur hexafluoride-filled microbubble contrast-enhanced pulse-inversion sonography. AJR Am J Roentgenol. 2009;193:709–21, http://dx.doi.org/10.2214/ajr.07.3988.
23. Stang A, Keles H, Hentschke S, von Seydewitz CU, Dahlke J, Habermann C, et al. Incidentally detected splenic lesions in ultrasound: does contrast-enhanced ultrasonography improve the differentiation of benign hemangioma/hamartoma from malignant lesions? Ultraschall Med. 2011;32:582–92, http://dx.doi.org/10.1055/s-0031-1282034.
24. Martel M, Cheuk W, Lombardi L, Lifschitz-Mercer B, Chan JK, Rosai J. Sclerosing angiomatoid nodular transformation (SANT): report of 25 cases of a distinctive benign splenic lesion. Am J Surg Pathol. 2004;28:1268–79, http://dx.doi.org/10.1097/01.pas.0000138004.54274.d3.
25. Cao JY, Zhang H, Wang WP. Ultrasonography of sclerosing angiomatoid nodular transformation in the spleen. World J Gastroenterol. 2010;16:3727–30, http://dx.doi.org/10.3748/wjg.v16.i29.3727.
26. Palmucci S, Torrisi SE, Caltabiano DC, Puglisi S, Lentini V, Grassedonio E, et al. Clinical and radiological features of extra-pulmonary sarcoidosis: a pictorial essay. Insights Imaging. 2016;7:571–87, http://dx.doi.org/10.1007/s13244-016-0495-4.
27. Compérat E, Bardier-Dupas A, Camparo P, Capron F, Charlotte F. Splenic metastases: clinicopathologic presentation, differential diagnosis, and pathogenesis. Arch Pathol Lab Med. 2007;131:965–9, http://dx.doi.org/10.5858/2007-131-965-SMCPDD.
28. Picardi M, Soricelli A, Pane F, Zeppa P, Nicolai E, De Laurentiis M, et al. Contrast-enhanced harmonic compound US of the spleen to increase staging accuracy in patients with Hodgkin lymphoma: a prospective study. Radiology. 2009;251:574–82, http://dx.doi.org/10.1148/radiol.2512081293.
29. Görg C, Faoro C, Bert T, Tebbe J, Neesse A, Wilhelm C. Contrast enhanced ultrasound of splenic lymphoma involvement. Eur J Radiol. 2011;80:169–74, http://dx.doi.org/10.1016/j.ejrad.2009.11.012.