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## Use of contrast-enhanced ultrasonography in hepatosplenic sarcoidosis: Report of 2 cases

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### Summary

**Background:**

Sarcoidosis is a multisystemic granulomatous disease of unknown etiology that predominantly affects lungs and intrathoracic lymph nodes; in rare cases (approx. 10%), infiltration of the spleen and liver may be observed. In order to identify hepatosplenic infiltration, MRI/CT of the abdomen and different ultrasound techniques (PD US, US D) are usually performed. Contrast enhanced ultrasound (CEUS) is a new technique in this diagnostic algorithm, but the fact that this is a safe, accurate, and widely available method opens a new perspective for the detection of abdominal lesions in sarcoidosis.

**Case Reports:**

We report 2 cases of hepatosplenic sarcoidosis – a 41-year-old woman with splenic lesions and a 46-year-old man with liver infiltration.

**Results:**

On the basis of these 2 cases we intended to show the diagnostic potential of contrast enhanced ultrasound for the recognition of focal lesions of the spleen and liver in patients suffering from sarcoidosis.

**Key words:**

contrast enhanced ultrasound • CEUS • sarcoidosis • hepatosplenic sarcoidosis

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### Background

Sarcoidosis is a multisystemic granulomatous disease of unknown etiology that predominantly affects lungs and intrathoracic lymph nodes. In rare cases (approx. 10%), infiltration of the spleen and liver may be observed. Early detection of organ lesions in the course of sarcoidosis is crucial as it changes the classification of the disease and treatment strategy, thus influencing the long-term results of therapy. Unfortunately, the infiltration of abdominal organs is usually asymptomatic, which delays diagnosis [1].

HRCT is currently the standard diagnostic tool for monitoring patients with sarcoidosis. In the cases of organ involvement localized subdiaphragmatically, MRI/CT of the abdomen and different ultrasound techniques (PD US, US D) are performed. There is a need to find new, sufficiently sensitive and noninvasive screening methods to screen for systemic sarcoidosis. MRI is already well-established in this

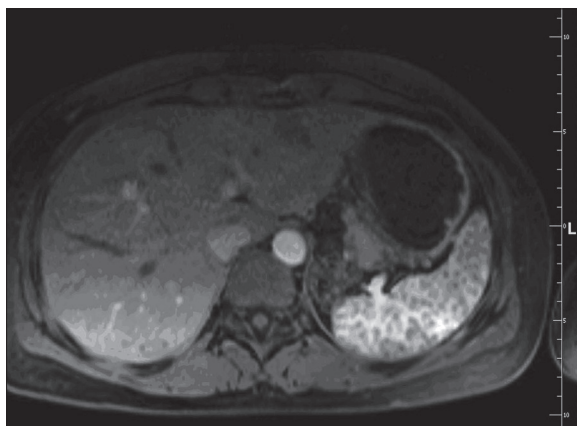
algorithm as a safe, accurate, and reliable method, but its wide use is limited. Consequently, the implementation of contrast enhanced ultrasound opens new perspectives for the detection of abdominal lesions in sarcoidosis.

The purpose of this report was to analyze the diagnostic potential of CEUS for the recognition of focal lesions of the spleen and liver in patients suffering from sarcoidosis.

### Case Report

#### Case 1

A 41-year-old woman treated for pulmonary sarcoidosis for 10 years was referred to the Department of Radiology and Diagnostic Imaging with the complaint of vague pain in the epigastric region of the abdomen. Initial ultrasound (US) examination, performed using the GE Vivid 7 scanner and a 3 MHz convex transducer, revealed that the spleen was enlarged, heterogeneous but without any focal lesions.

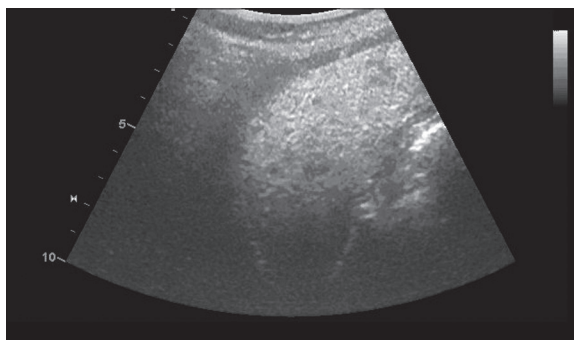


**Figure 1.** Case 1: 41-year-old woman. MRI images. After administration of contrast medium, numerous small, well-limited nodules are visible in the spleen.

As spleen infiltration was suspected, a magnetic resonance imaging (MRI) examination was conducted using a Siemens-Avanto scanner. After contrast medium administration (ProHance) multiple low-signal lesions with a maximum diameter of 12 mm were visualized in the spleen parenchyma (Figure 1). CEUS was the last diagnostic step, performed using GE Vivid 7 and microbubble contrast medium (SonoVue) at a dose of 2.4 ml/study. It confirmed the MRI findings: numerous hypoechoic lesions on the background of homogeneously enhancing spleen parenchyma with an average diameter of 10 mm (Figure 2). Liver image was normal during the whole diagnostic pathway. Biopsy of the spleen was not performed due to a high risk of bleeding.

### Case 2

A 46-year-old man treated for pulmonary sarcoidosis for 12 years was admitted to the Department of Pulmonology for follow-up examinations. Computed tomography (CT) of the chest performed using GE-Light-Speed 64 raised a suspicion of liver infiltration. The patient was referred



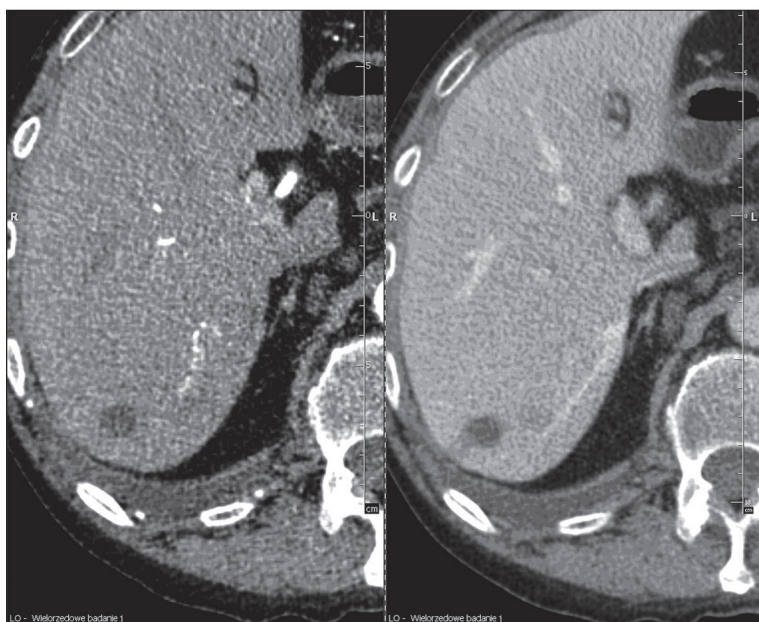
**Figure 2.** Case 1: 41-year-old woman. CE-US images. After administration of contrast medium, numerous small, well-limited nodules are visible in the spleen.

for abdominal CT (4-phase protocol) with contrast administration (Iomeron 400) which visualized 5 nonenhancing hypodense nodules with a diameter of 5–18 mm in the right hepatic lobe (Figure 3). CEUS, which was performed later on, was consistent with the results of CT imaging: after administration of contrast, 4 hypoechoic lesions became visible (diam. 7–19 mm) within the right lobe of the liver (Figure 4). In order to confirm the diagnosis of sarcoidosis, a biopsy of the liver was conducted. It revealed the presence of noncaseating granulomas. Spleen image was normal during the whole diagnostic pathway.

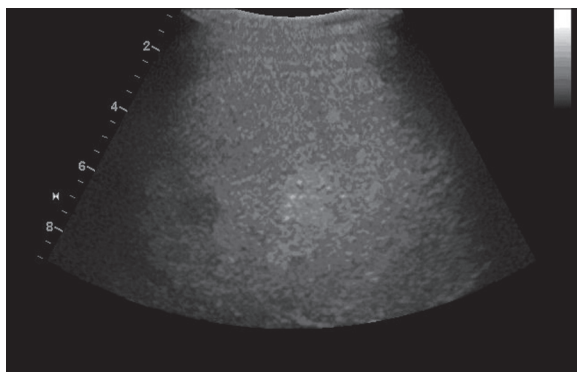
### Discussion

Early detection of lesions in patients suffering from sarcoidosis affects the treatment strategy and improves prognosis. Respiratory involvement presents as cough and dyspnea, whereas liver and spleen infiltration is usually asymptomatic. Manifestations such as abdominal pain, portal hypertension, pancytopenia, and spleen capsule rupture are observed in only 2–5% hepatosplenic sarcoidosis cases [2].

On CT and MRI, small nodules in the liver and spleen are often invisible. This is the reason why despite the



**Figure 3.** Case 2: 46-year-old man. CT images. After contrast administration. On the left: the arterial phase; on the right: the venous phase. A small and well-demarcated nodule in segment VII is visible in both phases.



**Figure 4.** Case 2: 46-year-old man. CE-US images. After contrast administration, a small, well-demarcated nodule in segment VII of the liver is visible.

development of imaging techniques, liver biopsy is still the diagnostic gold standard. In the cases of a seemingly normal liver image on CT and MRI, a biopsy revealed the presence of nodules in 40–70% cases [3,4]. Similar dissonance may be observed at autopsy, in which the extrapulmonary form is recognized more often than it is diagnosed based on the current routinely used imaging methods. Biopsy is still regarded as the reference method for diagnostic imaging. For the liver, this treatment is considered to be safe, with occasional complications. This is different when it comes to spleen biopsy which is a procedure burdened with considerable risk of bleeding and therefore not recommended. Spleen sarcoidosis, although not uncommon, is also difficult to confirm using solely diagnostic imaging [5].

Due to the invasive nature of biopsy and the risk of significant complications, we are looking for different diagnostic tools that are less invasive and have fewer contraindications. CT and MRI are good diagnostic methods, but in some cases they are contraindicated (CT – contrast allergy, MRI – pacemakers, metallic foreign bodies). The use of a contrast agent to visualize focal lesions in parenchymal organs is the imaging diagnostic standard in CT and MRI [6]. Administration of a contrast agent is burdened with, sometimes, severe complications related to the contrast medium, which eliminates them from diagnostic screening and limits their use in systemic sarcoidosis monitoring. The great advantage of the contrast media used in ultrasonography is their safety, which has been confirmed by clinical trials [7]. Moreover, in the diagnosis of sarcoidosis it is important to eliminate the nephrotoxicity of the administered contrast.

Hepatosplenomegaly and lymphadenopathy are the most common discoveries on CT and MRI scans, whereas granulomas are rare (about 5% cases) [8,9]. They occur most often in the form of multiple, well demarcated and nonenhancing

(after contrast administration) nodules with a diameter of up to 0.8 mm [10,11]. This allowed us to reach a conclusion that sarcoid nodules in the liver and spleen, as non-vascularized structures which do not impair the surrounding vascular architecture [12], will be visualized in CEUS as hypoechoic nodules, which was confirmed in this study. The CEUS allowed us to distinguish healthy (hyperechoic) liver and spleen parenchyma from numerous small, avascular (hypoechoic) granulomas.

In the literature, there are first attempts to use CEUS in the diagnosis of systemic sarcoidosis. For example, a case of a 74-year-old woman suffering from sarcoidosis, in whom CEUS confirmed the presence of nonenhancing nodules in the parenchymal organs [13]. Another one is a case of a 38-year-old woman with atypical pain in the left lower hemi-abdomen, in whom CEUS revealed the presence of hypoechoic nodules in the liver [14]. The authors of those papers observed a pattern of post-contrast behavior similar to that demonstrated in our study.

CEUS in a clear and transparent way shows the vascular structure of focal lesions on the background of a homogeneously enhancing liver parenchyma, which allows differentiation between them, with efficacy similar to MRI [15]. In the literature, the nature of post-contrast enhancement is widely raised as a feature differentiating focal lesions of the liver in CEUS. Focal liver lesions vary in the degree of enhancement, contrast saturation time and the phenomenon called “washout”, but there are no well-demarcated, nonenhancing solid lesions in these diagnostic algorithms, and such a pattern of behavior is represented by sarcoid nodules. This feature creates a prospect of high sensitivity and specificity of CEUS in granuloma diagnostics.

## Conclusions

Based on our observations, it seems that the main way of CEUS implementation could be by searching for systemic sarcoidosis in patients already diagnosed with pulmonary sarcoidosis (based on biopsy, HRCT, biochemical, and serological tests). This method has a potential to become a reliable screening tool in these patients (replacing more expensive and less available imaging methods, such as MRI, CT). It also seems that CEUS could be an important method of monitoring the effects of therapy. CEUS has all the qualities to play an important role in the examination of lesions occurring in systemic sarcoidosis.

## COI disclosure

No potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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