71-Year-Old Patient with Chronic Lymphocytic Leukemia (CLL) and Hypoechoic Nodular Spleen and Liver Lesions with Fatal Outcome: Presentation of Mucormycosis in B-Mode Imaging and Contrast-Enhanced Ultrasound (CEUS)

Introduction

Mucormycosis is a fungal infection that can potentially manifest in any organ system. It mainly affects immunocompromised patients with diabetes mellitus type II or malignant hematologic diseases, especially after stem cell transplantation [1,2]. In a study of 929 patients facing zygomycosis, infestation of the sinus cavities (39%) was observed most frequently, followed by pulmonary (24%) and cutaneous manifestations (19%) [1]. However, mucormycosis of the liver and spleen is rare and has been documented only in several case reports [3].

Contrast-enhanced ultrasound (CEUS) is an established and important method for the diagnosis of focal liver lesions. The first guidelines for CEUS of the liver were published in 2004, followed by updates in 2008 and 2012 [4]. CEUS imaging of mucormycosis has not been described in the literature. To our knowledge, this case report describes hepatic and splenic mucormycosis using CEUS for the first time.

History and Clinical Findings

A 71-year-old CLL male patient was admitted to our hospital with increasing abdominal pain, general malaise and new focal liver lesions. He had been diagnosed with chronic lymphocytic leukemia (CLL) 9 years ago and had received multiple systemic therapies in the past. Due to progressive disease, a tyrosine kinase inhibitor (TKI) therapy had been started approximately 2 months ago. The patient reported ongoing B symptoms with night sweats and weight loss. Laboratory tests showed marked leukocytosis, thrombocytopenia, anemia and elevated transaminases. A preclinical computed tomography scan (CT) showed hypodense, non-enhancing hepatic and splenic lesions on contrast CT (**Fig. 1**).

Investigations

B-mode imaging showed multiple hypoechoic hepatic nodules with diameters of up to 4 cm, and a large hypoechoic splenic lesion with a diameter of 7 cm, which initially indicated lymphoma involvement of the liver and spleen (**Fig. 2a**). CEUS was performed for further diagnostics. For this purpose, 2.4 ml of SonoVue contrast media were administered and then rinsed with 10 ml of NaCl. The study was carried out in a contrast-specific examination mode (Acuson Sequoia, Siemens) with a low mechanical index ("low MI" imaging). Both the hepatic and the splenic lesions presented no enhancement in the arterial and parenchymal phase, which is not characteristic for lymphoma infiltration (**Fig. 2b**).

Therapy, Course, Diagnosis

Clinically, the patient presented with an infection without a clear focus rather than a progressive disease. A broad empirical antibacterial and antifungal therapy was initiated. Based on our initial ultrasound findings of multiple lesions lacking vascularization, we ruled out abscesses and discussed necrotizing, atypical CLL infiltrates or focal hemorrhage. Both differential diagnoses explained the acute illness of the patient poorly. For further differentiation, a sonographically guided biopsy of a liver lesion was performed. The patient developed progressive liver failure and his condition worsened rapidly. He died within 24 h of admission, prior to the final biopsy report. Histopathological findings showed extensive necrosis with evidence of fungal hyphae in small thrombosed vessels, which, according to their location, were identified as mucor species (**Fig. 3**).

In summary, this case report describes the diagnosis of hepatic and splenic mucormycosis using CEUS with fulminant course and fatal outcome.

Discussion

The dual blood supply of the liver via the hepatic artery and the portal vein is an important property that can be exploited by CEUS. The portal venous blood flow creates a distinct contrast agent phase (portal venous phase) between the arterial and parenchymal phase [4]. In CEUS,

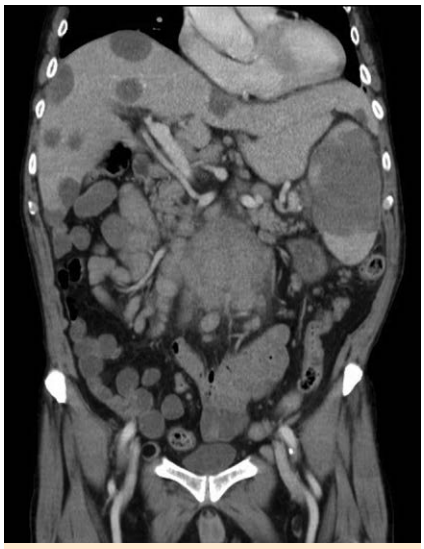

Fig. 1 CT scan with hypodense hepatic and splenic lesions.

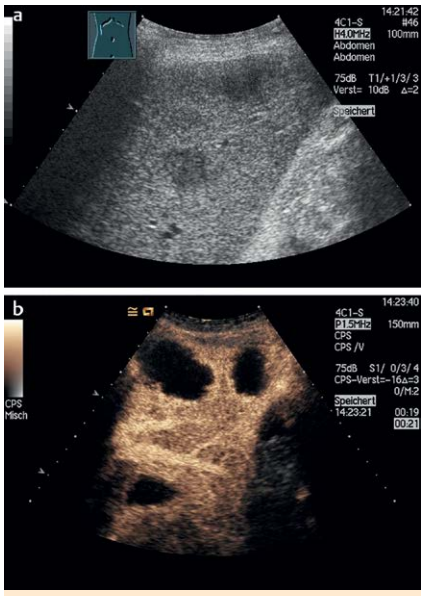

Fig. 2 **a** Hypoechoic hepatic lesions in B-mode imaging. **b** No enhancement of the hepatic lesions during the arterial phase of CEUS.

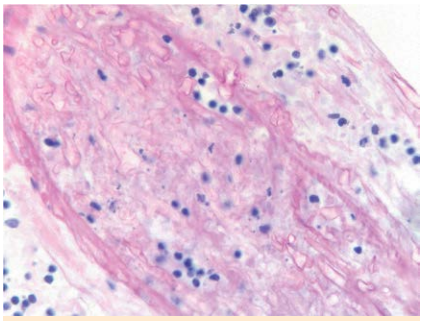

Fig. 3 Liver biopsy (PAS staining 1: 630): Partially necrotic vessel which is almost completely filled with the tubular material. From size and morphology according to a thrombus of mucor hyphae, here with detection of PAS-positive hyphae.

malignant hepatic lesions predominantly show rapid flushing of contrast medium with parenchymatous hypoenhancement ("washout phenomenon") [4]. Avascular hepatic tumors such as cysts or hematomas show no enhancement in all contrast medium phases of CEUS [4]. Liver abscesses can also exhibit a lack of enhancement because of necrotic areas [4].

In the described case, the hepatic and splenic lesions were hypoechoic in B-mode imaging, which is characteristic for CLL-related lymphoma infiltration [5]. However, in CEUS, the splenic and hepatic lesions presented as avascular tumors, not characteristic for lymphoma infiltration [5]. Hepatic lymphomas can present as well as arterial hyper-, iso- or hypoenhancement. However, they show rapid flushing of the contrast agent during the parenchymal phase with hypoenhancement in the late phase, matching the behavior of malignant hepatic lesions [5]. Thus a progression of CLL with lymphoma infiltration of the liver and spleen was unlikely. Histological analysis of a liver lesion provided evidence of mucormycosis, excluding an atypical form of lymphoma involvement. Mucormycosis of the liver and spleen is a rare but an important differential diagnosis in immunocompromised patients. The lack of enhancement in CEUS may help to distinguish mucormycosis from parenchymal lymphoma infiltration. This case report underlines the demand of a histological confirmation of suspected tumor progression in known malignant systemic disease.

References

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