Case Report
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Focal Hepatic Eosinophilic Infiltration in Contrast-Enhanced Ultrasonography with Sonazoid: A Case Report
간 내 호산구 침윤의 Sonazoid 조영 초음파 소견: 증례 보고

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Focal eosinophilic infiltration in the liver is often associated with various eosinophil-related conditions. Focal eosinophilic infiltration in the liver is often identified incidentally by radiologic examinations ordered for other reasons, and is usually visualized radiographically as small, ill-defined, oval or round nodules. Focal eosinophilic infiltration in the liver may sometimes mimic hepatic metastases in those patients who present with a history of malignancy. Here, we present two cases of contrast enhanced ultrasonography findings of focal hepatic eosinophilic infiltration using Sonazoid (perfluorobutane; Daiichi-Sankyo, GE, Tokyo, Japan).

Index terms
Sonazoid
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INTRODUCTION

Focal eosinophilic infiltration in the liver is related to various eosinophil-related conditions and is incidentally found on ultrasonography (US) or computed tomography (CT). The imaging findings of focal lesions are relatively well known, but it is often difficult to differentiate metastasis in patients with malignancy history (1, 2).

Sonazoid (perfluorobutane; Daiichi-Sankyo, GE, Tokyo, Japan) is a third-generation contrast agent that enables low mechanical index, continuous real-time imaging, and Kupffer imaging. It shows rapid enhancement of the vascular pool after intravenous injection and can be phagocytosed by Kupffer cells in the Kupffer phase (3).

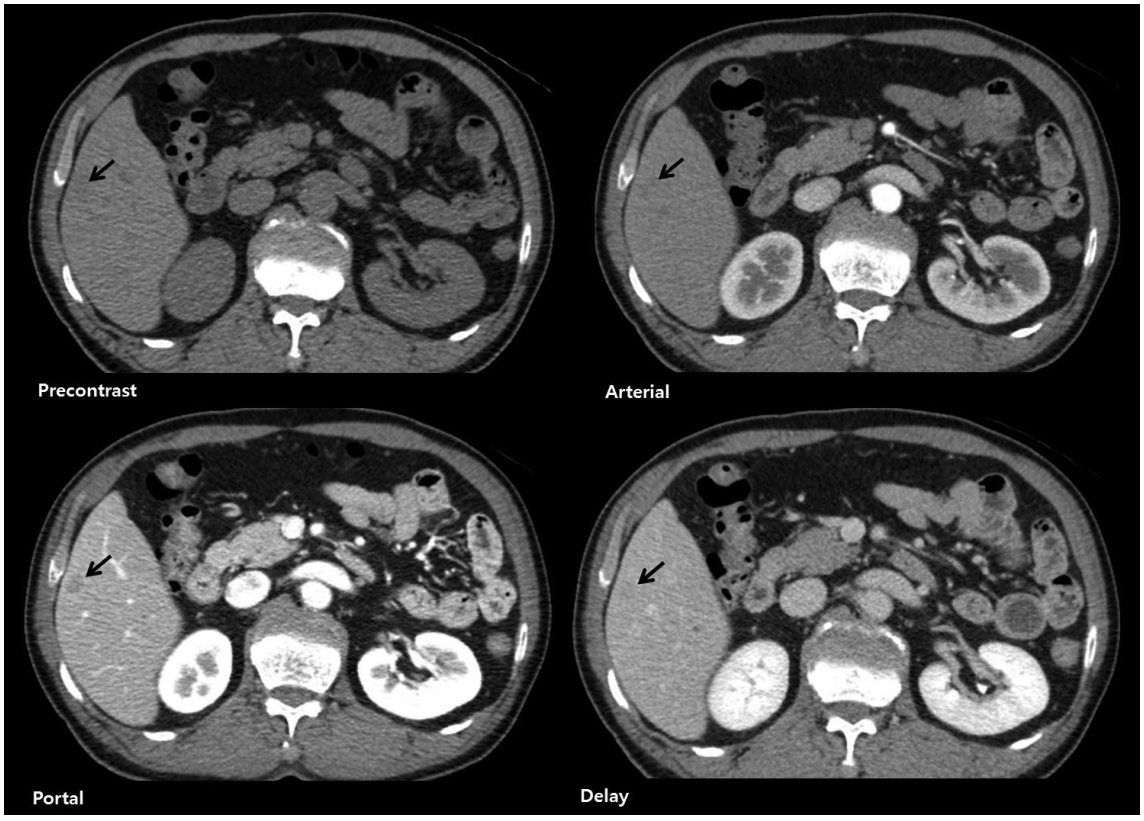
To our knowledge, sonographic findings of eosinophilic liver infiltration using Sonazoid have not been reported in the English literature. Here, we report two cases of sonographic findings of focal eosinophilic infiltration in the liver using Sonazoid.

CASE REPORT

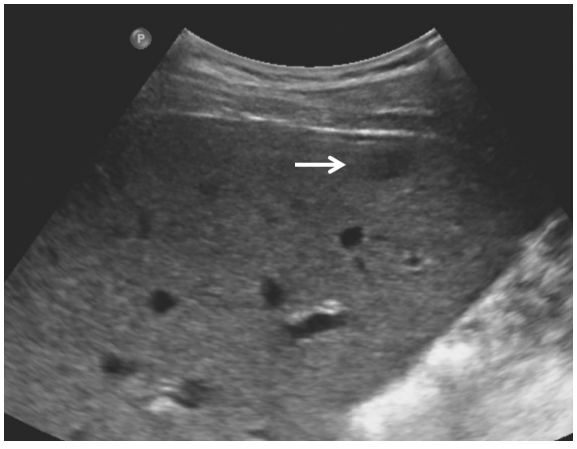
Case 1

A 63-year-old male patient with lung cancer underwent dynamic contrast-enhanced abdominal CT for distant metastasis evaluation. He had no specific symptoms, such as abdominal pain, fever, fatigue, etc. The dynamic contrast-contrast enhanced CT scan showed a 1.4 cm low-attenuation lesion at S5 of the liver on dynamic portal phase CT scan (Fig. 1A). For metastasis evaluation, the clinician determined a US-guided percutaneous gun biopsy. Examination was performed using an IU-22 (Philips Medical Systems, Bothell, WA, USA) equipped with a 3–5 MHz convex-array transducer. B-mode US revealed an ill-defined low echoic lesion on S5 of the liver (Fig. 1B). For contrast-enhanced US examination (CEUS), Sonazoid was prepared by mixing it with 2 mL of saline and was injected by hand injection as slowly as possible. Approximately 1 mL of the Sonazoid was injected through into an antecubital vein with a 21-gauge

peripheral intravenous cannula, followed by a 10-mL saline flush. For preserving the microbubbles, US was set with a mechanical index of 0.2. CEUS demonstrated iso-enhancement on the arterial phase (40 seconds), hypo-enhancement on the portal phase (70 seconds), and a 3 minute delay phase and hypo-enhancement on the 10 minute Kupffer phase (Fig. 1C). US-guided percutaneous gun biopsy was performed, and pathologically eosinophilic infiltration was diagnosed (Fig. 1D). The patient's white blood cell count was 8.51 × 10^3/uL with 58.1% neutrophils, 27.8% lymphocytes, and 6.5% eosinophils on the day of

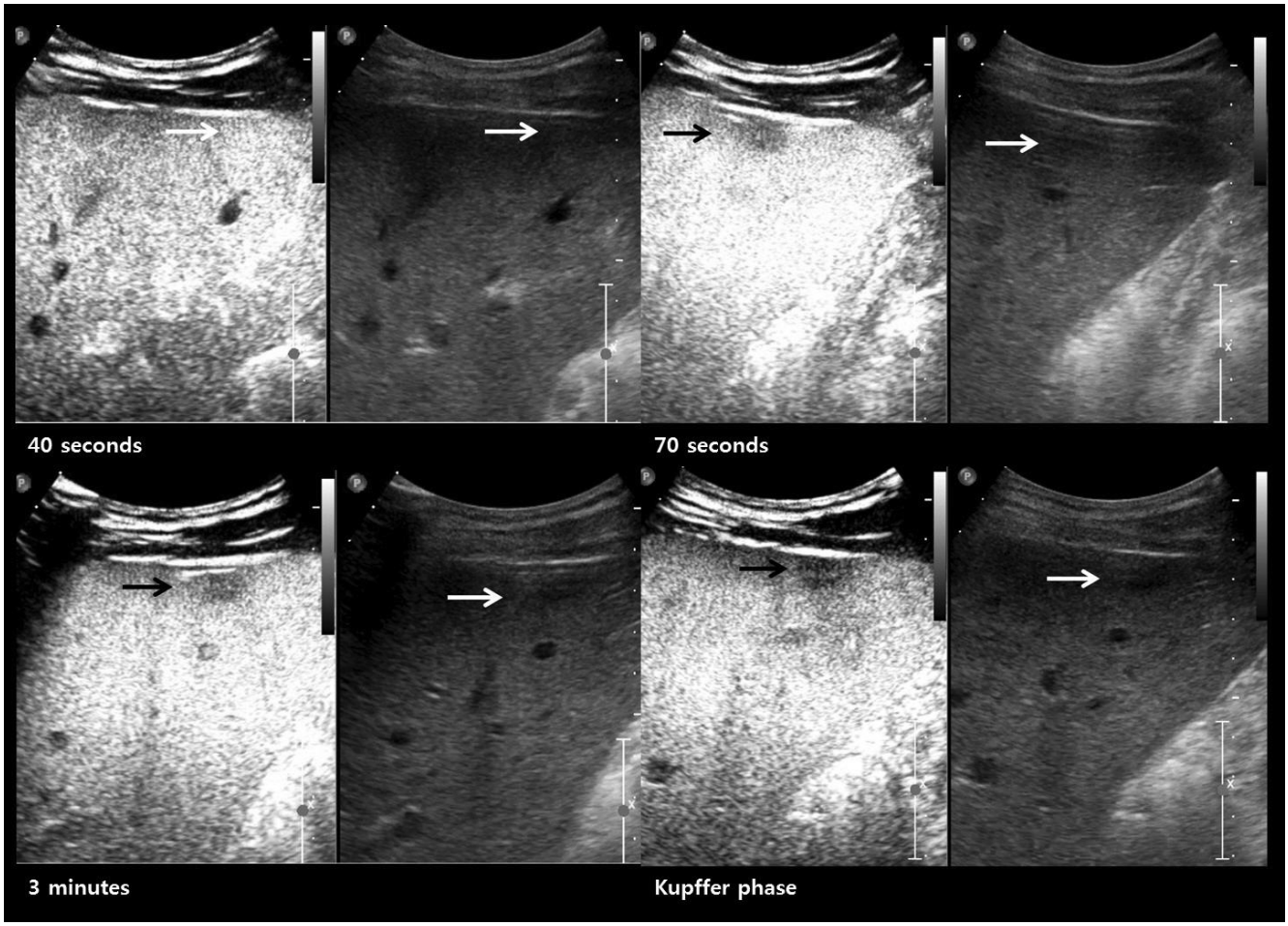


A



B

Fig. 1. Focal hepatic eosinophilic infiltration in a 63-year-old male patient with lung cancer (case 1).
A. Portal phase of contrast-enhanced CT scan shows an approximately 1.4 cm low-attenuated lesion on S5 of the liver (arrows). On pre-contrast CT scan and arterial phase of contrast-enhanced CT scan and 3-minute delay phase of contrast-enhanced CT scan, the lesion reveals iso-attenuation to slight low-attenuation.
B. B-mode ultrasonography shows an ill-defined low echoic lesion on S5 of the liver (arrow).
CT = computed tomography



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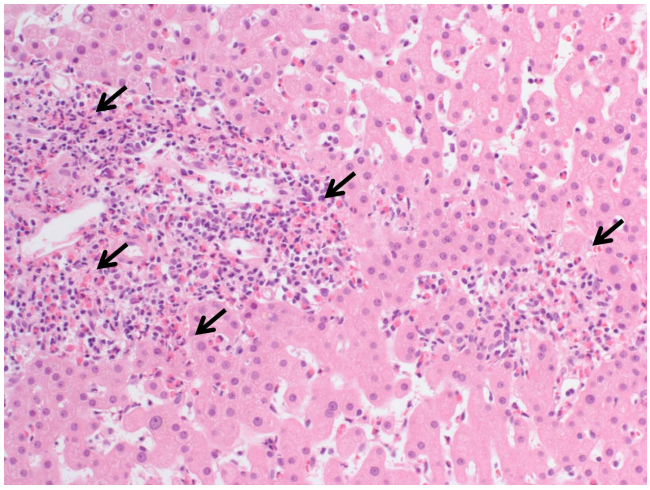

D

Fig. 1. Focal hepatic eosinophilic infiltration in a 63-year-old male patient with lung cancer (case 1).
C. Forty seconds after injection of Sonazoid, showing an iso-enhanced lesion. Seventy seconds after injection of Sonazoid, showing a hypo-enhanced lesion (arrows). Three minutes after injection of Sonazoid, showing a hypo-enhanced lesion (arrows). In the Kupffer phase (10 minutes after injection of Sonazoid), showing a hypo-enhanced lesion (arrows).
D. Photomicrograph of biopsy specimen shows inflammatory cell infiltrations at hepatic parenchyma, predominantly composed of eosinophils (arrows) (hematoxylin and eosin stain, × 200).

the CT exam. After 10 days, eosinophil was elevated to 9.6%.

Case 2

A 55-year-old male patient with diabetes mellitus and hypertension complained of abdominal pain that had persisted for 2 days. He didn't complain any other symptoms, such as fever or fatigue, etc. The patient's white blood cell count was 9.59 × 10^3/uL with 77.3% neutrophils, 14.2% lymphocytes, and 1.6% eosino-

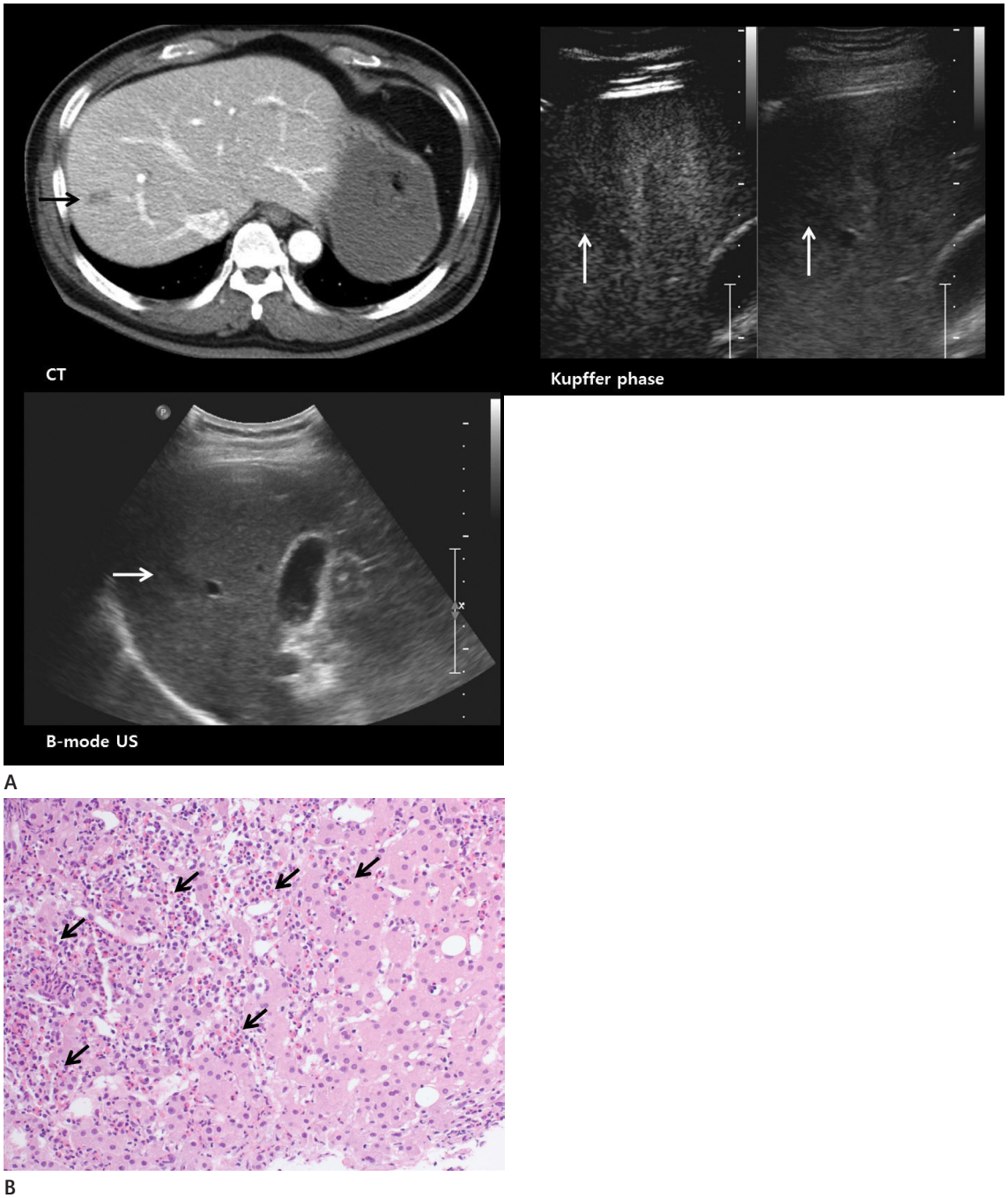

Fig. 2. Focal hepatic eosinophlic infiltration in a 55-year-old male with an incidentally found lesion of the liver (case 2).
A. Axial contrast-enhanced computed tomography scan shows an approximately 1.7 cm low-attenuation lesion on S8 of the liver (arrow). B-mode ultrasonography shows an ill-defined low echoic lesion on S8 of the liver (arrow). In the Kupffer phase (10 minutes after injection of Sonazoid), showing a hypo-enhanced lesion (arrows).
B. Photomicrograph of biopsy specimen shows inflammatory cell infiltrations at hepatic parenchyma, predominantly composed of eosinophils (arrows) (hematoxylin and eosin stain, × 200).

phils. Contrast-enhanced abdominal CT was performed and showed a 1.7 cm low-attenuation lesion on S8 of the liver (Fig. 2A). The clinician determined US-guided percutaneous gun biopsy for histologic evaluation. B-mode US revealed an ill-defined slight low echoic lesion on S8 of the liver (Fig. 2A). CEUS demonstrated hypo-enhancement on the 10 minute Kupffer phase (Fig. 2A). Eosinophilic infiltration was pathologically diagnosed (Fig. 2B), and the patient's eosinophil was elevated to 11.8%.

DISCUSSION

Eosinophilic infiltration in the liver histologically includes eosinophilic infiltrations in the periportal space, eosinophilic abscess, and eosinophilic granuloma. Eosinophilic infiltration in the liver is often associated with various eosinophil-related conditions, such as parasitic infestation, allergic reactions, hypereosinophilic syndrome, and internal malignancies including lymphoma, leukemia, and cancer of the lung, stomach, pancreas, or ovary. In two cases, the etiology was uncertain through clinical and patient information, except lung cancer history. It is almost usually correlated with eosinophilia (defined as 500 eosinophils/μL in the peripheral blood) and is incidentally discovered on radiologic examinations, such as US or CT.

The imaging findings of focal eosinophilic infiltration in the liver are well known and morphologic findings are similar in US, CT and magnetic resonance image (MRI). At CT, characteristically portal phase of dynamic enhanced study reveals conspicuously multiple, small, round or oval, low attenuated nodular lesions with fuzzy margins in the liver (2, 4, 5). On MRI, these lesions are iso- or slightly low signal intensity on T1 weighted images and have high signal intensity on T2 weighted images. Dynamic MRI more easily demonstrates lesion enhancement on the arterial phase than does dynamic CT (5, 6). On era of hepatobiliary MRI contrast agent, one study using gadobenate dimeglumine-enhanced MRI revealed that the hepatic focal eosinophilic infiltration showed intermingled low signal intensity and isosignal intensity (67%) and homogenous low signal intensity (24%) on hepatobiliary phase. Another study using gadoxetic acid-enhanced MRI revealed that all hepatic focal eosinophilic infiltration lesions showed mixed hypointensity, irregular margins and nonspherical shapes on hepatobiliary phase (7, 8).

Sonazoid is a contrast agent with a low mechanical index and is phagocytosed by Kupffer cells. CEUS with Sonazoid can assess the vascularity in the vascular phase and the presence of Kupffer cells in the post-vascular phase after 10 minutes in real time. The presence of Kupffer cells indicates normal hepatic tissue, and the absence of Kupffer cells indicates a pathologic lesion (3). In the first case, the lesion shows iso-enhancement at the arterial phase of the vascular phase and hypo-enhancement at the portal phase, as seen in dynamic enhanced CT. At 3 minutes delay phase of CT in this case, the lesion reveals iso-enhancement, however, the lesion still reveals hypo-enhancement after 3 minutes and is sustained on the Kupffer phase after 10 minutes of CEUS. This is an important distinction between dynamic enhanced CT and dynamic enhanced CEUS using Sonazoid. We hypothesized that this finding was related to early contrast agent uptake, as seen in gadoxetic acid. Superparamagnetic iron oxide (SPIO)-enhanced MRI works on a similar principle to Sonazoid, as it is phagocytosed by Kupffer cells. A study using SPIO-enhanced MRI revealed that most cases of hepatic focal eosinophilic infiltration showed a reduction in the extent of hyperintense area and differentiation of lesion size compared to the T2-weighted images (9). In our cases, two lesions on the Kupffer phase showed the same lesion size compared to the B-mode US images.

Most of the metastases showed rim-like enhancement on arterial phase of CEUS and hypoenhancement on the Kupffer phase of CEUS (10). In our cases, rim-like enhancement is not seen on arterial phase of CEUS, but these lesions show hypoenhancement on portal and delay phase and are sustained on the Kupffer phase after 10 minutes of CEUS. Hatanaka et al. (10) reported that small portion of metastatic lesions show atypical arterial enhancement pattern which may be caused by different characteristics of the primary cancer. Although rim-like enhancement on arterial phase of CEUS is not visible, we can't exclude metastasis in the case of hypoenhancement on Kupffer phase.

In conclusion, imaging findings on CEUS with Sonazoid of focal eosinophilic infiltration in the liver show different features on the vascular phase compared to CT and MRI and present indistinctive findings on the Kupffer phase. Nonspecific imaging features of CEUS with Sonazoid were not helpful for distinguish these lesions from metastatic lesions in our cases.

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간 내 호산구 침윤의 Sonazoid 조영 초음파 소견: 증례 보고

이동준[1] · 김대중[1]* · 김광일[2]

간 내 호산구 침윤은 종종 다양한 호산구 관련 질환과 연관이 있다. 간 내 호산구 침윤은 영상의학적 검사에서 우연히 발견되며 대개 작고 다수며, 형태가 명백하지 않으며 타원형 혹은 둥근 형태의 병변으로 발현된다. 때때로 간 내 호산구 침윤은 암 병력이 있는 환자의 경우 간 내 전이로 오인되기도 한다. 저자들은 초음파 조영제인 Sonazoid를 이용한 간 내 호산구 침윤의 조영초음파 소견을 보고하고자 한다.

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