*Case report*

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# Contrast-enhanced ultrasound findings of gallbladder tuberculosis: a case report

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**Abstract**

Preoperative diagnosis of gallbladder tuberculosis (TB) is difficult, and the contrast-enhanced ultrasound (CEUS) pattern has never been reported before. We present a case of TB in which CEUS had some special findings that were helpful for early diagnosis. The thickened gallbladder wall presented in the arterial phase of CEUS the "sandwich biscuit" sign with no enhancement in the middle layer and hyperenhancement in the inner and outer layers.

**Keywords:** gallbladder; tuberculosis; contrast-enhanced ultrasound

## Introduction

Gallbladder tuberculosis (TB), a type of extrapulmonary TB, is extremely rare with limited case reports and literature reviews. In this paper, we report a case of gallbladder TB, with an emphasis on the ultrasound (US) and contrast-enhanced US (CEUS) findings.

## Case report

A 63-year-old man developed yellow staining of the skin and sclera 2 days before admission, accompanied with distending pain in the upper abdomen. He had a 10-year history of diabetes but no history of TB. The laboratory examination showed leucocytes $10.07\times10^9$/L, total bilirubin 146.4 μmol/L, direct bilirubin 116.7 μmol/L, alanin amino transferase 96 U/L, aspartate amino transferase 65 U/L, and tumor marker CA199 54.06 U/mL. The chest computed tomography (CT) showed no abnormalities, while the abdominal contrast-enhanced CT suggested gallbladder cancer.

The patient underwent US and CEUS using an ACUSON Sequoia machine from Siemens with a 5C1 (3.5–5 MHz) probe, and SonoVue (Bracco, Milan, Italy) as the contrast agent. The conventional US revealed an enlarged gallbladder with multiple stones, the wall thickened by about 1.7 cm, uneven echo, and an unclear boundary with liver tissue and duodenal wall (fig 1a). After 1.6 mL of a US contrast agent was injected through the left cubital vein, followed by flushing with 5 mL of normal saline, the patient underwent CEUS with low acoustic power (the mechanical index setting was 0.09). CEUS showed a "fast-in and slow-out" contrast pattern. In the arterial phase, the gallbladder wall started to be visualized synchronously with the surrounding liver tissue, 12 s after injection of the contrast agent. The thickened gallbladder wall showed three layers, resembling a "sandwich biscuit": the inner and outer layers presented uniform hyperenhancement, whereas the middle layer indicated no enhancement, with slightly irregular septa in it showing hyperenhancement (fig 1b). The inner layer of the lesion was smooth and complete; by contrast, the outer layer was not smooth, and the boundary with the surrounding tissues was unclear. The enhancement peaked at 24 s. The contrast agent began to subside at 1 min 02 s in the venous phase; the inner and outer layers of the gall-

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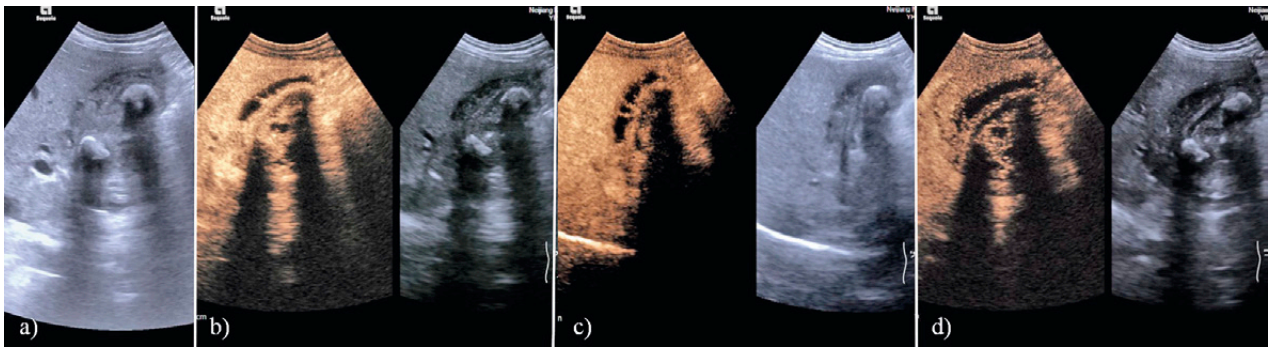


**Fig 1.** a) Greyscale US showed enlarged gallbladder with stones, wall thickening and blurred borders; b) at 23s in the arterial phase, the gallbladder wall showed the "sandwich biscuit" sign with no enhancement in the middle layer and hyperenhancement in the inner and outer layers; c) at 1min 03s in the venous phase, the contrast agent fades to slightly hypoenhancement, and the middle layer remains nonenhancement; d) at 2min 05s in the venous phase, the contrast agent further subsided.

bladder wall showed slight hypoenhancement, whereas the middle layer still showed nonenhancement (fig 1c-d). The scanning of the liver, starting 120 s after contrast agent administration, found no abnormally enhanced hepatic lesions. The diagnosis suggested the possibility of inflammatory lesions of the gallbladder.

The patient was surgically treated, and postoperative pathology showed granulomatous inflammation of the gallbladder wall with caseous necrosis, positive acid-fast bacilli, consistent with TB (fig 2).

## Discussion

Mycobacterium tuberculosis (MTB) commonly affects the lungs and solitary TB of the gallbladder is one of the rarest sites of extrapulmonary TB infection. The reason the gallbladder is less susceptible to infection is related to the highly alkaline environment of bile and the inhibitory effect on MTB of the bile acids [1-2]. The pathogenesis of gallbladder TB is unknown, and the route of infection is mostly considered to be caused by hematogenous or lymphatic spreading. Cholelithiasis and biliary obstruction are considered the most important factors in the development of gallbladder TB [2-4]. The clinical manifestations of gallbladder TB are not typical, with most patients presenting chronic cholecystitis with right upper quadrant pain or gallbladder mass.

There are insufficient imaging data for gallbladder TB, and although a few reports on CT and Magnetic resonance imaging (MRI) exist, the manifestations of CEUS have not been documented. The purpose of this report is to discuss some characteristic manifestations of CEUS in the diagnosis of gallbladder TB through the comparative analysis of CEUS and pathological examination to improve the diagnostic accuracy. Xu et al [5] proposed three morphology features of gallbladder TB, namely, micronodular lesion of the gallbladder wall, a thickened wall, and a gallbladder mass. Our case was the most common type – thickened wall type. The thickened gallbladder wall in the arterial phase of CEUS exhibits a "sandwich biscuit" sign. CEUS findings were compared with histopathological sections. The nonenhancement area in the middle layer was the area involved in TB lesions, presenting a large number of caseous necrosis and tuberculous granulomas. The hyperenhancement area with irregular septa inside was the residual gallbladder wall tissue between tuberculous granulomas and was accompanied with inflammatory reaction. The hyperenhancement area

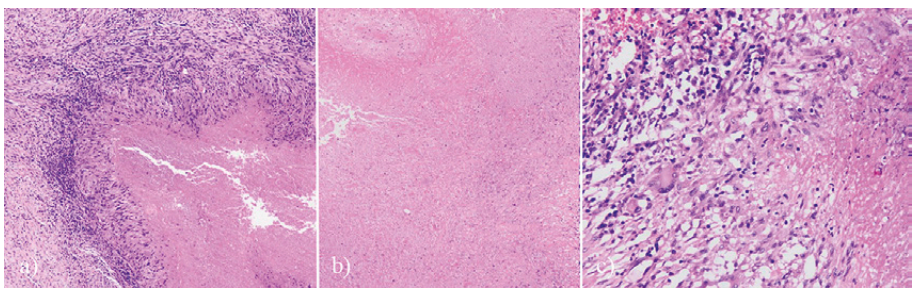


**Fig 2.** a) Microscopical view showing tuberculous granuloma with surrounding fibrous hyperplasia (H&E staining ×100); b) caseous necrosis (H&E staining ×40); c) epithelioid cells and multinucleated giant cells are present at the margin of the tuberculous granuloma (H&E staining ×100).

of the inner and outer layers was the residual tissue not involved in TB on the mucosal and serosal surfaces, accompanied with inflammatory reactions, such as interstitial edema and lymphocyte infiltration.

Xanthogranulomatous cholecystitis (XGC) and thick-walled gallbladder carcinoma (GBC) can show localized or diffuse thickening of the gallbladder wall, which may infiltrate adjacent tissues. In conventional US the distinction between XGC, GBC, and TB is difficult, but CEUS add some specific findings, which are helpful for early diagnosis. XGC is a rare and special type of cholecystitis; the lesion is located in the gallbladder wall, characterized by the formation of yellow plaques or waxy granulomas, and the mucosal line is mostly intact. CEUS showed a "fast-in and slow-out" contrast pattern, with uniform or inhomogeneous hyperenhancement in the arterial phase and equal-enhancement or slight hypoenhancement in the venous phase. By contrast, the mucosal line became clearer and smoother. Gallbladder TB and XGC are both benign lesions, and CEUS can show complete and continuous mucosal lines. A sign similar to "sandwich biscuit" can also appear in contrast-enhanced CT and MRI of XGC: the mucosal and serosal surfaces are significantly enhanced, and the middle layer is weakly enhanced [6]. Although in both images can be found the "sandwich biscuit" sign, the histologic aspect is distinct. The middle layer of gallbladder TB indicates massive caseous necrosis. The wall of XGC comprises xanthogranulomas composed of numerous chronic inflammatory cells, foamy histiocytes, and proliferating fibroblasts. It is an inflammatory lesion with contrast medium entering, showing a hypoenhancement band or an overall hyperenhancement of the gallbladder wall. GBC originates from the glandular epithelium of the mucosa and grows invasively, which can cause changes in the hierarchical structure of the gallbladder wall. CEUS showed irregular mucosal surfaces, lesions demonstrating a "fast-in and fast-out" contrast pattern, hyperenhancement in the arterial phase, mostly tortuous and irregular vascular distribution, and hypoenhancement in rapid washout in the venous phase [7]. Accordingly, typical CEUS findings make this case of thick-walled gallbladder TB largely distinguishable from XGC and GBC. However, when caseous necrosis is not evident in the early stage of the disease, when XGC inflammation intensifies and invades the surrounding liver tissue to form abscess, or when GBC has large necrosis, the identification is still difficult, and the diagnosis depends on pathology.

Our case describes for the first time the peculiar "sandwich biscuit" sign in CEUS of gallbladder TB, and to provide a correlative analysis in conjunction with histopathology, which can serve as a basis for further studies.

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