

A Case of Xanthogranulomatous Cholecystitis Preoperatively Diagnosed with Contrast-enhanced Ultrasonography

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Abstract

We report a case of xanthogranulomatous cholecystitis (XGC) that was diagnosed preoperatively by means of ultrasonography (US) with the contrast-enhancement agent Sonazoid after a false-positive result had been obtained with fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET). A 69-year-old woman was admitted because of right upper quadrant pain. Blood tests revealed a serum CA19-9 level of 749.8 IU/L. Computed tomography (CT), US, and magnetic resonance imaging of the abdomen showed abnormal thickening of the gallbladder wall but no stones. The border between the gallbladder and the liver was unclear. FDG-PET revealed a lesion with increased uptake of tracer in the gallbladder wall. The thickness of the lesion was similar to that on CT. We suspected gallbladder carcinoma with hepatic invasion. To confirm the tentative diagnosis, we performed US with the contrast-enhancement agent Sonazoid. The gallbladder wall was homogeneously enhanced in the early vascular phase and remained enhanced for 90 seconds. Enhancement of the gallbladder wall was smooth and regular. The border between the gallbladder and liver was clear and smooth. On the basis of these examinations, we diagnosed chronic cholecystitis (XGC suspected), not gallbladder carcinoma. At surgery, the gallbladder wall was observed to be extremely thick because of severe inflammation, and cholecystectomy was performed. XGC was diagnosed on intraoperative pathological examination. Histopathological examination showed XGC, severe proliferative fibrosis with formation of multiple yellow-brown intramural nodules, and foamy histiocytes without malignant cells. In conclusion, the present case of XGC was diagnosed preoperatively with contrast-enhanced US after a false-positive result had been obtained with FDG-PET. Contrast-enhanced US can thus play important roles in diagnosing gallbladder disease and selecting treatment.

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Key words: xanthogranulomatous cholecystitis, contrast-enhanced ultrasonography, positron emission tomography

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Introduction

Xanthogranulomatous cholecystitis (XGC) is a rare inflammatory lesion of the gallbladder, characterized by marked proliferative fibrosis, macrophage infiltration, and foam cells involving the gallbladder wall¹. It is often difficult to distinguish XGC from gallbladder carcinoma by means of conventional imaging techniques, such as ultrasonography (US), computed tomography (CT), and magnetic resonance imaging²⁻⁷. Some patients with XGC have undergone excessive surgical resection after XGC was misdiagnosed preoperatively as advanced gallbladder carcinoma^{8,9}.

Several recent studies have demonstrated that fluorine-18 fluorodeoxyglucose positron emission

tomography (FDG-PET) is useful for distinguishing between benign and malignant lesions in the gallbladder¹⁰⁻¹⁴. However, FDG-PET is not specific for malignant lesions, and tracer can accumulate in inflammatory lesions with increased glucose metabolism¹⁵. Contrast-enhanced US is reportedly useful for diagnosing gallbladder lesions, particularly for distinguishing malignant and benign lesions¹⁶. We report a case of XGC that was diagnosed preoperatively by means of US with the contrast-enhancement agent Sonazoid (Daiichi Sankyo Co., Tokyo, Japan), after a false-positive result had been obtained with FDG-PET.

Case Report

A 69-year-old woman was admitted because of right upper quadrant pain. An abdominal CT scan revealed thickening of the gallbladder wall. The past history included thymoma, which was resected 5 years earlier, and pure red-cell aplasia, which was not treated medically. Blood tests revealed a serum CA19-9 level of 749.8 IU/L (normal, <37 IU/L). Magnetic resonance, US, and CT of the abdomen showed abnormal thickening of the gallbladder wall but no gallstones. The border between the gallbladder and liver was unclear (**Fig. 1, 2**). FDG-PET revealed a lesion with increased uptake of tracer in the gallbladder wall. The thickness of the lesion was similar to that on CT (**Fig. 3**). Gallbladder carcinoma with hepatic invasion was suspected. To confirm the diagnosis, we performed US with the

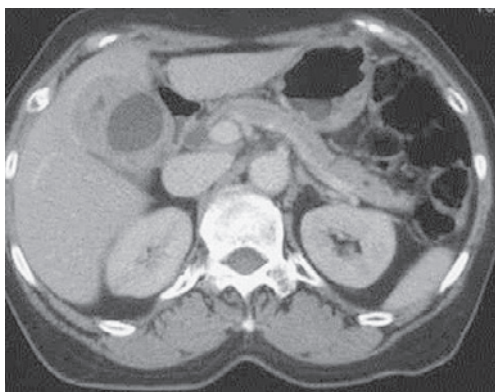


Fig. 1 CT showed an abnormally thickened gallbladder wall without stones. Invasion of the liver bed was suspected.

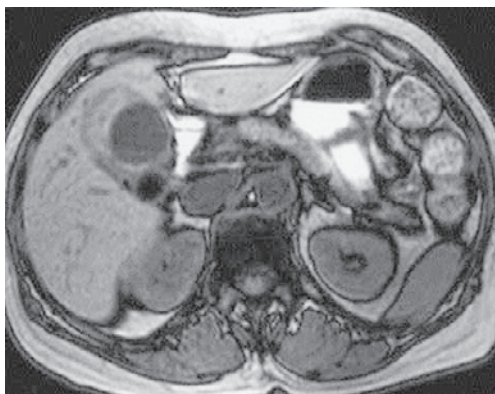


Fig. 2 Magnetic resonance imaging (T1-weighted) showed an abnormally thickened gallbladder wall without gallstones. Invasion of the liver bed was suspected.

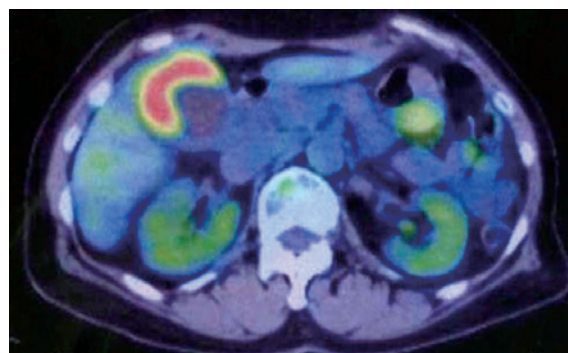


Fig. 3 FDG-PET revealed a lesion with increased uptake of tracer in the gallbladder wall. The thickness of the lesion was similar to that on CT.

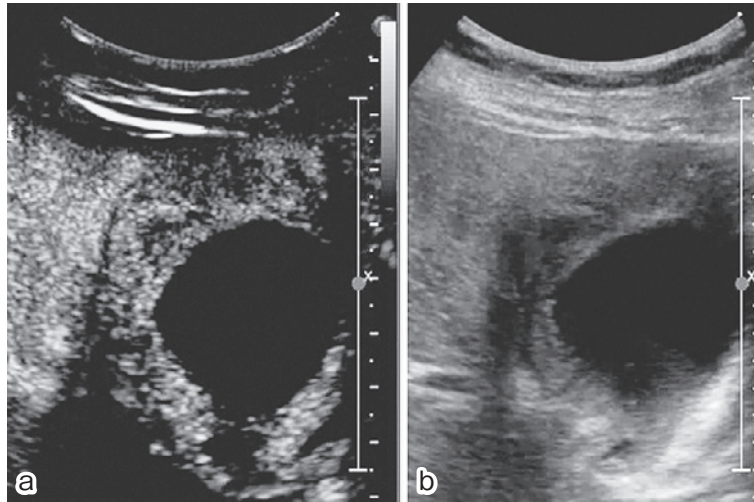


Fig. 4 US enhanced with the contrast agent Sonazoid showed that the gallbladder wall was homogeneously enhanced in the early vascular phase and remained enhanced for 90 seconds. Enhancement of the gallbladder wall was smooth and regular. The border between the gallbladder and liver was clear and smooth.

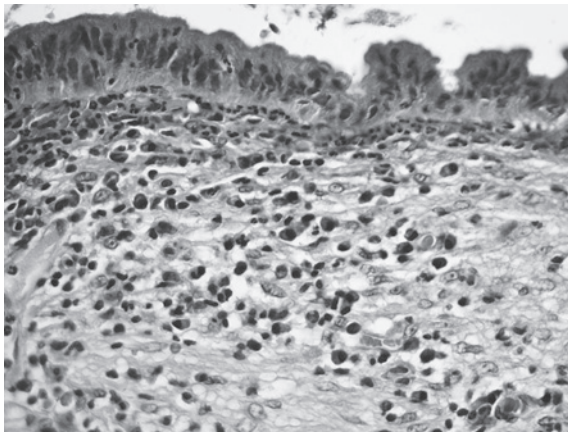


Fig. 5 Pathological examination revealed XGC, severe proliferative fibrosis with formation of multiple yellow-brown intramural nodules, and foamy histiocytes without malignant cells.

contrast agent Sonazoid. The gallbladder wall was homogeneously enhanced in the early vascular phase and remained enhanced for 90 seconds. Enhancement of the gallbladder wall was smooth and regular. The border between the gallbladder and liver was clear and smooth (**Fig. 4**). On the basis of these results, we diagnosed chronic cholecystitis (XGC suspected), not gallbladder carcinoma.

At surgery, the gallbladder wall was observed to be extremely thick because of severe inflammation,

and cholecystectomy was performed. XGC was diagnosed on intraoperative pathological examination. Histopathological examination revealed XGC, severe proliferative fibrosis with formation of multiple yellow-brown intramural nodules, and foamy histiocytes without malignant cells (**Fig. 5**). The postoperative course was uneventful, and the patient was discharged on postoperative day 14.

Discussion

XGC was first reported and named by McCoy and colleagues¹⁷. It accounts for only 0.7% to 13.2% of all inflammatory diseases of the gallbladder and occurs predominantly in middle-aged and elderly persons^{18,19}. The low incidence of XGC sometimes leads to misdiagnosis²⁰.

XGC is characterized by a destructive inflammatory process of the gallbladder, associated with deposition of bile pigments and cholesterol in the gallbladder wall. Macroscopically, lesions vary from a small limited focus within a yellow-brown nodule in the gallbladder wall to diffuse involvement of the entire gallbladder with extension to surrounding structures²¹. Gallbladder stones were present in 85% to 100% of patients in different series, with obstruction of the cystic duct in 80% of

cases^{1,18}. The pathogenesis of XGC is uncertain, but the current opinion favors a combination of acute inflammation of the gallbladder and outflow obstruction due to gallbladder stones^{18,22}. Bile enters the stroma of the gallbladder wall through ruptured Rokitansky-Aschoff sinuses or mucosal ulcerations due to gallbladder stones, acute inflammation, or both. Extravasated bile in the stroma causes intense inflammatory reactions with accumulation of histiocytes, which engulf insoluble cholesterol and other bile lipids to form large, round xanthoma cells. Microabscesses form in the gallbladder wall, eventually resulting in xanthogranulomata. Finally, a fibrous reaction and scarring result from healing of the inflamed tissue²³. Both intramural poorly echogenic nodulated zones on US and intramural hypoattenuated nodules on CT are specific for XGC. Despite these distinctions, it is difficult to distinguish XGC from gallbladder carcinoma⁸.

Several recent studies have shown that FDG-PET is useful for differentiating between benign and malignant lesions in the gallbladder. The sensitivity and specificity of FDG-PET for the diagnosis of gallbladder carcinoma range from 75% to 100% and 75% to 89%, respectively¹⁰⁻¹⁴. However, FDG-PET is not specific for malignant lesions, and tracer can accumulate in inflammatory lesions with increased glucose metabolism. Indeed, false-positive results have been obtained with benign lesions, including chronic cholecystitis, tuberculosis, and adenomyomatosis of the gallbladder^{13,24,25}. In our patient, FDG-PET/CT scans showed increased activity in the thickened wall of the gallbladder which was associated with an inflammatory, not malignant, lesion. In the near future, FDG-PET may be used more frequently to diagnose gallbladder carcinoma. We should consider the risk of misdiagnosing inflammatory lesions as carcinoma, because inflammatory diseases occur frequently in the gallbladder¹⁵.

Contrast-enhanced US has been reported to be useful for diagnosing gallbladder lesions, particularly for differentiating malignant and benign lesions¹⁶. Contrast-enhanced US provides the advantages of real-time, repeatable, multiplanar imaging without compromising patient safety or exposing patients to

radiation²⁶. When the tumor is more mass-like or the gallbladder wall is diffusely thickened, hyperenhancement followed by rapid washout of contrast agent within 35 seconds after administration is highly suggestive of gallbladder malignancy¹⁶. Disruption of gallbladder wall integrity, a feature not seen in benign gallbladder diseases, has been demonstrated in up to 85% of gallbladder carcinomas¹⁶. Improved mural visualization after contrast-agent administration and the malignant feature of late-phase hypovascularity relative to the hepatic parenchyma might help to sharply delineate the tumor²⁶. Hirooka et al. have reported that the 3-layer structure of the gallbladder wall is intact on contrast-enhanced US in patients with cholecystitis. They suggested this finding will prove important for differentiating carcinoma from cholecystitis²⁷. Numata et al. have reported that the observation of tumor vessels is useful for differentiating gallbladder carcinoma from adenomas, inflammatory polyps, and cholesterol polyps on contrast-enhanced harmonic US²⁸. The arterial branches supplying a gallbladder carcinoma tend to show irregularly tortuous extension. Benign gallbladder lesions are also hypervascular and contain arteries of almost normal caliber which taper normally and subdivide normally into small vessels²⁸. We performed contrast-enhanced US with Sonazoid. The gallbladder wall was homogeneously enhanced in the early vascular phase and remained enhanced for 90 seconds. The enhancement of the gallbladder wall was smooth and regular, no mucosal irregularity was detected, and the border with the liver was clear and smooth. The third layer of the gallbladder wall was intact. The arterial branches supplying this lesion did not show irregularly tortuous extension. These findings led to a diagnosis of chronic cholecystitis, (XGC suspected), not gallbladder carcinoma, and cholecystectomy was performed. The diagnosis on intraoperative pathological examination was also XGC.

In conclusion, we have reported a case of XGC diagnosed preoperatively with contrast-enhanced US after a false-positive result had been obtained with FDG-PET. Contrast-enhanced US can thus play an important role in diagnosing gallbladder disease and

selecting treatment.

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