

Gallbladder Tuberculosis: CT Findings with Histopathologic Correlation

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Objective: We wanted to describe the computed tomography (CT) findings of gallbladder tuberculosis (TB) and to correlate them with pathologic findings.

Materials and Methods: There were seven patients (M:F = 3:4; mean age, 46.3 years; age range, 32 to 78 years) in whom gallbladder TB was eventually diagnosed. All of them underwent cross-sectional imaging with CT, a pathologic examination and a retrospective review. CT imaging evaluation was done in each case, including the findings of a mass versus nodule, wall thickening (uniform or irregular) and the enhancement patterns (homogeneous or heterogeneous).

Results: All the cases of gallbladder TB revealed the following three different CT findings: micronodular lesion of the gallbladder wall (n = 1), a thickened wall (n = 4) and a gallbladder mass (n = 2). There were three cases of homogeneous enhancement of the lesions, including homogeneous enhancement with nodular lesion, homogeneous uniform thickness enhancement and homogeneous thickness enhancement in one case each, and these cases pathology showed tuberculous granuloma with a little caseating necrosis in one case and tuberculous granuloma with rich fibrous tissue, but little or no evident caseating necrosis in two cases. Four cases of heterogeneous enhancement of the lesions, including heterogeneous uniform-thickness enhancement in two cases, heterogeneous enhancement with a local mass lesion in one case and heterogeneous enhancement with a mass that replaced the gallbladder in one case; in these cases, pathology showed tuberculous granuloma with marked caseation or liquefaction necrosis in three cases and tuberculous granuloma by fibrous and calcifications accompanied by caseating necrosis in one case. Among the seven cases of gallbladder TB, six cases were accompanied by abdominal extra-gallbladder TB, including abdominal lymph node TB in five cases and hepatic TB in four cases.

Conclusion: Gallbladder TB has various CT manifestations, and the enhanced CT findings are well matched with pathological features. An irregularly thickened gallbladder wall or a gallbladder wall mass with multiple-focus necrosis or calcifications accompanied by the typical CT findings of abdominal extra-gallbladder TB should suggest the diagnosis of gallbladder TB.

Index terms: Gallbladder; Tuberculosis; Computed tomography (CT); Diagnosis; Pathology

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INTRODUCTION

Abdominal tuberculosis (TB) is one of the most common types of extra-lung TB. Its prevalence in developing countries has been estimated to be as high as 12% (1). In recent years, the increasing incidence of TB has been attributed to several causes, including the acquired immunodeficiency syndrome (AIDS) epidemic, intravenous (IV) drug abuse and the increasing number of immunocompromised patients

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(2–4). But gallbladder TB is still extremely rare, and the diagnosis of this disease is almost always overlooked unless there is a high index of suspicion (5, 6). Since the first case of gallbladder TB reported in 1870 by Gaucher, less than 120 cases have been reported in the English medical literature, according to the reported literature (5, 7–9) and the statistics results of searching PubMed.

There are not many reports on the computed tomography (CT) and cholecystography imaging features of gallbladder TB, so the imaging appearance of these lesions is considered as nonspecific and a histopathological confirmation is often required (5–8). In the present study, we retrospectively reviewed seven patients in whom gallbladder TB was eventually diagnosed and the CT manifestations were correlated with the pathologic results.

MATERIALS AND METHODS

Subjects

This study was approved by the Institutional Research and Ethics Board of Zhejiang University, School of Medicine, and all the patients' medical and radiological information was obtained from the Second Affiliated Hospital, Zhejiang University School of Medicine.

In this retrospective study, we reviewed the records of seven patients with gallbladder TB that was proved by surgery or laparoscopic biopsy over a 25-year period (from 1984 to 2009). The histological findings of granuloma with caseation necrosis or identification of acid fast bacilli was used as the criteria for making the diagnosis of TB. Among the seven gallbladder TB patients, three were male and four were female and their ages ranged from 32 to 78 years (mean: 46.3 years). The duration of symptoms ranged from 16 days to six months. The most frequent clinical signs and symptoms were abdominal pain ($n = 7$), abdominal swelling ($n = 4$), low-grade fever ($n = 2$), night sweats ($n = 1$), weight-loss ($n = 3$) and an abdominal mass ($n = 1$). Among the seven cases, five were accompanied by extra-gallbladder abdominal TB. The laboratory tests showed anemia ($n = 4$), an increased erythrocyte sedimentation rate ($n = 5$) and abnormal liver function ($n = 2$). Tuberculin tests (PPD tests) were positive in one out of the two patients tested. The chest X-ray was normal in all patients except one who had evidence of old, healed pulmonary TB.

CT Scanning

CT was performed on Siemens Somatom DR3, HiQ and

Volume Zoom 4 slice CT scanners with the patients in a routine fasting state. All the patients were given 500 mL of oral diluted iodinated contrast medium (10 g/L meglumine diatrizoate) 30 minutes before the scan. The scan ranged from at least the dome of the diaphragm to the last plane of the gallbladder, and for some of the patients the scan ranged from the dome of the diaphragm to the pubic symphysis. All the patients were examined with plain scanning at first, and then five cases were scanned by the DR3 or HiQ scanner using a bolus injection of 80 mL of 600 g/L meglumine diatrizoate for enhanced scanning using a section thickness of 8–10 mm and an interval of 5–10 mm, 120 kV and 165 mAs (the same as the technical parameters for the Volume Zoom 4 slice CT scanner). Two cases scanned by the Volume Zoom 4 slice CT scanner used a bolus injection (2.5–3.0 mL/s) of Ultravist (300 mg I/L) 80 mL that was given through the antecubital vein. Images were obtained separately at the arterial phase (25 s after injection), the portal venous phase (65 s after injection) and the parenchymal phase (100 s after injection).

Image Analysis

The CT images were reviewed by two radiologists who had no knowledge of the pathologic findings, and their consensus opinions were obtained. The CT imaging evaluation included nodular lesion of the gallbladder wall, wall thickened or not (uniform or irregular; local or diffuse), the size of the mass and the contrast material-enhanced CT manifestations (homogeneous or heterogeneous).

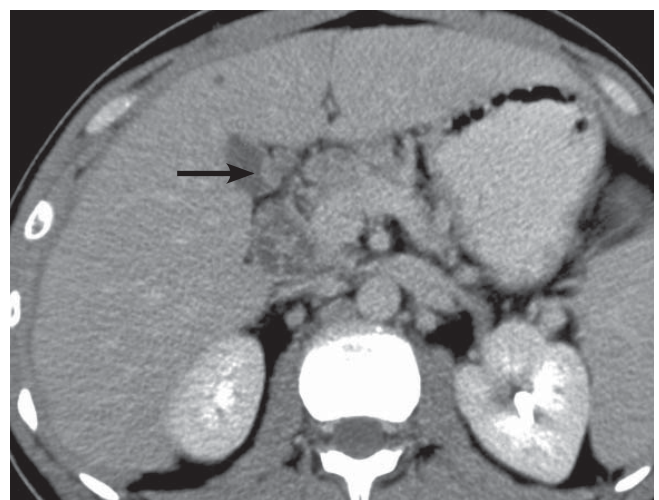


Fig. 1. Gallbladder tuberculosis in 35-year-old man.

Transverse contrast-enhanced CT scan shows micronodular lesion (black arrow) with significant homogeneous enhancement. Multiple enlarged lymph nodes with multilocular enhancement are seen in porta hepatis.

Pathologic Analysis

The pathologic specimens were obtained from the seven patients with gallbladder TB for the pathological correlation. The correlation between the enhanced CT findings and the pathologic features was assessed by a radiologist who reviewed the CT images and a pathologist who reviewed the pathologic reports and the histological slices. Pathologic reviews were made with taking special care for the specific features in the tuberculous lesions (i.e., caseation or liquefaction necrosis, and the presence of fibrosis or calcifications).

RESULTS

CT Findings of Gallbladder TB

All the cases of gallbladder TB revealed the following three different CT morphology findings: 1) micronodular lesion of the gallbladder wall in one case, and this case showed homogeneous enhancement with nodular lesion (Fig. 1), 2) a thickened wall of the gallbladder in four cases, with a diffuse uniform thickened wall in three of the four cases (Figs. 2-4) and local irregular wall thickening in one case (Fig. 5) and 3) a gallbladder mass in two cases: a large

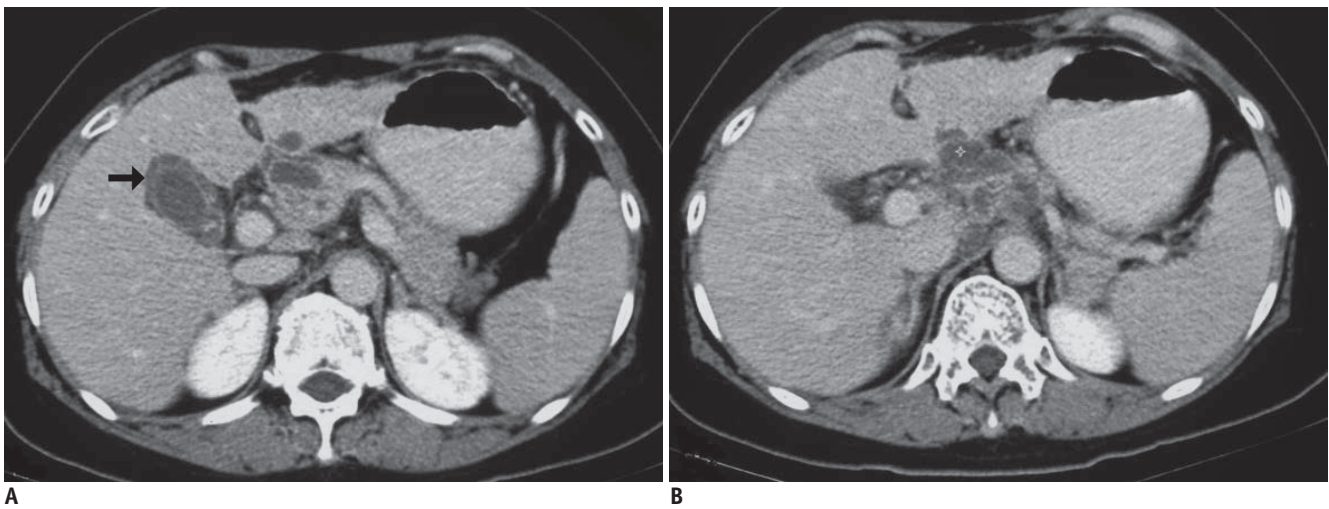


Fig. 2. Images show gallbladder tuberculosis in 58-year-old woman.

A. Transverse contrast-enhanced CT scan shows diffuse uniform-thickness wall with gallbladder stones and heterogeneous enhancement (black arrow). There are low-attenuation nodular lesion in lateral segment of left lobe of liver, and enlarged lymph node with peripheral enhancement in head of pancreas region. **B.** Multiple enlarged lymph nodes with peripheral or multilocular enhancement are seen in region around head of pancreas.

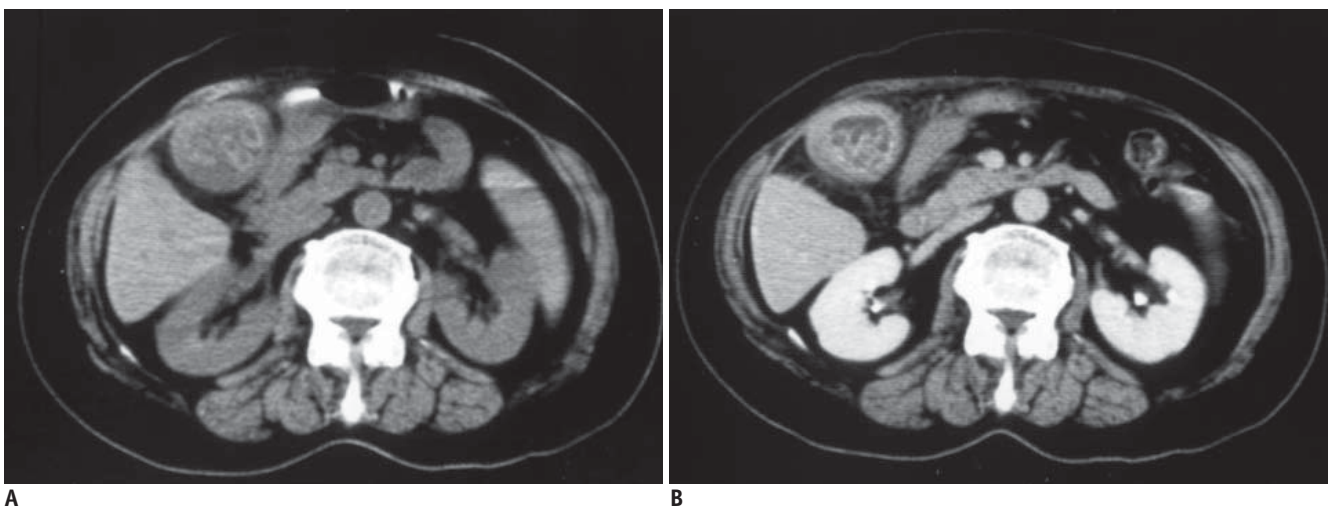


Fig. 3. Gallbladder tuberculosis in 32-year-old woman.

A. Transverse pre-contrast CT scan shows diffuse uniform-thickness wall with multiple gallbladder stones. **B.** Contrast-enhanced CT scan shows homogeneous enhancement of thickened wall.

gallbladder mass (Fig. 6) replaced the gallbladder or there was a local mass (Fig. 7) with flecked calcifications of the gallbladder wall in one case each. Those CT features and the clinical and pathologic findings are summarized in Table 1.

Enhanced CT of the Gallbladder TB as Correlated with the Pathological Features

Two kinds of CT enhancement patterns in the seven cases of gallbladder TB were seen; among them, three were homogeneous enhancement and four were heterogeneous

enhancement. The different enhancement patterns were correlated with different pathological features (Table 2). According to Table 2, homogeneous enhancement of the lesions usually showed tuberculous granuloma with little caseating necrosis or tuberculous granuloma with rich fibrous tissue, yet there was little or no evident caseating necrosis, but the heterogeneous enhancement of those four cases usually showed tuberculous granuloma with marked



Fig. 4. Gallbladder tuberculosis in 35-year-old man. Transverse contrast-enhanced CT scan shows diffuse uniform thickened wall with heterogeneous enhancement and infiltration of liver parenchyma (low-density lesion near gallbladder, black arrows).

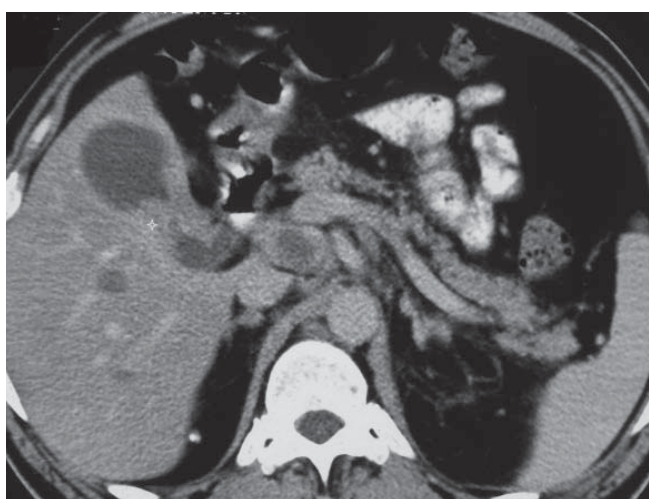


Fig. 5. Gallbladder tuberculosis in 47-year-old woman. Transverse contrast-enhanced CT scan shows local irregular wall thickening with homogeneous enhancement. Low-dense nodular lesion in right lobe of liver and enlarged lymph node in portocaval space were also found.

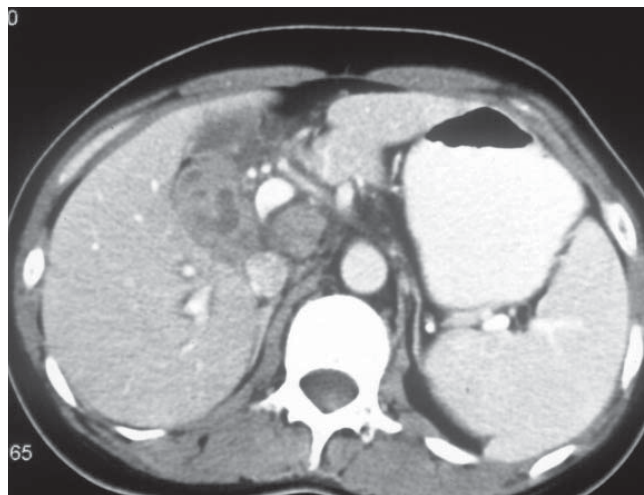


Fig. 6. Gallbladder tuberculosis in 39-year-old woman. Transverse contrast-enhanced CT scan shows large gallbladder mass with marked heterogeneous enhancement and multiple areas of necrosis. Markedly enlarged lymph node with slight heterogeneous enhancement is seen in portocaval space.



Fig. 7. Gallbladder tuberculosis in 78-year-old man. Transverse contrast-enhanced CT scan shows local mass with flecked calcifications of gallbladder wall (white and black arrows) with mild enhancement and central necrosis, and this was accompanied with hepatic tuberculosis, which showed massive low-density lesion with multiple flecked calcifications in liver surrounding gallbladder. Calcificated enlarged lymph nodes in peri-pancreatic area are also seen. Further, multiple renal cysts are also seen.

caseation or liquefaction necrosis on the pathology. Only one case with heterogeneous enhancement had different pathologic stages, including tuberculous granuloma with

fibrous and calcification stages accompanied with caseating necrosis.

Table 1. CT Findings of Gallbladder TB Correlated with Pathological Findings

Case	Sex	Age	CT Findings of Gallbladder	Pathology Findings	CT Findings of Abdominal Extra-Gallbladder Lesion
Case 1 (Fig. 1)	Male	35	0.7 × 1.2 cm micronodular lesion with significantly homogeneous enhancement	Tuberculous granuloma with little caseating necrosis	Multiple LAP
Case 2 (Fig. 2)	Female	58	Diffuse uniform thickened wall with gallbladder stones and heterogeneous enhancement	Tuberculous granuloma with marked caseation or liquefaction necrosis	Low-dense nodular TB lesion in lateral segment of left lobe of liver; multiple LAP
Case 3 (Fig. 3)	Female	32	Diffuse uniform thickened wall with multiple gallbladder stones and homogeneous enhancement of thickened wall	Tuberculous granuloma rich in fibrous tissue but little or no evident caseating necrosis	No abdominal extra-gallbladder lesion being found
Case 4 (Fig. 4)	Male	35	Diffuse uniform thickened wall with heterogeneous enhancement and infiltration of liver parenchyma	Tuberculous granuloma with marked caseation or liquefaction necrosis	Gallbladder TB with hepatic infiltration, showing low-density lesion near to gallbladder
Case 5 (Fig. 5)	Female	47	Local irregular wall thickening with homogeneous enhancement	Tuberculous granuloma rich in fibrous tissue but little or no evident caseating necrosis	Low-dense nodular lesion in right lobe of liver and enlarged lymph node in portocaval spacing
Case 6 (Fig. 6)	Female	39	Large gallbladder mass with marked heterogeneous enhancement and multiple necrosis areas	Tuberculous granuloma with marked, multiple-focus, caseating necrosis	Marked enlarged lymph node with slightly heterogeneous enhancement in portocaval spacing
Case 7 (Fig. 7)	Male	78	Local mass with flecked calcifications of gallbladder wall with mild enhancement and central necrosis, and infiltration of liver parenchyma	Tuberculous granuloma with large amount of fibrous tissue and calcifications, little caseating necrosis was found in center of mass	Massive low-density lesion with multiple flecked calcifications of liver surrounding gallbladder

Note.— LAP = enlarged lymph nodes including porta hepatis, hepatoduodenal ligament, and head of pancreas region, TB = tuberculosis

Table 2. Enhanced CT of Gallbladder TB Correlated with Pathological Features

CT Enhancement Patterns	Pathology Features
Homogeneous enhancement Homogeneous enhancement with nodular lesion (case 1) Homogeneous uniform enhancement (case 3) Homogeneous irregular enhancement (case 5)	Tuberculous granuloma with little caseating necrosis or tuberculous granuloma with rich fibrous tissue but little or no evident caseating necrosis
Heterogeneous enhancement Heterogeneous uniform enhancement (cases 2, 4) Heterogeneous enhancement with mass replaced gallbladder (case 6) Heterogeneous enhancement with local mass lesion (case 7)	Tuberculous granuloma with marked multiple-focus caseation or liquefaction necrosis (cases 2, 4, 6) Tuberculous granuloma with large amount of fibrous tissue and calcifications, little caseating necrosis within centre of mass (case 7)

DISCUSSION

Gallbladder TB can be manifested by a relatively nonspecific clinical presentation. It occurs most commonly in women over 30 years of age (7, 10). For our cases, all the patients were over 30 years old (mean: 46.4 years old). Compared to other abdominal TB, gallbladder TB is more often found in elder patients because the gallbladder is highly resistant to tubercular infection, which is possibly due to the inhibitory function of bile (7, 8, 10).

The gallbladders that harbor benign lesions such as gallstone, diffuse papillomatosis of the gallbladder, opisthorchiasis and cystic duct obstruction are prone to develop TB (7, 8, 11–15). Cholelithiasis and cystic duct obstruction are considered the most important factors in the development of gallbladder TB (7, 8, 11, 12). Majority of the case reports are of isolated gallbladder TB, but if postmortem examination is carried out, then multiorgan involvement may be found in more cases. Patients with gallbladder TB may display a wide spectrum of symptoms, but the most frequent clinical signs and symptoms were right upper abdominal pain and mass (5, 7). Anemia, an increased erythrocyte sedimentation rate and a positive tuberculin test may be found by laboratory examinations.

We found only a few papers on the radiological findings of gallbladder TB, and to the best of our knowledge, almost all these papers described one to two case reports. Moreover, the findings in these papers are considered to be non-specific (5, 8). Our seven case reports of gallbladder TB may be the largest so far. When correlating the retrospective analysis of the seven patients in this paper and the patients in the other previous reports, the CT morphology features of gallbladder TB can be summarized as three types: 1) the micronodular type, 2) the thickened-wall type and 3) the mass-forming type. Classifying the CT morphology of gallbladder TB may be helpful for us to understand the CT findings.

1) **Micronodular type:** In our study and the previous report (5), the CT findings of this type are micronodular or polypoid lesion of the gallbladder wall. This type of gallbladder TB may be nonspecific and it may mimic gallbladder polyp and early carcinoma on CT. But early gallbladder carcinoma with a polypoid mass is typically larger than 1 cm in the short diameter (16), and gallbladder polyp is usually a narrow-based lesion, which is different from the CT findings of our case, which showed a 0.7 cm short diameter and a broad-based lesion.

2) **Thickened-wall type:** This type may be the most

common form of gallbladder TB and it can be easily misdiagnosed as cholecystitis or carcinoma (5, 8, 12, 17, 18). Four of our patients belonged to this type and three were misdiagnosed based on the CT findings. The thickened wall may be diffuse or local, uniform or irregular, and the enhancement may be homogeneous or heterogeneous. The irregular thickened wall with heterogeneous enhancement in gallbladder TB may be helpful for making the differential diagnosis of cholecystitis. The “halo” of the edema of gallbladder TB can be seen on CT, and this is different from that of gallbladder carcinoma.

3) **Mass-forming type:** This type of gallbladder TB is commonly encountered according to the previous reports (5, 8, 18, 19). As for our experience and the previous report (5, 19), the CT findings of this type are similar to gallbladder carcinoma, showing the whole gallbladder mass or a local mass at the gallbladder wall with calcification. A large mass with multicentric necrosis on enhanced CT or a large mass with multiple flecked calcifications may be helpful to make the diagnosis of gallbladder TB. In addition, the mass-forming type of gallbladder TB with stone mimics actinomycosis of the gallbladder and this may be difficult to differentiate from actinomycosis of the gallbladder (20).

The enhanced CT findings of gallbladder TB were well correlated with the pathological features, and the different enhancement patterns may reflect different pathologic stages of lesions, including tuberculous granuloma, liquefaction necrosis or fibrosis. At the early and medium stage of granuloma with or without caseation or liquefaction necrosis, the CT images show homogeneous enhancement of lesions: at the caseation or liquefaction necrosis stage of gallbladder TB, the CT images usually show heterogeneous enhancement of lesions, as was seen in three cases respectively in our study. But at the fibrous stage associated with caseation or the liquefaction necrosis stage, the lesions also have heterogeneous enhancement, as was seen in our one case. The CT enhancement patterns of gallbladder TB are usually non-specific. For example, gallbladder TB with homogeneous uniform enhancement of the gallbladder wall mimics chronic cholecystitis and homogeneous irregular enhancement mimics carcinoma. But a large mass with multicentric necrosis (obvious heterogeneous enhancement with a mass replacing the gallbladder) may be the typical CT features of gallbladder TB.

Although the majority of the previously reported cases were isolated gallbladder TB, multiorgan involvement may be found in more cases when postmortem examination is carried

out (21). According to our report, most of the gallbladder TB was associated with intra-abdominal TB, i.e., tuberculous lymphadenopathy and hepatic TB. Only one of our cases did not have any evidence of extra-gallbladder TB. The typical CT findings of intra-abdominal TB, including enlarged lymph nodes with peripheral rim enhancement or a low-density mass with multiple flecked calcifications in the liver, may be helpful for making the diagnosis of gallbladder TB.

This study had some limits. First, only a small number of patients and lesions were included in this study. Second, direct comparison of CT with ultrasonography or MRI was not performed in our retrospective clinical study and this should be done in future clinical cases to confirm our results.

In conclusion, CT may be a good method for diagnosing gallbladder TB to identify the location and size of the lesion, and the enhanced CT findings of gallbladder TB are well correlated with the pathological features. Gallbladder TB is rare and making the preoperative diagnosis is difficult, and the definitive diagnosis relies on histological and bacteriological evidence of TB. Still, gallbladder TB should be considered in the differential diagnosis of diseases with an irregular, hypodense thickened gallbladder wall with pericholecystic edematous changes, a broad-based micronodular or polypoid lesion of the gallbladder wall or a gallbladder mass with multiple-focus necrosis or calcifications, and especially for those lesions associated with an infiltration of the liver parenchyma with multiple flecked calcifications, or abdominal enlarged lymph nodes with peripheral rim enhancement.

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