

Solitary schwannoma of the gallbladder: A case report and literature review

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Abstract

Schwannomas occurring in the gallbladder are extremely rare. Preoperative diagnosis of gallbladder schwannomas appears to be very difficult because they are normally asymptomatic and are often found incidentally. Until now, only five cases have been reported in the literature. To our knowledge, the contrast-enhanced ultrasound (CEUS) features of gallbladder schwannomas have not been reported before in other studies. We treated a 55-year-old male patient with gallbladder schwannoma in China. He had no symptoms, and the lesion was incidentally found by conventional ultrasound (US) when performing a health examination. The patient had normal liver function; moreover, serum carcinoembryonic antigen and alpha-fetoprotein were within the normal ranges. The lesion

showed no blood flow signals on color Doppler US, and the wall beneath the lesion was intact on CEUS. The lesion was believed to be a benign entity; in addition, gallbladder adenomyomatosis was suspected. A laparoscopic cholecystectomy was performed to remove the mass. Pathological examination revealed that the tumor was mainly composed of spindle-shaped cells; neither atypical cells nor signs of malignancy were found. Immunohistochemical staining showed a strong positive S-100 protein reaction. Vimentin and CD56 staining were also positive, whereas CD34 and CD117 were negative. Finally, the lesion was diagnosed as schwannoma. Herein, we report the case; the associated literature is also reviewed.

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Key words: Schwannoma; Gallbladder; Ultrasound; Contrast-enhanced ultrasound

Core tip: Gallbladder schwannoma, a benign tumor derived from the Schwann's cells in the gallbladder wall, is extremely rare. This paper describes the case of a 55-year-old man with a mass in the gallbladder but no other symptoms. The patient was treated by cholecystectomy. After 1 year of follow-up with clinical evaluation and ultrasound (US), it did not show any evidence of local recurrence. We learned through this rare case of gallbladder schwannoma that the imaging findings have not been reported in detail before. The US, especially contrast-enhanced ultrasound, features seemed to be helpful in excluding malignancy, and it was essential for treatment planning and the alleviation of patient anxiety in this case.

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INTRODUCTION

Schwannomas are benign neurogenic tumors that originate from the Schwann's cells of the peripheral nerves in young to middle-aged patients^[1]. Schwannoma can develop in any part of the body, but the most common sites include the head, neck, and flexor surfaces of the extremities^[2]. Schwannomas arising in the digestive tract are quite rare, and they occur most commonly in the stomach, followed by the colon and rectum^[3,4]. Primary benign schwannoma of the gallbladder is extremely rare. In this paper, we present a case of gallbladder schwannoma, with an emphasis on the imaging and pathological findings. Biliary system schwannomas in the literature are also reviewed.

CASE REPORT

A 55-year-old male patient was admitted to the hospital because a 2.1-cm mass was incidentally detected in his gallbladder by ultrasound (US) during a health examination. The patient had neither complaints nor symptoms. According to the physical examination, his abdomen was soft and flat; there was no evidence of jaundice or abdominal tenderness. He had no previous history of any other major illness, and his vital signs were stable. The blood laboratory study results were as follows: leukocyte count, $6.86 \times 10^9/L$; hemoglobin, 159 g/L; total protein, 80 g/L; total albumin, 50 g/L; total bilirubin, 13.4 $\mu\text{mol/L}$; direct bilirubin, 10.8 $\mu\text{mol/L}$; serum alanine aminotransferase 16.1 U/L; serum alkaline phosphatase, 53.4 U/L; and serum gamma-glutamyltranspeptidase, 31.4 U/L. The laboratory studies revealed almost normal liver function. Carcinoembryonic antigen and alpha-fetoprotein were within the normal ranges.

US was performed using a LogiQ E9 scanner (GE Healthcare, Milwaukee, WI, United States) with a convex transducer (frequency range, 2-6 MHz). Conventional US showed a 2.1-cm iso-echoic mural mass in the gallbladder. The mass was solid, homogeneously echogenic, and well defined with no infiltration into the liver (Figure 1A). Color Doppler US showed no flow signals within the mass (Figure 1B). Contrast-enhanced ultrasound (CEUS) was then performed using the low acoustic power contrast-specific imaging mode. The contrast agent used was SonoVue (BR1; Bracco SpA, Milan, Italy), a sulfur hexafluoride-filled microbubble contrast agent. The contrast agent was injected into the antecubital vein as a bolus (within 1-2 s) at a dose of 1.5 mL, followed by a flush of 5 mL of normal saline. The mass appeared slightly hyper-enhanced in the arterial phase and slightly hypo-enhanced in the venous phase. The gallbladder wall under the mass was intact (Figure 1C, 1D and 1E). A diagnosis of gallbladder adenomyomatosis was suspected before surgery.

Contrast-enhanced computed tomography (CECT) was subsequently performed to examine the gallbladder within 1 wk after the US examination, using a 64-slice computed tomography (CT) scanner. An un-enhanced CT scan of the gallbladder region showed a well-defined

round mass in the gallbladder. The mass showed homogeneous hypo-attenuation without internal calcification or liquefaction (Figure 2A). On CECT, the mass showed slight enhancement in the arterial phase (Figure 2B) and delayed enhancement until the late venous phase (Figure 2C). A CT diagnosis of a gallbladder polyp was suspected before surgery.

A laparoscopic cholecystectomy was performed to remove the mass. The gross specimen showed a 2.5-cm-sized, well-circumscribed, localized mass, which was surrounded by a fibrous capsule. Microscopic examination revealed that the tumor mainly consisted of spindle-shaped cells; neither atypical cells nor signs of malignancy were found (Figure 3A). Immunohistochemical staining showed a strong positive S-100 protein reaction (Figure 3B). Vimentin and CD56 staining were also positive (Figure 3C), whereas CD34 and CD117 were negative (Figure 3D). The final diagnosis of gallbladder schwannoma was made. Until now, twelve months after operation, the patient remained alive and in good status, without signs of recurrence of the lesion.

DISCUSSION

Schwannoma is a benign tumor derived from the Schwann's cells that encapsulates the nerve sheath, so it is known as a neurilemoma. Malignant schwannomas are extremely rare and are always associated with von Recklinghausen's disease^[5,6]. Schwannoma usually occurs in the extremities, but it can also be found in head, neck, trunk, retroperitoneum or mediastinum^[5]. It can also develop in the gallbladder due to the abundant anastomotic network of sympathetic and parasympathetic nerve fibers in the wall of the gallbladder and bile duct^[7]. However, schwannomas arising in gallbladder are extremely rare.

As a result of lacking of adequate knowledge of this tumor and low incidence in clinical practice, correct pre-operative diagnosis is hard to achieve. When tumor was small, patient normally appeared asymptomatic; on the contrary, jaundice and vague pain may happen when tumor was too large to compress surrounding organs. Until now, only five similar cases have been reported (Table 1). In the reported cases of gallbladder schwannomas, two cases revealed obstructive jaundice and vague pain; the other three cases were asymptomatic.

Imaging modalities, such as CT, magnetic resonance imaging (MRI), and US, are useful for detecting and locating tumors; however, definitive diagnosis is rarely achievable. Some cases might even be not visible on imaging examinations when the lesions coexist with cholecystolithiasis or are overly small^[5]. Generally speaking, an unenhanced CT scan depicts a schwannoma as a well-defined hypoattenuating area, and CECT shows peripheral enhancement with an irregular pattern. Delayed peripheral enhancement until the late venous phase on the CT scan reflects a fibrous capsule and an internal fibrillary element^[1,8]. In our case, however, no obvious enhancement during the arterial phase was observed on

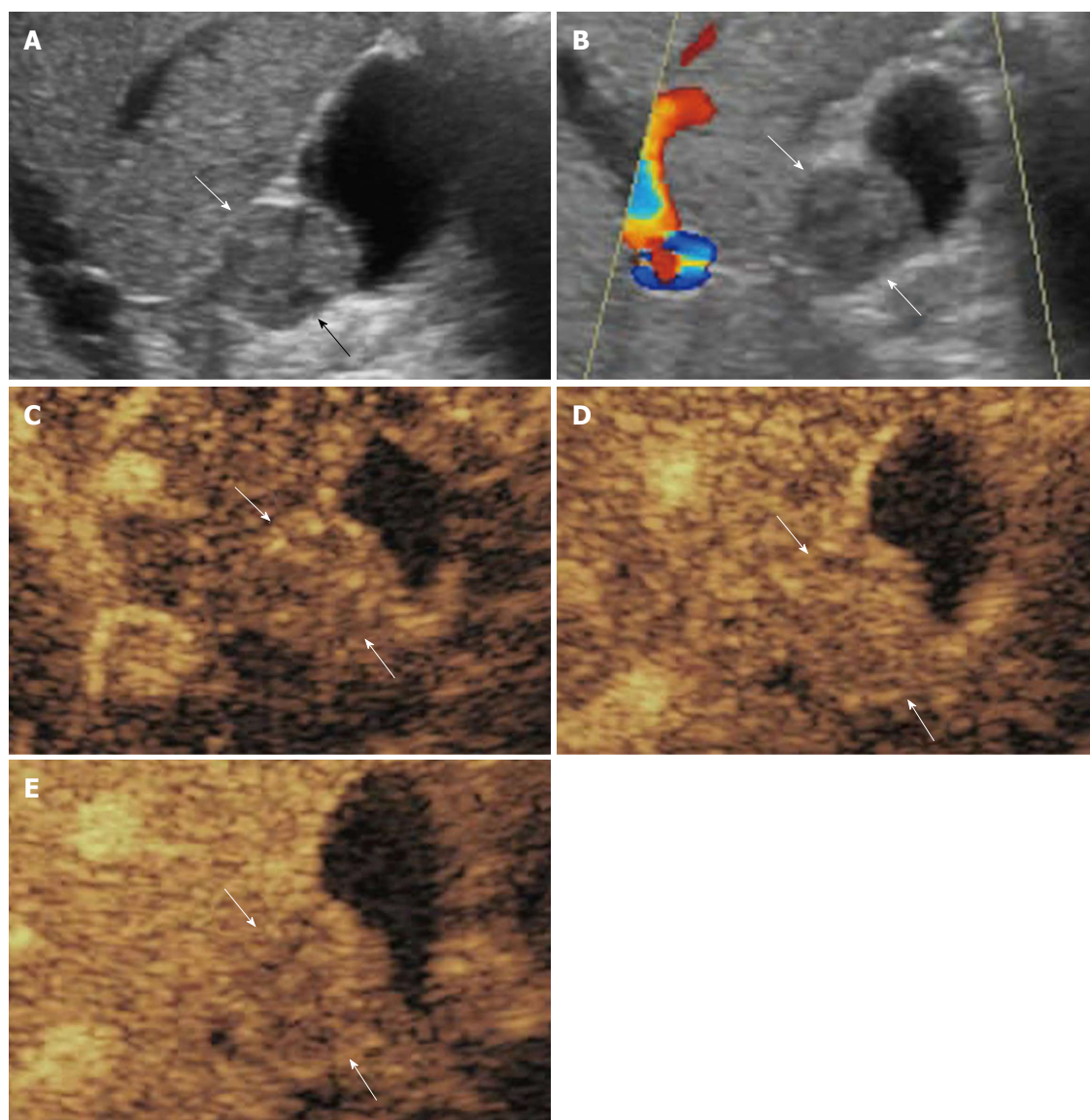


Figure 1 Ultrasound and contrast-enhanced ultrasound imaging. A: Conventional ultrasound shows a lesion (arrows) sized 2.1 cm in diameter in the gallbladder; B: Color Doppler ultrasound shows no blood supply in the mass (arrows); C: The lesion (arrows) shows hyper-enhancement 21 s after contrast agent injection; D: The lesion (arrows) shows iso-enhancement 34 s after contrast agent injection; E: The lesion (arrows) shows slight hypo-enhancement 54 s after contrast agent injection.

CECT. On MRI, schwannomas present as masses of low signal intensity on T1-weighted images and of high signal intensity on T2-weighted images^[2,9].

The US features of this lesion are unknown and non-specific. Ohta *et al*^[5] reported a lesion appearing on US as local gallbladder wall thickening at the fundus of the gallbladder with cholecystolithiasis. The lesion was diagnosed as chronic cholecystitis before surgery. In the present case, the lesion was visualized as a well-defined round isoechoic mass originating from the gallbladder wall on gray-scale US, and no intra-lesional blood flow signals were visible on color Doppler US. Although the lesion was larger than 2 cm in diameter, the wall beneath the mass was intact. No infiltration into the adjacent liver was present. CEUS with SonoVue was used for the preoperative diagnosis, which has not been reported before. The contrast arrival time to the lesion was 19 s after administration of the contrast agent. The lesion showed hyper-

enhancement in the arterial phase of CEUS and began to be hypo-enhanced 54 s after contrast administration. The gallbladder wall under the mass was intact in all of the phases. According to the previous literature regarding gallbladder CEUS^[10-12], malignant gallbladder lesions usually fade more quickly than benign gallbladder lesions, and most malignant gallbladder lesions begin to be hypo-enhanced 50 s before contrast administration. In addition, the gallbladder wall beneath the malignant lesion is usually destroyed, whereas it remains intact with benign gallbladder lesions.

Immunohistochemical analysis is necessary to distinguish schwannomas from neurofibromas, gastrointestinal stromal tumors and leiomyomas^[13]. Schwannomas are strongly positive for vimentin and S100 protein while negative for muscle cell markers; CD117 and CD34 are also useful clues for schwannoma, whereas positive staining has been helpful for the immunohistochemical diag-

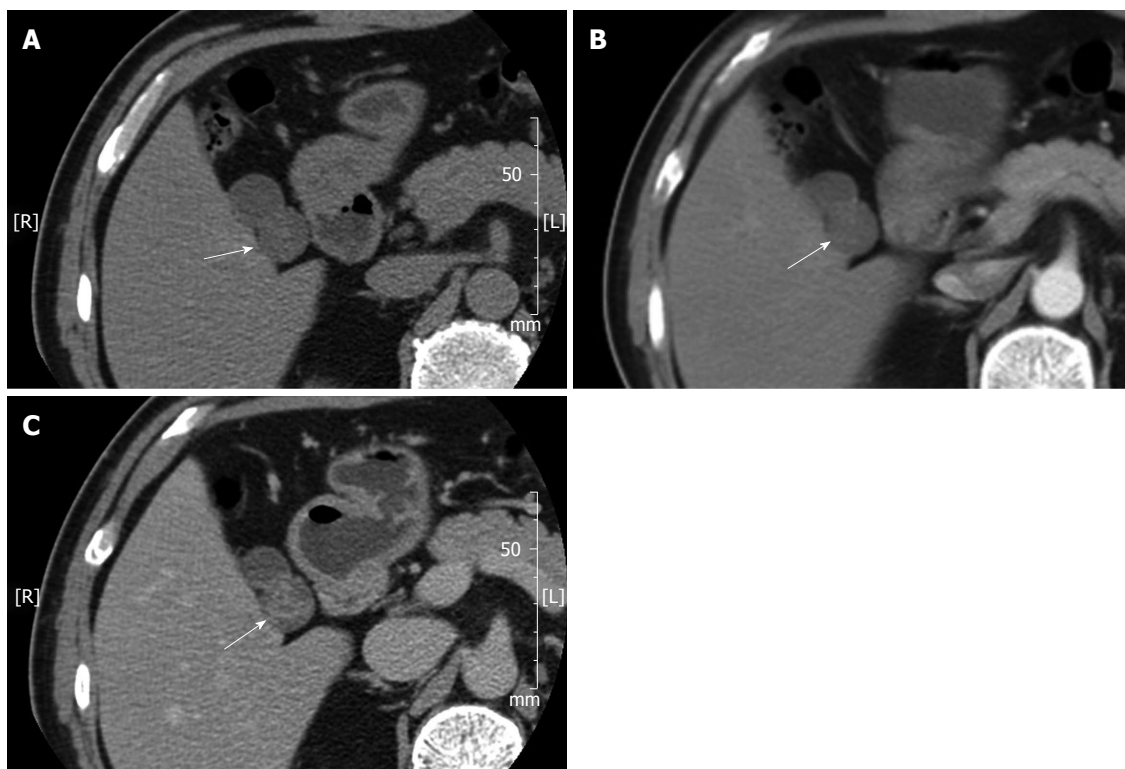


Figure 2 Gallbladder computed tomography imaging. A: Unenhanced computed tomography shows an iso-attenuating mass (arrow) in the gallbladder; B: No obvious enhancement (arrow) was found in the arterial dominant phase; C: The mass (arrow) shows slight hyper-attenuating in the late venous phase.

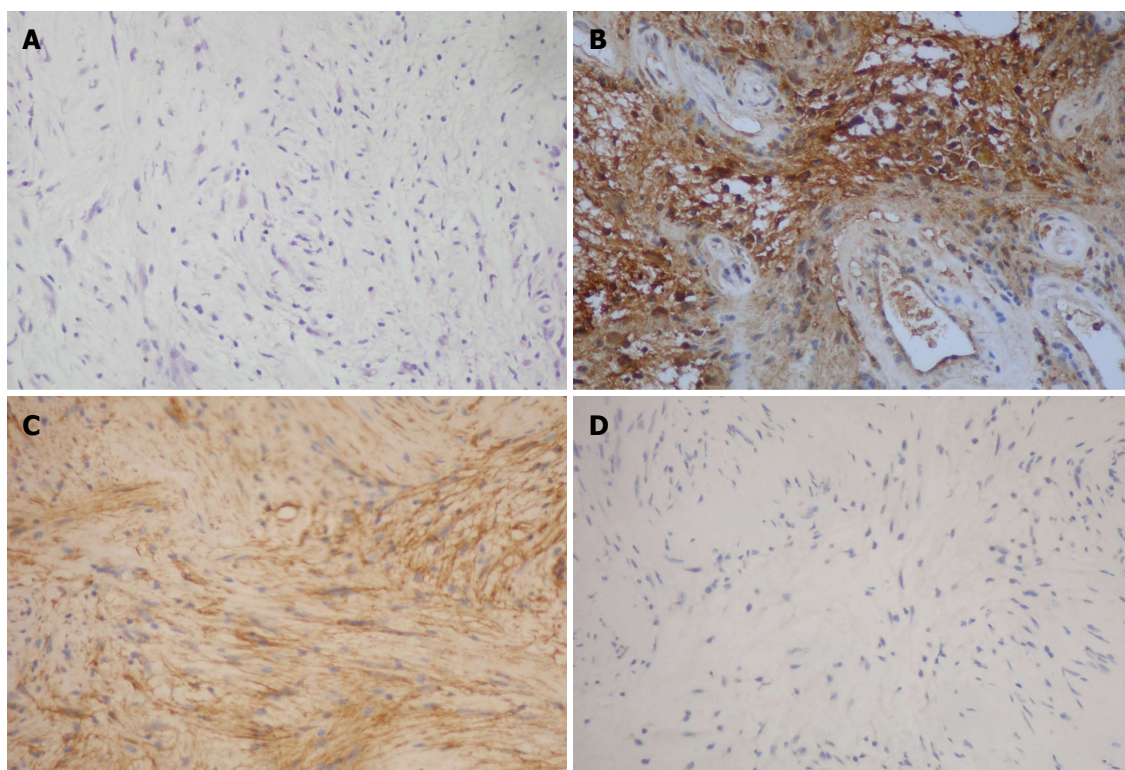


Figure 3 Pathological examinations. A: Microscopic examination shows that the tumor mainly composes of spindle-shaped cells and no atypical cells are found (HE staining; magnification: 10×30); B, C, D: Immunohistochemical staining shows the tumor is positive for S-100 protein (10×30) (B) and CD56(10×30) (C), whereas negative for CD117 (10×30) (D).

Table 1 Reported cases of schwannomas of the gallbladder

Ref.	Year	Sex	Age	Symptom	Imaging method	Location	Size (mm)	Preoperative diagnosis	With GB stones	Treatment	Follow-up	Status
Yamagiwa <i>et al</i> ^[18]	1991	M	58	Jaundice	NA	Neck	4	Bile duct cancer	NA	Cholecystectomy	NA	NA
Matsuoka <i>et al</i> ^[19]	1996	M	74	Asymptomatic	US MRI CT and endoscopy	Fundus	10	Adenomyomatosis	N	Cholecystectomy + hepatectomy	NA	NA
Ren <i>et al</i> ^[20]	2001	F	26	Vague pain	US and CECT	Neck	110	Tumor of GB	N	Cholecystectomy	NA	NA
Colović <i>et al</i> ^[21]	2003	F	61	NA	NA	Whole	90	Tumor of GB	N	Cholecystectomy	10 Y	Survived
Ohta <i>et al</i> ^[5]	2008	M	58	Asymptomatic	CT and US	Fundus	3	Cholecystolithiasis	Y	Cholecystectomy	16 M	Survived
Current case	2012	M	55	Asymptomatic	CEUS and CECT	Neck	22	Adenomyomatosis	N	Cholecystectomy	12 M	Survived

NA: Not available; CEUS: Contrast-enhanced ultrasound; CECT: Contrast-enhanced computed tomography; US: Ultrasound; CT: Computed tomography; MRI: Magnetic resonance imaging.

nosis of gastrointestinal stromal tumors^[5,14].

Histologically, schwannomas originating in the digestive tract are S-100 protein-positive spindle cell tumors that consist mainly of cellular (Antoni A) areas, and they generally do not show a nuclear palisading pattern, which is usually found in conventional schwannomas of the soft tissue and central nervous system^[2,15,16]. Whether lack neurofibromatosis-2 genetic alterations might be the key point to distinct schwannomas of the digestive tract from conventional schwannomas^[2,17].

Schwannomas of the gallbladder can be successfully treated surgically, like schwannomas in other locations^[1]. The treatment of choice is cholecystectomy due to the diagnostic uncertainty before surgery, even with extensive application of various imaging modalities. To our knowledge, this was the first time to evaluate the features and usefulness of CEUS in diagnosing solitary schwannoma of the gallbladder. CEUS can easily excluding the possibility of malignant GB disease.

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COMMENTS

Case characteristics

A rare case of gallbladder schwannoma was incidentally detected in a 55-year-old man by ultrasound (US) during a health examination.

Clinical diagnosis

The patient had no symptoms, such as obstructive jaundice or pain.

Differential diagnosis

Gallbladder polyp; gallbladder adenomyomatosis; gallbladder cancer.

Laboratory diagnosis

Leukocyte count, $6.86 \times 10^9/L$; hemoglobin, 159 g/L; total protein, 80 g/L; total albumin, 50 g/L; total bilirubin, 13.4 $\mu\text{mol/L}$; direct bilirubin, 10.8 $\mu\text{mol/L}$; serum alanine aminotransferase 16.1 U/L; serum alkaline phosphatase, 53.4 U/L; serum gamma-glutamyltranspeptidase, 31.4 U/L; carcinoembryonic antigen, alpha-fetoprotein and liver function tests were within the normal limits.

Imaging diagnosis

US showed a 2.1-cm, iso-echoic, well-defined, mural mass in the gallbladder;

contrast-enhanced ultrasound (CEUS) showed the mass slightly was hyper-enhanced in the arterial phase and slightly hypo-enhanced in the venous phase; moreover, the gallbladder wall under the mass was intact.

Pathological diagnosis

Microscopic examination revealed that the tumor mainly consisted of spindle-shaped cells; it was S-100/Vimentin/CD56-positive and CD34/CD117-negative.

Treatment

The patient was treated with cholecystectomy.

Related reports

Schwannomas arising in the gallbladder are extremely rare, and preoperative diagnosis appears to be very difficult because these tumors are commonly asymptomatic and are often discovered incidentally.

Term explanation

To our knowledge, the CEUS features of gallbladder schwannomas have not been reported before in the other literature.

Experiences and lessons

This report not only presents the details of the US and CEUS features in this case, but it also indicates the usefulness of CEUS in excluding malignancy before surgery.

Peer review

This article presents a case of gallbladder schwannoma with an emphasis on the imaging and pathological findings; also, biliary system schwannomas in the literature are reviewed.

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