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Single Case

Laparoscopic Excisional Cholecystectomy with Full-Thickness Frozen Biopsy in Suspected Gallbladder Carcinoma

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Keywords

Gallbladder carcinoma · Cholecystectomy · Intraoperative histological examination

Abstract

Owing to the advantages of a laparoscopic approach, laparoscopic cholecystectomy (LC) is thought to be the treatment of choice in gallbladder disease, even in cases of suspected malignancy. However, it is difficult to differentiate between cholecystitis and gallbladder carcinoma (GBC). We performed radical hepatectomy in patients with pT2 GBC diagnosed by full-thickness frozen biopsy. A 75-year-old Japanese man presented to our hospital with discomfort in the right upper quadrant of the abdomen. This patient was diagnosed with suspected GBC and was scheduled to undergo LC and intraoperative histological examination. Following the procedure, we made a diagnosis of GBC with negative invasion of the cystic duct stump. We converted the laparoscopic procedure to an open surgery involving wedge liver resection with lymphadenectomy. The patient was discharged from our hospital in remission 14 days

following the radical hepatectomy. Histological examination showed that the GBC had invaded the liver (T3a), but there was no lymph node metastasis (N0): stage IIIA. Between April 2009 and September 2018, 580 patients underwent cholecystectomy for gallbladder disease at our hospital. Among these, 8 (1.4%) were suspected to have GBC preoperatively and underwent laparoscopic excisional cholecystectomy. We performed elective surgery in the early stage in two patients and second-look surgery in two patients recently. We were able to perform what we termed a laparoscopic excisional cholecystectomy, involving LC with a full-thickness frozen biopsy, even in situations where intraoperative histological examination was not available. Altogether, laparoscopic excisional cholecystectomy is an effective surgical treatment for suspected early GBC.

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Introduction

Laparoscopic cholecystectomy (LC) has become the gold standard approach for managing benign biliary diseases such as stones, polyps, and cholecystitis. In contrast, LC is not recommended for suspected gallbladder carcinoma (GBC). However, the question of how to treat suspected early GBC remains. There are many advantages to the laparoscopic approach, and LC can play a significant role in the treatment of gallbladder disease, including suspected malignancy. However, it is difficult to differentiate between cholecystitis and GBC. The treatment strategy for cases of gallbladder polyps over 10 mm in size or where there is suspicion of liver invasion of GBC is controversial. We performed radical hepatectomy in patients with pT2 GBC diagnosed by full-thickness frozen biopsy intraoperatively, and in this report, we describe the treatment strategy followed at our hospital.

Case Presentation

A 75-year-old Japanese man presented to our hospital with discomfort in the right upper quadrant of the abdomen. The patient was admitted to the Gastroenterological Center of our hospital for surgery. The laboratory findings on admission were as follows (Table 1): white blood cells, 3,300/mm³; C-reactive protein, 0.53 mg/dL; and tumor marker (CEA and CA19-9), negative. Abdominal enhanced computed tomography showed a tumor in the gallbladder. The tumor in the gallbladder did not extend beyond the liver and serosa, indicating Hinf0 and S0 if the tumor is GBC (Fig. 1). MRI showed slight thickening of the wall and a localized protruding lesion on the hepatic side wall of the gallbladder.

Based on these findings, this patient was diagnosed to have a malignancy of the gallbladder and was scheduled to undergo laparoscopic treatment. Initially, intracorporeal procedures were performed laparoscopically through four trocars, and the gallbladder was found to be swollen. An intraoperative view showed a gallbladder remnant, along with no inflammation at the Calot's triangle. The patient then underwent an LC for suspected GBC (Fig. 2).

First, we performed the LC and an intraoperative histological examination followed by skeletonization of the cystic artery and the cystic duct with blunt dissection. The cystic duct was identified and resected with the harmonic scalpel to prevent tumor dissemination (Fig.

3). Based on the frozen section biopsy, we made a diagnosis of GBC stage T2 with negative invasion of the cystic duct stump. The procedure was converted to open surgery and we performed wedge liver resection with lymphadenectomy.

The patient had an uneventful postoperative period with good recovery and was discharged from our hospital in remission 14 days after the radical hepatectomy. Histological examination showed GBC stage IIIA with invasion of the liver (T3a) and no lymph node metastasis (N0) (Fig. 4).

Discussion

GBC is generally associated with a poor prognosis with a reported 5-year survival rate of 5% [1, 2]. The overall 5-year survival rate is currently reported to be 5–13% [1–3], with a mean overall survival of 3–11 months [4]. Biliary tract carcinoma, including GBC, is the eighth most common malignancy in Japanese men and the seventh in Japanese women according to the National Cancer Center 2016 [5]. GBC is, therefore, not very rare. However, only 30% of GBC patients were suspected of having the condition preoperatively, whereas the remaining 70% were diagnosed incidentally following a pathological examination either during or after surgery [6]. This could be the reason why GBC is mistakenly assumed to be a rare, highly malignant tumor. It is extremely rare to find a diagnosis of GBC preoperatively in the early stages of the malignancy. Unfortunately, over 75% of GBC is not resectable due to its aggressive pathophysiology [1, 6].

The prognosis for GBC is poor due to the significant difficulties associated with its diagnosis. Surgical resection is the only potentially curative therapy for GBC [7], although obviously, it is difficult to differentiate between GBC and cholecystitis as many authors report [8, 9] because both present with thickening of the gallbladder wall.

It is also difficult to select the proper radical surgery for GBC resection. However, when the GBC is discovered in its early stages, the 5-year survival rate can approach 75%, which is a high rate [10]. The surgical management of GBC varies depending on the stage of the malignancy, especially T staging to assess the depth of tumor invasion, and this contributes to the high survival rates [11].

We advocate additional radical surgery depending on the T staging because preoperative diagnosis of GBC is rare with a variable prognosis based on the extent of tumor invasion [11]. The importance of T staging in the diagnosis of GBC has been stated above. When the diagnosis of GBC is made accurately, curative resection should consist of cholecystectomy with resection of the adjacent liver segments, such as wedge resection of the gallbladder bed and 4b+5 liver segmentectomy, right or left lobectomy of the liver to obtain an R0 resection, and lymphadenectomy including prophylactic common bile duct excision.

As discussed in our previous paper [12], the rationale for our treatment strategy was that as there is no defined surgical approach for suspected GBC, an intraoperative histological examination would be useful before proceeding to open surgery. Intraoperative diagnosis by histological examination facilitates proper management in case of doubt and allows for the opportunity to perform radical surgery [12, 13]. Actually, we were able to obtain an intraoperative diagnosis and convert from cholecystectomy to radical surgery in the present case according to our surgical strategy (Fig. 5). The ability to obtain full-thickness frozen biopsies

through LC allows for the diagnosis of GBC intraoperatively and also provides information on tumor depth. Therefore, surgeons have the ability to convert the procedure to an open radical surgery for GBC [12] (except for pTis and pT1a cases). We therefore have emphasized the effectiveness of intraoperative histological examination in our treatment strategy.

However, according to an article in *JAMA Surgery* in 2017 [14], the optimal time interval for re-resection for incidentally discovered GBC appears to be between 4 and 8 weeks following the initial cholecystectomy. There was no significant difference in the point of overall survival. Finding this to be a suitable interval (between 4 and 8 weeks after the initial cholecystectomy), we changed our strategy (Fig. 6). A laparoscopic approach, especially cholecystectomy, for suspected GBC is not recommended (CQ21) according to the guidelines for the management of biliary tract cancers [15]. The laparoscopic approach for suspected GBC is controversial indeed. We were able to diagnose the GBC as well as get accurate information about the depth of the tumor through a procedure we termed laparoscopic excisional cholecystectomy involving LC followed by a full-thickness frozen biopsy. LC with a full-thickness frozen biopsy occasionally can involve LC combined with partial resection of the liver.

Between April 2009 and September 2018, 580 patients underwent cholecystectomy for gallbladder disease at our hospital. Among these, 8 (1.4%) (Table 2) were diagnosed with suspected GBC preoperatively. We performed laparoscopic excisional cholecystectomy for suspected GBC because we thought that the open surgical approach would be an overtreatment in case of benign biliary diseases. Of the 8 patients, 5 were confirmed to have GBC. Overtreatment (open approach) was avoided in 3 cases who were diagnosed to have a benign biliary disease (37.5%). We performed elective surgery in the early stage (case 2, case 4) and second-look surgery recently (case 6, case 7). There were no differences in the findings between intraoperative histological diagnosis and final (postoperative) diagnosis in our cases, although the diagnostic accuracy was not 100%. Intraoperative histological examination has certain limitations in spite of the high sensitivity and specificity. It is important to make an accurate diagnosis of GBC for selecting the appropriate radical surgery. Our treatment strategy can be performed everywhere, even when intraoperative histological examination was not available. Therefore, we state that laparoscopic excisional cholecystectomy is an effective surgical method for managing suspected early GBC.

Statement of Ethics

The authors and co-authors have no ethical conflicts to disclose.

Disclosure Statement

The authors declare that there are no conflicts of interest.

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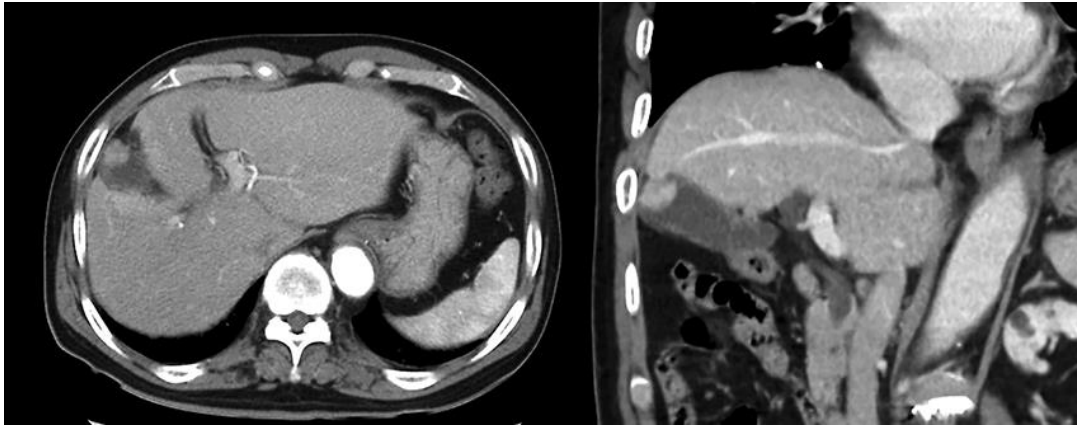


Fig. 1. Preoperative abdominal CT findings. Abdominal enhanced computed tomography showed the tumor in the gallbladder. The tumor in the gallbladder did not extend beyond the liver and serosa, indicating Hinf0 and S0 if the tumor is gallbladder carcinoma.

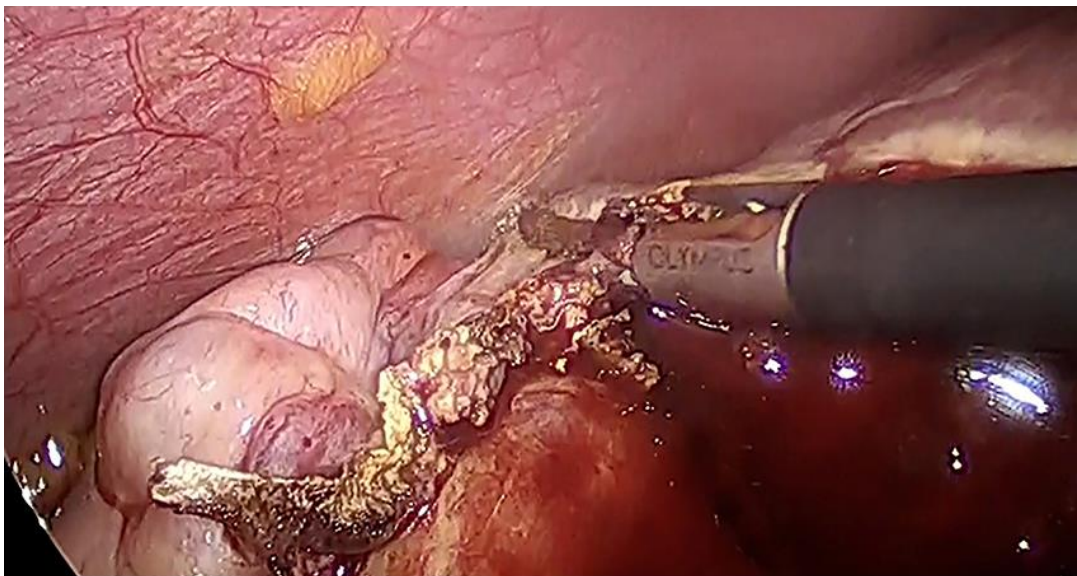


Fig. 2. Operative findings under laparoscopic view. We performed laparoscopic cholecystectomy combined with resection of partial liver. We could diagnose the gallbladder carcinoma due to this full-thickness frozen biopsy.

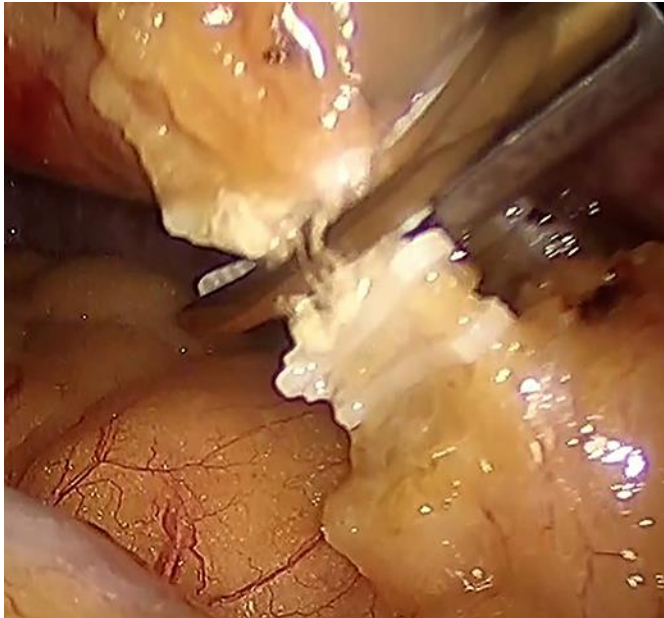


Fig. 3. Operative findings under laparoscopic view. The cystic duct was identified and resected with the harmonic scalpel (SONOSURGE) to prevent tumor dissemination.

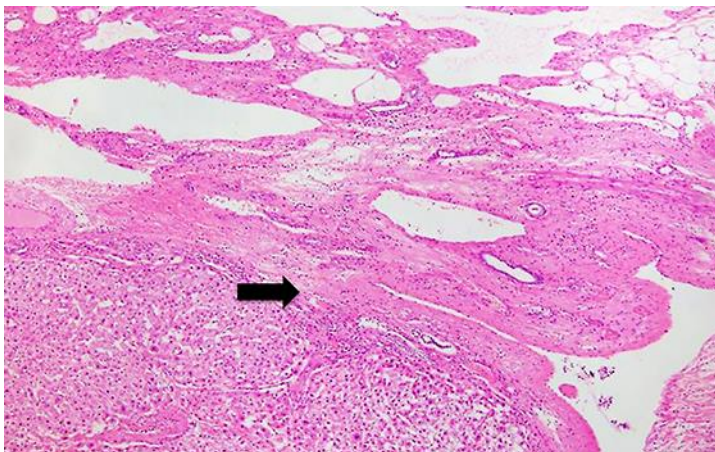


Fig. 4. Histological appearance (hematoxylin-eosin staining, $\times 40$). Histological findings of the tumor showed gallbladder carcinoma stage IIIA with invasion of the liver (T3a) (black arrow) and no lymph node metastasis (N0).

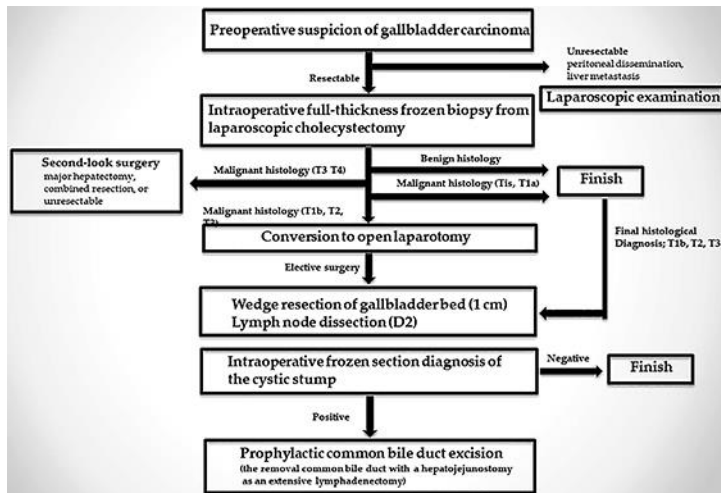


Fig. 5. Former surgical strategy for suspected gallbladder carcinoma in our hospital.

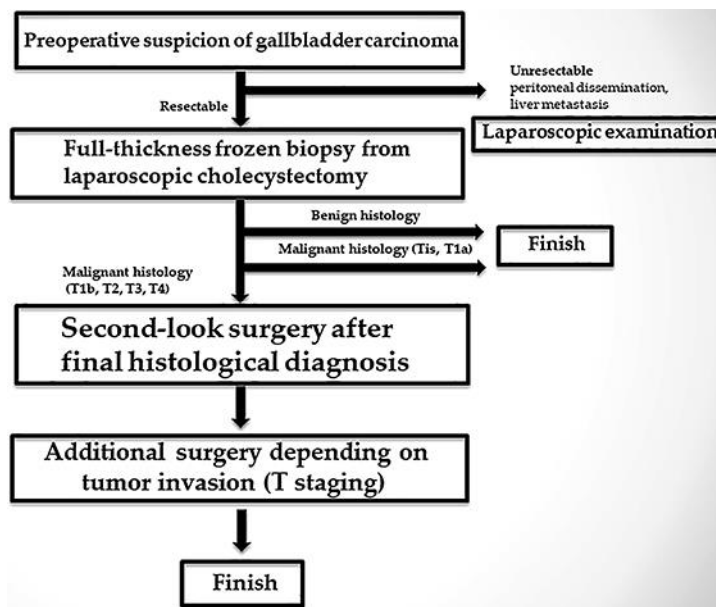


Fig. 6. New surgical strategy for suspected gallbladder carcinoma in our hospital.

Table 1. Laboratory findings

Variable	Range	On admission	Variable	Range	On admission	Variable	Range	On admission
Peripheral blood			Blood chemistry			Serological tests		
WBC, <i>n</i> /μL	3,900–9,800	3,000	TP, g/dL	6.5–8.3	6.1	CRP, mg/dL	0–0.30	0.53
RBC, <i>n</i> /μL	430–570	344×10 ⁴	ALB, g/dL	3.8–5.2	3.5	HBsAg		(–)
Hb, g/dL	13.5–17.6	11.5	T.Bil, mg/dL	0.2–1.2	0.3	HBsAb		(–)
Hct, %	40.0–52.0	34.7	AST, IU/L	10–40	19	HCVAb		(–)
Plt, <i>n</i> /μL	12.0–34.0	9.6×10 ⁴	ALT, IU/L	5–45	16			
Tumor markers			ALP, IU/L	110–340	288	Coagulation		
CEA	0–5	0.7 ng/mL	γ-GTP, U/L	12–87	34	PT, s	10.5–13.5	13.0
CA19-9	0–37	3 U/mL	LDH, IU/L	107–230	192	PT, %	70–130	80.4
			BUN, mg/dL	8.0–20.0	18.0	aPTT, s	25–40	42.3
			Cr, mg/dL	0.61–1.04	1.30			
			Na, mEq/L	135–147	139			
			K, mEq/L	3.3–5.0	3.8			
			Cl, mEq/L	98–108	107			
			CPK, IU/L	45–190	61			

Table 2. Laparoscopic cholecystectomy for gallbladder tumor in our hospital

Case	Age, years	Sex	Preoperative diagnosis	Intraoperative diagnosis	Intra-histological examination	Postoperative diagnosis	TNM stage	Operation	Time, min	Bleeding, mL	Complication	Hospital stay, days	Outcome (recurrence)
1	72	male	Acute cholecystitis, cholecystolithiasis, xanthogranulomatous cholecystitis	Acute cholecystitis, cholecystolithiasis, xanthogranulomatous cholecystitis	yes	Acute cholecystitis, cholecystolithiasis, xanthogranulomatous cholecystitis	++	Laparoscopic cholecystectomy	225	A little	none	8	1 year 9 months (benign)
2	67	female	Suspected gallbladder carcinoma	Gallbladder carcinoma	yes	Gallbladder carcinoma Cy (-)	T2N1M0 stage IIIB	Laparoscopic cholecystectomy → Wedge resection of the gallbladder bed (1 cm)	305	460	none	14	2 years 1 month, alive
3	59	female	Gallbladder polyp	Gallbladder adenoma	no	Gallbladder adenoma	++	Laparoscopic cholecystectomy	50	A little	none	7	5 years 5 months (benign)
4	75	male	Suspected gallbladder carcinoma	Gallbladder carcinoma	yes	Gallbladder carcinoma Cy (+)	T3a (liver) N0M0 stage IIIA	Laparoscopic cholecystectomy → Wedge resection of the gallbladder bed (1 cm)	295	300	none	16	6 months (brain hemorrhage), dead
5	77	female	Suspected gallbladder carcinoma	Acute cholecystitis, cholecystolithiasis	yes	Acute cholecystitis, cholecystolithiasis, inflammatory change of the RAS	++	Laparoscopic cholecystectomy	115	A little	none	5	2 months (benign)
6	81	male	Suspected gallbladder carcinoma	Gallbladder carcinoma	yes	Gallbladder carcinoma Cy (+/-)	T2N0M0 stage II	(1) Laparoscopic cholecystectomy (2) Segmental resection of IVb + V	(1) 150 (2) 350	(1) 5 (2) 520	(1) none (2) none	(1) 5 (2) 15	3 months, alive
7	75	male	Suspected gallbladder carcinoma	Gallbladder carcinoma	yes	Gallbladder carcinoma Cy (+)	T2N0M0 stage II	(1) Laparoscopic cholecystectomy (2) Segmental resection of IVb + V	(1) 105 (2) 321	(1) A little (2) 360	(1) none (2) none	(1) 5 (2) 10	3 months, alive
8	59	male	Gallbladder polyp	Gallbladder carcinoma	no	Gallbladder carcinoma Cy (-)	TisN0M0 stage 0	Laparoscopic cholecystectomy	75	A little	none	5	1 year 1 month, alive