

Anticipatory extended cholecystectomy: the ‘Lucknow’ approach for thick walled gall bladder with low suspicion of cancer

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Background: Gall stones (GS) cause inflammation of the gall bladder (GB) i.e., chronic cholecystitis (CC) and xantho-granulomatous cholecystitis (XGC) which can result in a thick walled GB (TWGB). Gall bladder cancer (GBC) may also present as TWGB. While CC and XGC can be treated with simple cholecystectomy (SC), GBC merits extended cholecystectomy (EC). We propose a new surgical approach, anticipatory extended cholecystectomy (AEC), for doubtful TWGB in the belief that AEC would not violate the sacrosanct cholecysto-hepatic plane in doubtful cases and thereby not ruin the chances of cure for a patient whose GB demonstrates malignancy on frozen section histopathology. The addition of lymphadenectomy in cases which turn out to be malignant completes the procedure for GB cancer, but spares all problems related to lymphadenectomy in an undeserving patient.

Methods: AEC involves removal of GB with a 2-cm wedge of liver, which is then subjected to frozen section histological examination. Lymphadenectomy is performed if GBC is confirmed. AEC was performed in 13 patients between January 2011 and June 2014. During the same period, 1,673 SC for CC/XGC and 116 EC for GBC were performed.

Results: All patients were symptomatic for GS (3 with acute cholecystitis). Ultrasonography (US) raised suspicion of GBC in 11 patients. CT raised suspicion of GBC in 9 patients. Preoperative FNAC was done in 2 patients; in 1 it was negative and in 1 it was suspicious for malignancy. Preoperative diagnosis was GBC in 8, TWGB in 2, XGC, porcelain GB and GB perforation in 1 each. AEC and frozen section was done in all 13 patients. It was reported as GBC in 2 patients and as suspicious of GBC in 1 patient; lymphadenectomy was performed in these 3 patients. Final histopathology revealed XGC in 9, CC in 2 and GBC in 2 patients.

Conclusions: In patients with TWGB on US/ CT with low suspicion of cancer, AEC serves as a triage—if frozen section biopsy turns out to be positive for GBC, AEC can be completed to EC by performing lymphadenectomy. We wish to name this approach as the ‘Lucknow’ approach for TWGB.

Keywords: Chronic cholecystitis (CC); extended cholecystectomy (EC); gall bladder cancer (GBC); thick walled gall bladder (TWGB); xantho-granulomatous cholecystitis (XGC)

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Introduction

Gall stone disease (GSD) causes inflammation of the gall bladder (GB) in the form of acute cholecystitis (AC) and chronic cholecystitis (CC), both causing thickening (>3 mm) of the GB wall. The GB wall thickening in AC is transient and reversible but that in CC persists. Xantho-granulomatous cholecystitis (XGC), a variant of CC, also causes GB wall thickening. GB wall thickening in AC, CC and XGC is usually diffuse, uniform and regular.

Gall bladder cancer (GBC) also results in GB wall thickening but it is usually focal, non uniform and irregular but may sometimes be diffuse, uniform and regular as in AC, CC and XGC. A diffuse, uniform and regular thick walled GB (TWGB), thus, may be AC, CC, XGC or GBC and it may be difficult to differentiate between these on ultrasonography (US) or even computed tomography (CT) (1). As a matter of fact, it may be difficult or even impossible to differentiate between these even at surgery and, at times, XGC and GBC may even coexist (2). In some patients, an episode of AC may get complicated by intrahepatic GB perforation leading on to an abscess which may look like a mass lesion on US/CT.

While simple cholecystectomy (SC) is the treatment for AC, CC and XGC, GBC should be treated by extended cholecystectomy (EC) (cholecystectomy with liver wedge and lymphadenectomy). In presence of a TWGB, if SC is performed and it turns out to be GBC, it will be inadequate treatment; although completion extended cholecystectomy (CEC) including liver wedge and lymphadenectomy can still be performed at reoperation but tumor planes would have already been breached and outcome compromised. This is more likely to happen if GB perforation and bile spill occurs during cholecystectomy. On the other hand, if EC is performed for a TWGB on suspicion of GBC and it turns out to be AC, CC or XGC it will be an over kill. EC is a safe procedure but operation time is longer than SC and lymphadenectomy can add to post-operative complications e.g., ascitic fluid/chylous leak.

Patients with high suspicion of GBC on US/CT should be taken up directly for EC (3). We propose a new surgical approach, anticipatory extended cholecystectomy (AEC), for TWGB where differentiation between benign (complicated AC, CC or XGC) and malignant (GBC) is not possible on imaging (US or CT) or at operation but there is low suspicion of GBC. This new approach, while being complete treatment for benign disease (AC, CC and XGC), does not violate oncological planes in case the disease is malignant (GBC).

Patients and methods

A retrospective analysis of patients with TWGB (>3 mm) which was suspicious for malignancy on US and CT who were treated with AEC as a prospective protocol from January 2011 to June 2014 at a tertiary-level referral hospital in northern India. Patients with obvious findings suggestive of GBC such as GB mass, GB polyp, significant lymphadenopathy, presence of liver metastasis or ascites on US or CT were excluded from the analysis.

Patients with TWGB (GB wall >3 mm) on US were further evaluated by triple phase (arterial phase, portal phase and hepatic venous phase) CT abdomen. FNAC was not performed as a protocol because a negative FNAC does not rule out GBC and a resectable GBC does not need preoperative histological confirmation.

Details of clinical presentation, findings on imaging (US and CT), results of fine-needle aspiration cytology (FNAC), operation details (findings and procedure), frozen section biopsy and histopathology reports were reviewed.

AEC was performed in the form of removal of the GB with a non-anatomical 2 cm wedge of liver in segments IVB and V (in relation to the fundus and body of GB) and frozen section histopathological examination; lymphadenectomy was not done (cf. EC which includes lymphadenectomy also).

Results

A total of 13 AECs were performed over a period of 3 years; during the same period, 1,673 simple and 116 extended cholecystectomies were performed. The mean age of these 13 patients was 45 (range, 22–67) years; there were 7 men and 6 women. All 13 patients were symptomatic; median duration of symptoms was 3 (range, 2–58) months. All 13 patients had pain abdomen, of which 12 had biliary colic and 1 had continuous dull ache—2 patients reported a recent change in the character of pain (the final histopathology in these 2 patients was XGC). Three patients had history of AC. Two patients also had fever, 2 had weakness and 1 had anorexia; none had jaundice. GB was palpable in five patients.

US was done in all 13 patients. GB calculi were detected in all 13 patients. GB wall was thickened (irregular in 10 and diffuse in 2 patients) in 12 patients and was normal in 1 patient. GB wall thickness was mentioned in US reports in four patients and ranged from 5–10 mm; in other patients it was mentioned that GB wall is thick but the exact thickness was not mentioned. GB mass was seen in seven patients. US raised the suspicion of GBC in 11 patients and CC in



Figure 1 Computed tomography showing thick-walled gall bladder.

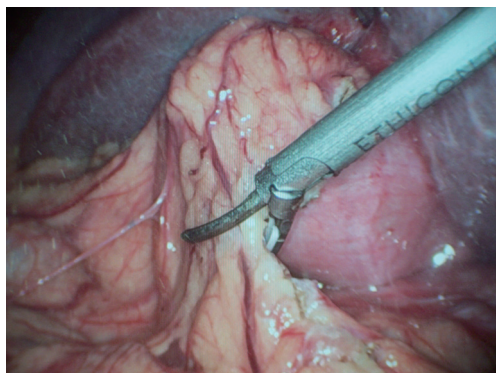


Figure 2 Omentum adherent to gall bladder.

2 patients.

All patients were evaluated with CT because of suspicion of GBC. CT report was available in 12 patients. GB wall was thickened in all 12 patients (irregular in 8 and diffuse in 4 patients) (*Figure 1*). GB mass was seen in 3 patients; in 2 of these patients, interface between GB mass and liver was lost. Liver infiltration was seen in three other patients. In three patients, pericholecystic stranding was present. CT raised the suspicion of GBC in nine patients; CT diagnosis was XGC, porcelain GB, GB perforation and TWGB in one patient each.

Based on clinical presentation and US/ CT findings, it was not possible to differentiate between CC/XGC and GBC but the suspicion of GBC was low in all the 13 cases.

FNAC had been done in 2 of 13 patients before they were referred to us. In one patient, laparoscopic cholecystectomy was attempted when a GB fundus mass with pericholecystic omental and colonic adhesions was found. Because of

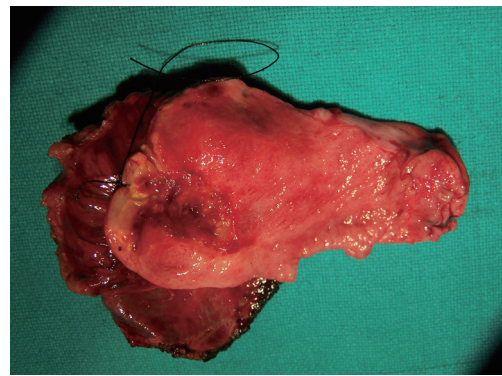


Figure 3 Specimen of gall bladder with wedge of liver.

suspicion of GBC, intraoperative FNAC was done which was inconclusive. The final histological diagnosis in this patient was XGC. In another patient, FNAC was done because of suspicion of GBC on CT; it was negative for malignancy. The final histological diagnosis in this patient was also XGC.

Preoperatively, there was suspicion of GBC in eight patients, TWGB in two patients, XGC, GB perforation and porcelain GB in one patient each. Because of suspicion of GBC, staging laparoscopy (*Figure 2*) was done to rule out peritoneal dissemination in all 13 patients. After staging laparoscopy, all patients were converted to open procedure for further surgery. GB was removed with 2 cm liver wedge (*Figure 3*) and the specimen was subjected to frozen section histological examination in all patients. In one patient (in whom frozen section turned out to be positive for malignancy), the GB was adherent to the common hepatic duct which was excised and Roux-en-Y hepaticojejunostomy was done.

Frozen section histological examination reported malignancy in two patients and suspicious of malignancy in one patient; in ten patients, frozen section was reported as negative for malignancy. Standard lymphadenectomy was done in three patients in whom frozen section report was malignancy or suspicious of malignancy to complete the EC. Two of these were finally confirmed as GBC while one in whom frozen section report was suspicious of malignancy was finally found to have XGC (*Table 1*).

One patient developed fever after discharge from the hospital and was found to have an intra-abdominal collection; percutaneous catheter drain (PCD) was placed after readmission which drained bile. Hepato-biliary isotope scan revealed bile leak from the cut liver surface and bilioenteric ductal continuity was present; endoscopic stenting

Table 1 Details of patients

Patient No.	Age	Sex	US diagnosis	CT diagnosis	Frozen report	Final diagnosis
1	50	F	GBC	GBC	XGC	XGC
2	35	F	GBC	GBC	XGC	XGC
3	46	F	GBC	XGC	No e/o malignancy	XGC
4	22	F	GBC	GBC	XGC	XGC
5	45	M	GBC	GBC	XGC	XGC
6	60	M	GBC	GBC	Suspicion for malignancy	XGC
7	34	M	GBC	Porcelain GB	No e/o malignancy	CC
8	48	F	GBC	GB perforation	Malignancy	GBC
9	35	F	GBC	GBC	No e/o malignancy	XGC
10	33	M	CC	GBC	No e/o malignancy	XGC
11	40	M	GBC	TWGB	No e/o malignancy	XGC
12	64	M	Cholelithiasis	GBC	No e/o malignancy	CC
13	67	F	GBC	GBC	Malignancy	GBC

GBC, gall bladder cancer; XGC, xantho-granulomatous cholecystitis; GB, gall bladder; CC, chronic cholecystitis.

controlled the bile leak and PCD was removed. One patient had high drain output but it was serous; one patient had a minor wound seroma. Median postoperative hospital stay was 4 (range, 3–14) days. There was no mortality.

Final histopathology was XGC in eight patients, CC in three patients and GBC in two patients. Frozen section histological diagnosis in both patients with GBC was positive and both had T2 N0 disease.

Discussion

We have proposed a new surgical approach, AEC, for TWGB with low suspicion of GBC on imaging (US and/ or CT). AEC involves removal of the GB with wedge of liver (but without lymphadenectomy) and frozen section histological examination. If frozen section reveals malignancy (GBC), lymphadenectomy is added to complete EC. AEC is technically easy to perform and does not carry major morbidity. AEC in itself provides complete treatment for benign TWGB (AC, CC and XGC) and at the same time avoids inadequate oncological treatment for malignant TWGB (GBC) also.

GB wall >3 mm on US is defined as TWGB. TWGB on US should be further evaluated with CT (3). Focal, non-uniform and irregular TWGB is highly suspicious of GBC and should be treated as such—by open surgery and EC. Diffuse, uniform and regular TWGB is usually benign (AC, CC or XGC) but can rarely be malignant (GBC) (4).

XGC mimics GBC not only on imaging (US and/ or CT) but even intraoperatively and on gross examination of the resected specimen (GB); the two may also coexist (2). Preoperative FNAC may identify most GBC and some XGC (5) but a negative FNAC does not exclude GBC. Moreover, FNAC is not recommended in resectable GBC because of fear of tumor spread along the needle tract. EUS guided FNAC from TWGB has been reported (6) but requires equipment and expertise which is not available easily and everywhere. Again, negative FNAC does not exclude GBC. Diffusion weighted MR imaging (DWI) may help to differentiate between benign and malignant TWGB but is not accurate (7). Tumor markers e.g., CEA, CA 19-9 and CA 125 have not been found to be useful to differentiate between XGC and GBC (8).

Preoperative differentiation between benign and malignant TWGB thus is difficult, especially in a high GBC incidence geographical area such as northern India.

While SC is adequate for AC, CC or XGC, EC is required for GBC. If SC is performed for TWGB harboring GBC, it will result in breach of tumor planes between GB and liver and compromise oncological principles; this will deny the possible chance of cure in an early GBC. Moreover, if SC is done laparoscopically, GB perforation and bile spill are more likely to happen and may result in peritoneal dissemination and port site recurrence in malignant TWGB (GBC). On the other hand, if EC is performed for all TWGBs, it will be an overkill for majority

of TWGB which are benign (AC, CC and XGC) resulting in increased morbidity and even occasional mortality. Rammohan *et al.* (9) reported that 15 out of 77 patients who underwent EC on suspicion of GBC turned out to be XGC on final histology.

Jain *et al.* (10) reported 22 patients with XGC—radical (extended) cholecystectomy was performed in 11 patients; they used frozen section in 10 patients but after SC. As mentioned earlier, SC when performed in a patient with TWGB harboring GBC violates oncological principles. The authors argued that SC followed by immediate CEC will provide similar oncological outcome as EC but the report did not mention any patients who underwent SC only first and then underwent CEC after frozen section revealed GBC.

Agarwal (1) reported a large experience with 556 GB masses (seen on imaging)—239 were found to be inoperable on preoperative evaluation and 317 were operated. At operation, 129 were found to be unresectable and 198 were resected. Of the resected cases, 167 turned out to be GBC and 31 were XGC. In these 31 patients with XGC, 25 radical (extended) cholecystectomies (with adjacent organ resection in 10) were performed—an unnecessary procedure for XGC. They also used frozen section in six patients but after performing segment IVB +V resection, which is a major, difficult and more morbid procedure than wedge of liver resection proposed by us. This report also does not mention any patients who underwent SC only first and then underwent CEC after frozen section revealed GBC. In any case, for most patients with malignant TWGB (GBC) liver wedge is adequate (11) and is as good as segment IVB +V resection (12).

Shirai *et al.* (13) recently reported full thickness cholecystectomy (gall bladder with cystic plate) with limited lymphadenectomy of the first echelon (cystic and pericholedochal) lymph nodes, as an alternative to EC, in 12 elderly patients with GBC. Han (14) reported use of cholecystectomy with wedge of liver but in only 4 out of 39 patients with XGC.

Only one of our patients with benign TWGB (XGC) underwent an unnecessary lymphadenectomy; this was because of a suspicious frozen section report. Ishii *et al.* (15) also reported a similar patient with TWGB on CT where at operation it was thought to be GBC with infiltration of the transverse colon. Intra-peritoneal wash cytology was positive for malignancy and only palliative resection was done—final histology showed XGC. There was no false positive result of frozen section histological examination

in our experience. We, however, do not rely on intra-peritoneal wash cytology as we found it to be of no use in a trial (unpublished data).

Some recent reports describe laparoscopic EC (16) but long term results in terms of recurrence and survival are awaited. We do not practice and do not recommend laparoscopic EC for GBC; we advocate staging laparoscopy (17) followed by open EC. Even AEC can be performed laparoscopically; Cho *et al.* (18) reported laparoscopic resection of GB together with GB bed in some carefully selected patients with T2 GBC. Han and Cho (19) reported laparoscopic removal of GB with some attached liver tissue in 30 patients with suspected GBC on CT, EUS or lap US—in their experience, however, majority (18 out of 30) of patients turned out to be GBC. We disagree with them in using laparoscopic approach for AEC; also, we recommend AEC in patients with low suspicion of GBC.

Cholecystectomy with wedge of liver followed by frozen section histological examination has been reported by some surgeons earlier for TWGB but in small number of cases and in retrospective analyses. We have used it in 13 selected patients with TWGB with low suspicion of GBC as a prospective protocol and wish to name it as AEC. AEC triages patients with TWGB into benign (AC, CC and XGC) in whom it avoids an unnecessary lymphadenectomy (in our experience, only 1 out of 11 patients with benign TWGB underwent an unnecessary lymphadenectomy because of a false positive frozen section report) and malignant (GBC) in whom it is an oncologically adequate procedure. This surgical approach is likely to be useful particularly in areas with high incidence of GBC which also report large number of patients with TWGB. We wish to name this surgical approach as the Lucknow approach for TWGB.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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