

Xanthogranulomatous Cholecystitis: A Diagnostic Dilemma**Wasif Mohammad Ali¹, Imad Ali², Syed Amjad Ali Rizvi³, Manzoor Ahmad², Mohd. Sadik Akhtar¹**¹Associate Professor, Department of Surgery, Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, Uttar Pradesh, India 202002²Assistant Professor, Department of Surgery, Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, Uttar Pradesh, India 202002³Professor, Department of Surgery, Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, Aligarh, Uttar Pradesh, India 202002

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Conflict of interest: Nil

Abstract:**Introduction:** Xanthogranulomatous cholecystitis (XGC) is a benign gall bladder condition and an uncommon variant of chronic cholecystitis, which usually presents with non-specific symptoms. The dilemma of XGC is that it mimics gallbladder carcinoma (GBC) both preoperatively and intra-operatively. Hence it becomes very difficult to diagnose and manage these patients. Therefore, we have shared our experience of treating XGC and made an effort to develop a care pathway for XGC management.**Materials and Methods:** Retrospective review of clinical data of 1248 patients with the preoperative diagnosis of cholelithiasis, cholecystitis, or gallbladder carcinoma and had undergone surgery at our tertiary centre from May 2016 till December 2021. Twenty-six cases of XGC were identified and evaluated in terms of clinical features, laboratory examinations, radiological findings, the requirement of conversion from laparoscopic to open surgery, complications, length of hospital stay, endoscopic retrograde cholangiopancreatography (ERCP) and preoperative diagnoses.**Results:** In our study the incidence of XGC was 2.0%, mean age at presentation was 55.2 years, with female: male ratio of 1.8:1. In 3 patients, GBC was suspected preoperatively (11.4%), 14 patients (53.8%) had obstructive jaundice at first presentation and required an endoscopic retrograde cholangiopancreatography (ERCP) before LC. Of these, 7 had common bile duct stones. One patient had impacted stone for which choledochoduodenostomy was done. Abdominal ultrasound scan showed marked thickening of the gallbladder wall in 18 cases (70%). LC was attempted in 23 patients but converted to open in 15 patients (65% conversion rate). In 1 patient right hemicolectomy was done along with open cholecystectomy because of dense adhesions. A total cholecystectomy was possible in 19 patients and partial cholecystectomy was the choice in 7 (26%).**Conclusion:** Severe XGC can result in diagnostic dilemmas and difficulties both pre-operatively and intra-operatively due to very close resemblance to gallbladder malignancy. In our study we have devised a pre-operative decision-making algorithm to differentiate between the XGC and GBC and manage accordingly.**Keywords:** Xanthogranulomatous Cholecystitis, Carcinoma Gallbladder, Diagnostic prediction, Cholecystectomy.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Xanthogranulomatous cholecystitis (XGC) is a benign gall bladder condition and an uncommon variant of chronic cholecystitis. The destructive inflammatory infiltration and fibrosis cause the asymmetrical thickening of the gallbladder wall and the formation of multiple yellowish-brown nodules, which often extend into the neighboring organs, such as the liver, colon, omentum and duodenum [1, 2]. Goodman and Ishak described XGC as a separate pathological enti-

ty in 1981 [3]. The epidemiological data in previous studies have shown that there is a higher incidence of XGC in the Indian population, with little variation in gender¹. The dilemma of XGC is that it mimics gallbladder carcinoma (GBC) both preoperatively and intra-operatively. It can present with pericholecystic infiltration, hepatic involvement and lymphadenopathy [4, 5]. The perioperative findings in aggressive cases may be similar to those of gallbladder or

biliary tract carcinomas. It is important to develop a preoperative noninvasive method to differentiate XGC from GBC. In our study we investigated the differentiating radiological features between XGC and GBC, with the aim to devise a noninvasive differential diagnosis between the two diseases preoperatively.

Material and Methods

It is a retrospective study in which we reviewed the clinical data of 1248 patients with the preoperative diagnosis of cholelithiasis, cholecystitis, or gallbladder carcinoma and had undergone surgery at our tertiary centre from May 2016 till December 2021. Twenty-six cases of XGC were identified. The presence of xanthoma cells (foamy histiocytes containing lipids and bile pigment), enormous multinucleated histiocytes, and acute or chronic inflammatory cells in the mural alterations led to the histological diagnosis. Patients were retrospectively evaluated in terms of clinical features, laboratory examinations, radio-

logical findings, the requirement of conversion from laparoscopic to open surgery, complications, length of hospital stay, endoscopic retrograde cholangiopancreatography (ERCP) and preoperative diagnoses.

Results

After the examination of 1248 cholecystectomy specimens, 26 patients (2.1%) were histologically confirmed and diagnosed with XGC, of which 17 (65.4%) were female and 9 (34.6%) were male, meaning a female-to-male ratio of 1.8:1.

The patients in this study were on average 55 years old. Table 1 summarizes the clinical diagnosis at the time of presentation. Twenty patients (76%) required an emergency surgical admission at first presentation. A history of jaundice was obtained in 14 patients (53.8%). Three patients (11.5%) presented with a right upper quadrant mass, when a gallbladder carcinoma was suspected.

Table 1: Xanthogranulomatous cholecystitis: clinical presentation

Clinical Presentation	Number
Acute cholecystitis	15
Cholangitis	3
Biliary colic	2
Chronic RUQ pain	3
RUQ mass, RUQ, rig RUQ Right upper quadrant.	3

USG were obtained in all the patients. Gallstones were present in all the cases. The most common sonographic finding (Table 2) was a diffuse or focal thickening of the gallbladder wall, 18 patients (70%). 11 patients underwent computerised tomography. A gallbladder carcinoma was suspected radiologically in three patients (11.5%), 14 patients (53.8%) presented with obstructive jaundice and required an endoscopic retrograde cholangiopancreatography (ERCP).

Table 2: Xanthogranulomatous Cholecystitis: Sonographic Features

Features	Number
Wall thickness	
Thick walled	18
Thin walled	05
Not reported	03
Stones	
Multiple	20
Single	03
Sludge	03
No stones	0
Other features	
Pericyclic collections	07
Mass lesion (? carcinoma)	03

Table 3: Xanthogranulomatous cholecystitis: Operative findings

Features	Number
Thick-walled gallbladder	22
Adhesions	23
Omental	19
Duodenal	01
Colonic	02

Obscure Calot's triangle anatomy	16
Empyema of gallbladder	06
Features suggestive of gallbladder carcinoma	03
Gangrenous cholecystitis	0

Dilated common bile duct was found in 11 patients (7 with stones and 4 without stones). An elective open cholecystectomy was performed in three patients in preference to LC, due to anticipation of intra-operative technical difficulty.

One of them had a Mirizzi's syndrome and the other had a mass in the right hypochondrium from inflammatory adhesions to the right hepatic flexure and ascending colon and the third patient had adhesions with abscess formation. In the patient which was having dense adhesions between GB and hepatic flexure right hemicolectomy and loop ileostomy was done along with open cholecystectomy. Laparoscopic cholecystectomy was attempted in 23 patients but was unsuccessful in 15 cases (65% conversion rate). The most common reason for conversion was obscure

anatomy of Calot's triangle. In one patient there was hard impacted CBD stone for which choledochoduodenostomy with cholecystectomy was done. Thickening of the gallbladder wall was the most consistent feature found at operation (82%), followed by adhesions to surrounding organs (79%; see Table 3).

In another patient open cholecystectomy with duodenal repair and loop retrocolic Gastrojejunostomy was done due to dense adhesions with the surrounding structures. Partial cholecystectomy was carried out in 07 patients. Postoperative complications are shown in Table 4. The bile leak in one patient was managed conservatively. There were no deaths in this series. When compared to either LC or conversion, the average hospital stay was longer after an open surgery (Table 5).

Table 4: Xanthogranulomatous cholecystitis: Postoperative complications

Complications	Number
Bile leak	01
Biloma	02
Pneumonitis	0
Wound infection	01

Table 5: Xanthogranulomatous cholecystitis: in-patient length of stay.

Procedure	Number	Average (days)	Range (days)
LC	08	3.4	2-6
LC> Open	15	6.8	4-12
Open LC, laparoscopic cholecystectomy; LC > Open, conversion to open procedure.	03	8.4	7-15

Discussion

XGC is a rare clinical entity and is characterized by a diffuse, destructive inflammatory process. The gallbladder wall is infiltrated by histiocytes and macrophages causing a proliferative fibrosis. The clinico radiological picture of XGC closely resembles gallbladder carcinoma with pericholecystitic infiltration, hepatic involvement and lymphadenopathy.

It was termed as "pseudo tumour" by Christensen and Ishak in 1970 and later called a xanthogranulomatous gallbladder by McCoy in 1976 [6,7]. It commonly involves the population in the fifth and sixth decades of life [8,9] and is present in about 0.7-13.2% of all cholecystectomies [10,11]. In our study the average age was 60.2 years with slight female predominance and incidence was 2.2% of all the cholecystectomies done. The pathogenesis of XGC is uncertain, but usually there is a combination of acute inflammation

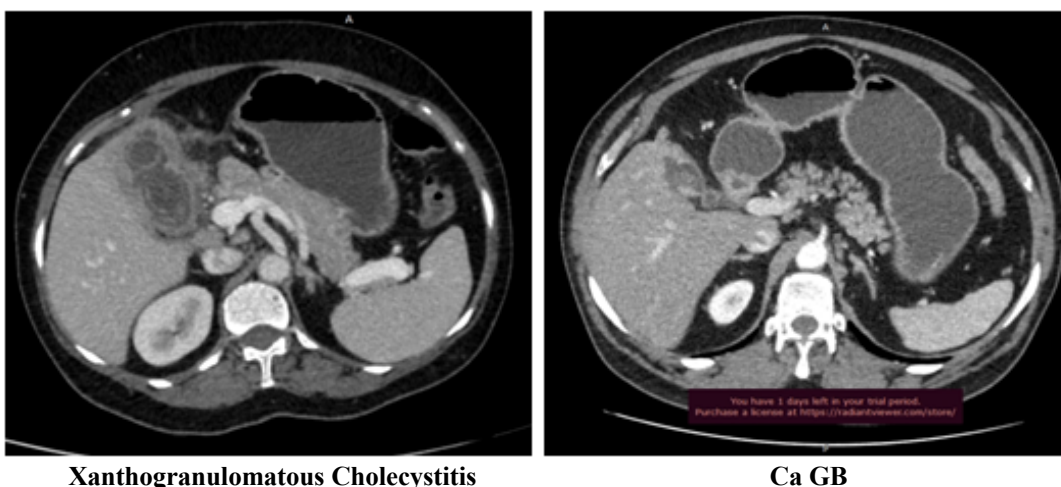
of the gallbladder and obstruction to its outflow due to gallstones [12,13]. Bile enters into the gallbladder wall stroma through ruptured Rokitansky–Aschoff sinuses or mucosal ulcerations secondary to the presence of gallstones or acute inflammation. The extravasated bile in the stroma causes inflammatory reactions of histiocytes accumulation, which engulf the insoluble cholesterol and other bile lipids to form large round xanthoma cells. Micro abscesses are then formed in the gallbladder wall eventually resulting in xanthogranuloma. Finally, the healing of the inflammatory reaction results in a fibrous reaction and scarring. The clinical manifestations of XGC can be those of acute or chronic cholecystitis. Clinical features like fever, recurrent abdominal pain and leucocytosis favours a diagnosis of XGC, while a history of anorexia and weight loss favours GBC. However, jaundice, vomiting and the presence of a palpable right upper quadrant mass are not distinguishing features

[14]. The severe inflammatory process often involves the surrounding structures and forms fistulous communications and can manifest as Mirizzi's syndrome with obstructive jaundice.

USG is the modality, which is done in all the patients. The presence of cholelithiasis, choledocholithiasis, cholecystitis, diffuse wall thickening with continuous mucosal enhancement of gallbladder and the presence of sub-mucosal hypoattenuating nodules favours XGC whereas focal gallbladder wall thickening and the presence of GB mass favours GBC [15,16,17]. Ultrasonography can also detect the conditions like gallbladder perforation with abscess formation and gas in the biliary tree due to fistula formation [18,19].

CT findings involve diffuse or focal wall thickening, intramural hypoattenuating nodules in thickened walls, luminal surface enhancement (LSE) with continuous mucosal lines or mucosal lines with focal breach. Cholelithiasis and choledocholithiasis are often seen associated with XGC [20].

Focal thickening is less commonly seen in xanthogranulomatous cholecystitis and is more likely to be associated with carcinoma of gallbladder. Specifically, the CT criteria for the diagnosis of xanthogranulomatous cholecystitis include diffuse wall thickening, continuity of the mucosal line, intramural hypoattenuated nodules, and absence of invasion to adjacent liver parenchyma [21].



Xanthogranulomatous Cholecystitis

Ca GB

Figure 1:

Proposed algorithm for patients with USG findings suggesting XGC/GB Ca

We reached the conclusion that in those cases where the preoperative diagnosis is more likely to be a gallbladder malignancy, it is worth referring these patients to a hepatobiliary unit for further management, which may involve a hepatic resection if needed.

Therefore, pre-operative counselling is very important in such patients. Whenever a thick-walled gallbladder is encountered, it is important to consider XGC and gallbladder cancer in the differential diagnosis, and to counsel the patients for possible difficulties and management protocols including referral to specialist centres. At operation, XGC may project the appearance of an advanced gallbladder carcinoma because of marked thickening of the gallbladder wall and local destructive picture as a result of intense inflammation. Therefore, an intraoperative frozen-section biopsy should be performed in such scenario [23,24]. Xanthogranulomatous cholecystitis is a condition that could only be diagnosed histopathological-

ly after cholecystectomy. Operative findings usually reveal the presence of prolific adhesions to surrounding tissues, thick-walled gallbladder associated with fistulous communications, gallbladder perforations and abscess formation, resulting in technical difficulties and prolonged operating time. Complete resection of the gallbladder is not always possible especially due to obliteration of Calot's triangle. In our study, a total cholecystectomy was possible in only 19 out of 26 patients (73%). A high conversion rate up to 80% is reported in XGC. Our conversion rate in these cases was 65% (15 cases out of attempted).

Xanthogranulomatous Cholecystitis – Per Operative Findings

The postoperative complication rate was noted to be higher in patients of XGC with 10.7% in partial cholecystectomy and 2.8% in total cholecystectomy [10,16].

The overall complication rate in our study was 20%. Furthermore, the period of stay in the hospital is usually greater for these individuals. The average hospital stay was reported to be 21 days (range, 9–60 days)

for open cholecystectomy as opposed to 5 days (range, 3–10 days) for LC [15]. In our patients, the average length of stay for open cholecystectomy was 8.4 days, compared to 3.4 days for a successful LC.

The present study provided a noninvasive method in

distinguishing XGC from GBC. By taking CT scan, we could distinguish most of the XGC cases from GBC and can take management decisions preoperatively.

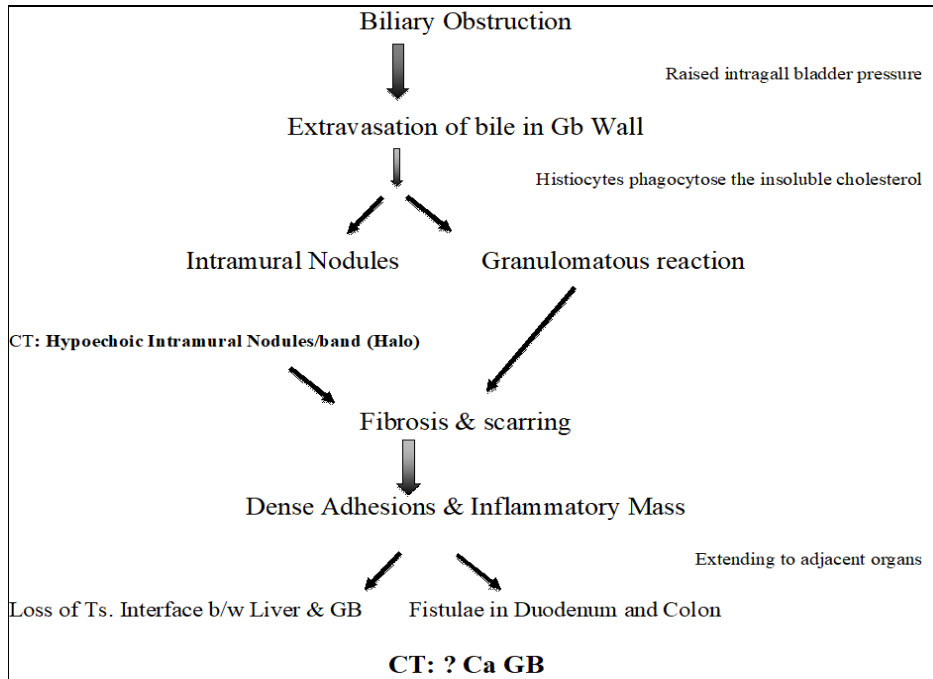


Figure 2:

Fine needle aspiration cytology (FNAC) has been reported to play an important role in making the preoperative diagnosis of GBC and XGC. The overall sensitivity of detecting carcinoma was 90.6% and specificity 94.7%. The sensitivity of detecting malignancy was 80% when adenocarcinoma was associated with XGC [22].

We have devised a pre-operative decision-making algorithm.

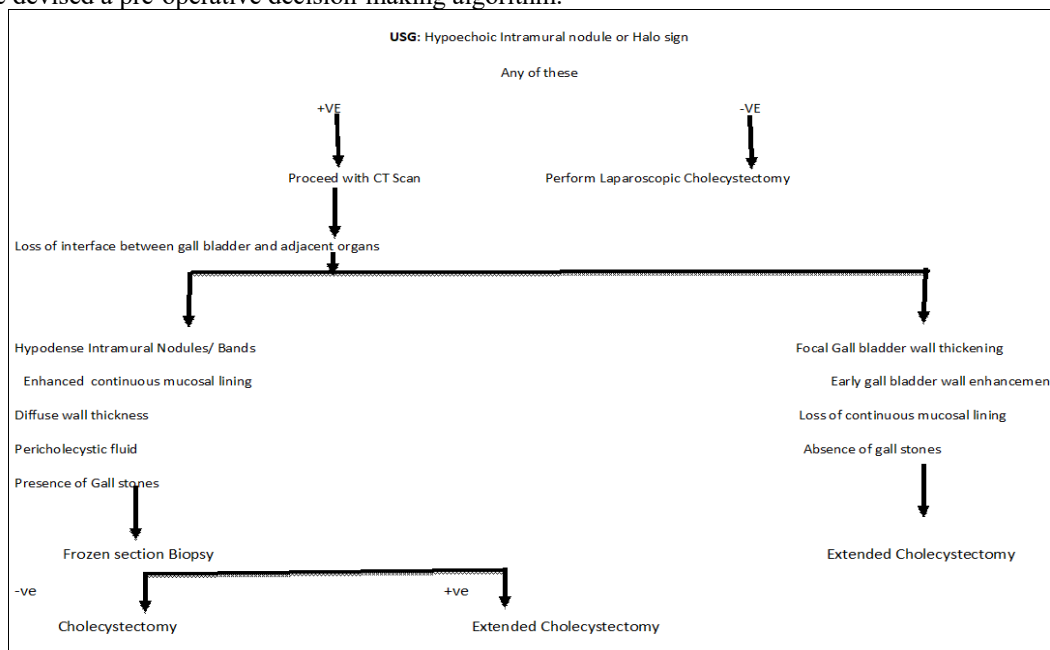


Figure 3:

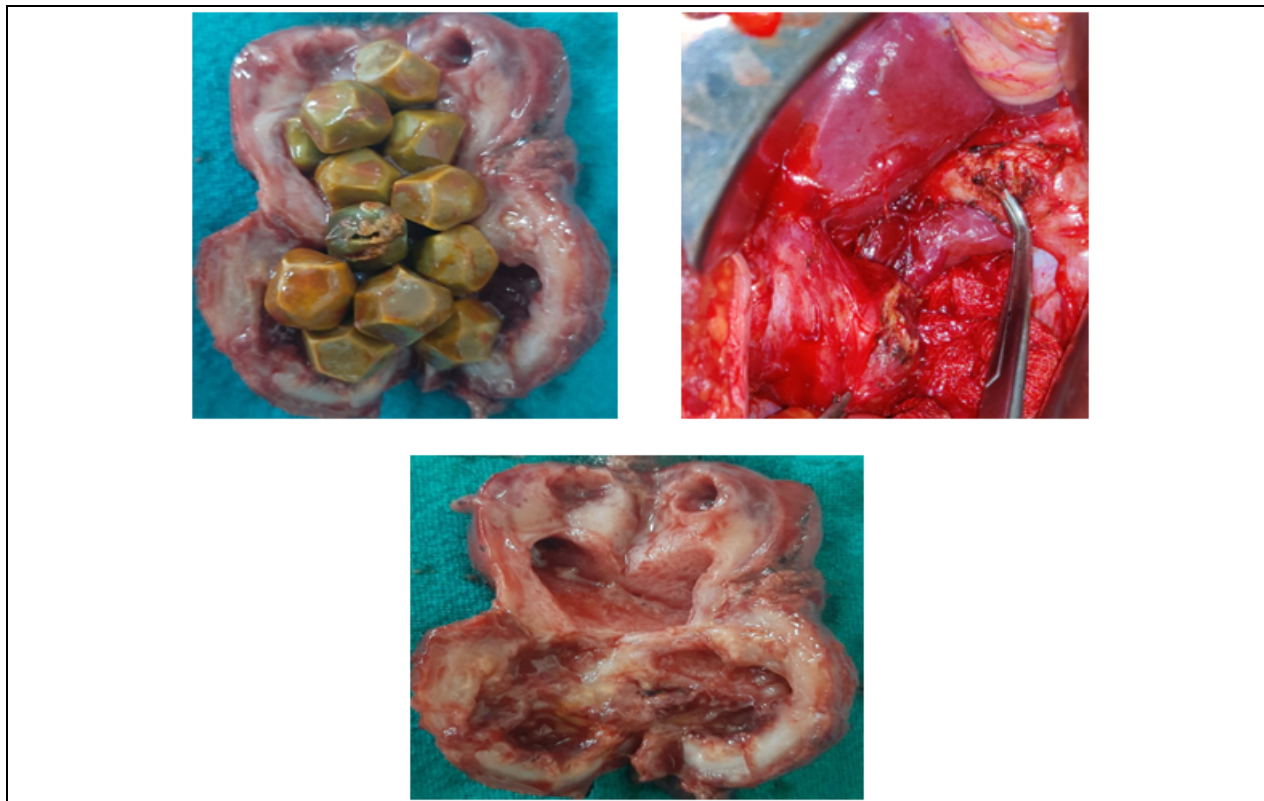


Figure 4:

Conclusion

Severe xanthogranulomatous cholecystitis can result in diagnostic dilemmas and difficulties both pre-operatively and intra-operatively due to very close resemblance to gallbladder malignancy. A correct preoperative diagnosis requires awareness and a high index of suspicion. USG, CT, and FNAC are useful preoperative diagnostic techniques. Preoperative counseling must include possible differential diagnosis of gallbladder cancer. It is possible to exclude gallbladder carcinoma with frozen section during the operation. LC is usually unsuccessful and often a partial cholecystectomy is the procedure of choice to avoid the complications of biliary injuries.

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