



RETROSPECTIVE STUDY OF CLINICAL, RADIOLOGICAL AND SURGICAL FINDINGS OF XANTHOGRANULOMATOUS CHOLECYSTITIS AN EXPERIENCE AT TERTIARY LEVEL INSTITUTION

General Surgery

Dr. Bhawana Kumari	M.S. (Gen. Surg.), DGO, Senior Resident, Department of Gen. Surgery, AIIMS, Patna, Bihar.
Dr. Hrishi Kumar*	M.S. (Gen. Surg.), Senior Resident, Department of Gen. Surgery, AIIMS, Patna, Bihar. *Corresponding Author
Dr. Manoj Kumar	M.S., FRCS, DNB, FACS, Additional Professor, Department of Gen. Surgery, AIIMS, Patna, Bihar.
Dr. Hari Prasad CP	Postgraduate Resident, Department of Gen. Surgery, AIIMS, Patna, Bihar.
Dr. Debarshi Jana	Young Scientist (DST), Institute of Post-Graduate Medical Education and Research, A.J.C. Bose Road, Kolkata-700020, West Bengal, India.

ABSTRACT

Background: Xanthogranulomatous cholecystitis is a benign disease of gallbladder which presents almost classically similar with the chronic calculus cholecystitis, but it mimics GB carcinoma intraoperatively. **Materials and methods:** In our study, 54 cases were found in a study period of 2 yr in which histopathological reports was xanthogranulomatous cholecystitis whether the pt underwent lap/radical/open or lap converted open cholecystectomy for cholelithiasis and chr. cholecystitis and suspicious carcinoma GB. They were retrospectively analysed for getting an idea preoperatively to differentiate them on clinicoradiological ground and while during surgery. **Results and Observation:** Data were retrospectively analysed and observed that clinical and biochemical features are non specific. Imaging in the form of USG and CT does help but not to that much extent to accurately diagnose them. Intraoperatively presence of dense adhesion and loss of fat plane to surrounding structures creates a big dilemma for the operating surgeon and multiple frozen section biopsy can be of immense help here in guiding further treatment course. Frozen section analysis was not present at our institution so we did not avail its use. **Conclusion:** Our study is an attempt to derive any correlation between clinicoradiological and intraoperative aspects preoperatively for the diagnosis of xanthogranulomatous cholecystitis. Although its incidence is greater here than other countries due to rising gallbladder diseases but till this time it is concluded that neither clinical nor radiologically xanthogranulomatous cholecystitis can be ruled out preoperatively. Only histopathological diagnosis is absolutely correct, and in our study we concluded that histopathological diagnosis is still the gold standard.

KEYWORDS

Xanthogranulomatous Cholecystitis, Histopathology, Ultrasound CECT, Gallbladder Carcinoma

INTRODUCTION

Xanthogranulomatous cholecystitis is one of the rare inflammatory disease of GB presenting as acute and chronic cholecystitis^[1] frequently associated with cholelithiasis. It is characterized by accumulation of lipid laden macrophages. It was first described in 1970 by Christensen et al^[2] and later nomenclatured by Mac Coy in 1976^[3]. Gallbladder related diseases are one of the common surgical entity in the northern India particularly in the state of Bihar. It ranges from benign pathology to malignant ones. Although XGC is a rare, benign disease but similarity with Ca GB makes it more important. Its growing incidence here, leads to a common mistake which is frequently occurring in our perspective is that persons being operated for malignancy later diagnosed to be a case of benign condition histopathologically. This increases morbidity to the patients in the form of radical surgery as well as increased hospital stay. Our study is an endeavor to get an idea preoperatively or intraoperatively to differentiate it from Ca GB.

MATERIALS AND METHODS.

This is a retrospective study conducted at AIIMS, Patna. Patients whose histopathological reports showed XGC and underwent lap/open/radical cholecystectomy were included in the study between January 2018 to March 2020. Clinical records of these patients were reviewed retrospectively for clinical features, laboratory investigations, and findings on radiological imaging. Majority of the pt were presented with pain upper abdomen, the duration varied between days to years. Age of the patients ranges from 17 years to 70 years. Biochemically raised alkaline phosphatase, raised leucocyte count & raised tumour marker also pointed about the possibility of malignancy. Ultrasonography (USG) abdomen was done as an initial examination in all patients; in case of suspicious GB ie thickened GB or contracted GB with mass lesion, a contrast-enhanced computed tomography (CECT) was done.

RESULTS

In our observation, 54 patients had histological findings of XGC in the

duration of the study period. Two of them had associated gbcarcinoma, and one had coexisted periampullary carcinoma. Clinical features are tabulated in Table No. 1. In our study, Females outnumbered males which was similar to the study. Among the 54 patients 34 were female and 20 were males. Male to female ratio was 0.588. This is contradiction to the previous study^[3,4]

Characteristic	Findings
1. Male	20
2. Female	34
3. Right upper quadrant pain Less than 6 month duration More than 6 month duration	54 40 14
4. Mass right upper abdomen	2
5. Nausea & vomiting	30
6. Jaundice	4

The most affected age group was between 50-60 years, although a second peak was also observed between age 30-40 years. The most common presenting symptom was right upper quadrant (RUQ) pain which was present in almost all patients. 40 out of 54 had multiple episode of pain abdomen for less than 6 months and rest 14 had history of pain abdomen for more than 6 months. 2 patient presented with mass per abdomen. Nausea vomiting was associated in almost half of the patients. Imaging findings are given in Table No. 2.

Symptoms	Number
1. Cholelithiasis	54
2. Thickened GB wall	45
3. Asymmetric wall thickness	10
4. Focal thickening of GB wall	10
5. Contracted GB	2
6. CBD calculi	3

Comparison of radiological findings to that of operative findings was done and tabulated in Table No. 3 about 50% pt. USG report showing thickened GB wall along with cholelithiasis.

Imaging finding	Number	Intraoperative findings
1.Simple gallbladder	9	Simple lap cholecystectomy
2.Difficult gallbladder	27	Dense adhesion at callots and loss of fat plane with adjacent structures
3.Simple gallbladder	18	Dense adhesion to surroundings present

About 50% of pt .usg report showed thickened GB wall along with cholelithiasis. Intraoperatively these cases were turned out to be difficult due to dense fibrosis secondary to XGC In about 49.99% cases there were no change in GB wall in USG but intraoperatively 18 {66.66%} of them had dense adhesion to surroundings. GB calculus was present in all cases.^[4,5]

In only 10 patients preoperative CT was done where USG showed asymmetrical thickened GB wall suspicious for malignancy. CT showed asymmetric wall thickening particularly at fundus, loss of fat plane with adjacent liver, duodenum and hepatic flexure, and some lymph node. Intraoperatively they were also the same as to the imaging findings and resulted in radical procedures. In CT we did not get report of intramural nodules in any cases which contradicts the previous study by K A CHUN^[6,7,8]. Two patient developed intraoperative complication in the form of stomach rupture, another developed increased drain output for around seven days. Bile spillage due to GB rupture while removing from GB bed or during extraction from epigastric port was also a significant association. Patients of radical cholecystectomy were discharged on 8th postoperative day. Final outcome was different forms of surgery and is tabulated in Table No. 4.

Lap cholecystectomy	32
Lap converted open cholecystectomy	4
Open cholecystectomy	4
Radical cholecystectomy	11
ERCP followed by lap cholecystectomy	1
ERCP followed by lap converted open cholecystectomy	1
Open cholecystectomy with choledocholithotomy	1

Among 54 patients 3 had associated CBD calculi. They underwent ERCP followed by lap cholecystectomy and another had lap conversion. One pt. underwent open cholecystectomy along with choledocholithotomy. Intraoperatively dense adhesion were present at hepatocystic triangle in 45, in two patients pyoceles were present & in one pt. mucocoele was present. One pt. presented with mirizzi type I. Rest of the patient had no difficult GB. We did not find any cholecystoduodenal fistula which disfavours the previous studies showing their association. In 4 cases lap converted open cholecystectomy was done. In cases where there were higher chances of malignancy radical cholecystectomy was done [11 cases]. In one case us guided FNAC of the GB mass done which was suggestive of adenocarcinoma but finally on histopathology, it was XGC. In 4 cases depending on USG findings open cholecystectomy was planned and resulted in subtotal cholecystectomy. Tumor markers and deranged LFT does not help to rule out XGC and carcinoma.

Three patient had associated carcinoma, out of them, two pt. had GB carcinoma and 1 had coexisted periampullary carcinoma. One patient had associated hydatid cyst of liver. One pt. had complaint of jaundice along with pain abd. for 1 month, Her USG report showed thick walled GB, cholelithiasis and choledocholithiasis with malignant distal CBD stricture. She underwent therapeutic ERCP for choledocholithiasis. Post ERCP, CT SCAN reported GB to be partially contracted with irregular wall thickening in fundal region, suspicious for being neoplastic. It also reported about the presence of organized peripancreatic collection in pancreatic tail region. Her tumour markers were in the normal range CA19-9-82.04,CEA-0.08. Her USG guided FNAC showed features of adenocarcinoma GB. Based on these observations and reports patient was assumed to have malignancy and planned for staging laparoscopy followed by radical cholecystectomy. Peroperatively there was dense adhesion near callots leading to conversion to open. In our setup we do not have the facility of frozen section, so the surgery was completed with doing extended cholecystectomy, along with choledochotomy and T tube placement. It was a histological surprise when final HPE report came and showed it to be a case of XGC. Two patients had associated GB carcinoma and managed by radical procedure. One patient had associated

periampullary carcinoma and managed with whipples procedure and histopathological report of GB came out to be XGC. One patient had associated hydatid cyst liver who presented with huge right abdominal lump along with pain abdomen for 2 months and managed accordingly.

DISCUSSION

Although XGC is a rare disease but it is an important GB pathology in northern states of India particularly Bihar due to growing incidences of cholelithiasis here. The pathogenesis is not clear but it may be postulated that outflow obstruction of GB secondary to calculus leads to bile extravasation into the GB wall. This produces intense inflammatory reaction, subsequent healing of which results in Fibrous reaction & scarring. This in turn creates a dense fibrosis with surrounding structures, and simulates with Ca GB^[9]. What make this disease important is its resemblance with Ca GB both preoperatively and intraoperatively, because the treatment options for both is quite different. In our study, female outnumbered the male patients which was similar to the previous study of Taskesen et al^[10]. The most common age group affected was between 50-60 years although a second peak was also observed between 30-40 years The clinical presentation is non specific, most of the patients presented with upper right quadrant pain abdomen associated with nausea & vomiting. 40 out of 54 had pain abdomen of less than 6 month duration^[11] and rest had history of more than 6 month. We did not find any correlation of tumour marker with XGC which is similar to the previous study^[14,15,16,17]. On imaging, USG reported thickened GB wall in 50 % cases^[11], in rest patients USG did not comment on GB thickening. Out of these, 10 patients are those which had asymmetrical GB wall thickening and underwent subsequent CT. CT reported asymmetric wall enhancement particularly at fundus and loss of plane with surrounding structures^[11,12]. None of the cases reported the thickening to be diffuse which was contradictory to the previous study of Rajguru et al^[12]. CT report here did not mention any intramural nodule or homogenous enhancement which was in contradiction to the previous study, Intraoperatively 83.33% cases were turned out to be difficult cholecystectomies [including radical] due to presence of dense adhesions at callots and surroundings. We have nonavailability of frozen section examination which can be of use in differentiating it to the Ca GB as studied in previous study^[13,15,19,20,21]. Simultaneous presence of Ca GB and XGC was seen in 2 cases which supported the existence of their association, analogous to the study conducted by Ros et al.^[12,22,25]

On pathological aspects, most of the patients showed smooth and congested serosa and some had rough. mucosa remained atrophied and denuded with loss of velvety mucosa in some case there were haemorrhagic areas on mucosa. There were abundance of foamy histiocytes, few patients had associated antral metaplasia. Features of XGC was associated with focal mucosal ulceration in most cases which supports the pathogenesis. On histopathologically gb wall thickness varied from 0.2mm -1.4 cm

CONCLUSION

XGC is now become an important gb pathology. in our setup due to rising trend of gallbladder related disease. What makes it more important is its resemblance to its malignant counterpartie ca gb. No definite diagnosis from prehand is available to us which can prevent increased mortality & morbidity of patients in the form of radical surgery. Aim of our study was to evaluate different clinico radiological & intraoperative criterias so as to derive an idea preoperatively about its existence. In our study ,we found that clinically both appears same ,biochemical reports also of not much help even imaging also does not help much^[23,24]. Imaging notifies the thickening but cannot rule out possibility of inflammatory or malignant. It has been concluded finally that histopathological diagnosis is still the gold standard^[19].

REFERENCES

1. Suzuki H, Wada S, Araki K, Kubo N, Watanabe A, Tsukagoshi M, Kuwano H. Xanthogranulomatous cholecystitis: Difficulty in differentiating from gallbladder cancer. *World J Gastroenterol*. 2015 Sep 21;21(35):10166-73.
2. Christensen AH, Ishak KG. Benign tumors and pseudotumors of the gallbladder. Report of 180 cases. *Arch Pathol*. 1970 Nov;90(5):423-32.
3. McCoy JJ Jr, Vila R, Petrossian G, McCall RA, Reddy KS. Xanthogranulomatous cholecystitis. Report of two cases. *J S C Med Assoc*. 1976 Mar;72(3):78-9. PMID: 1063276.
4. Guzmán-Valdivia G. Xanthogranulomatous cholecystitis in laparoscopic surgery. *J Gastrointest Surg*. 2005 Apr;9(4):494-7. doi: 10.1016/j.gassur.2004.09.036. PMID: 15797229.
5. Houston JP, Collins MC, Cameron I, Reed MW, Parsons MA, Roberts KM. Xanthogranulomatous cholecystitis. *Br J Surg*. 1994 Jul;81(7):1030-2.
6. K A Chun, H K Ha, E S Yu, K S Shinn, K W Kim, D H Lee, S W Kang, Y H Auh. Xanthogranulomatous cholecystitis: CT features with emphasis on differentiation

- from gallbladder carcinoma.
7. Parra JA, Acinas O, Bueno J, Güezmes A, Fernández MA, Fariñas MC. Xanthogranulomatous cholecystitis: clinical, sonographic, and CT findings in 26 patients. *AJR Am J Roentgenol*. 2000 Apr;174(4):979-83.
 8. Kim PN, Ha HK, Kim YH, Lee MG, Kim MH, Auh YH. US findings of xanthogranulomatous cholecystitis. *Clin Radiol*. 1998 Apr;53(4):290-2.
 9. Bo X, Chen E, Wang J, Nan L, Xin Y, Wang C, Lu Q, Rao S, Pang L, Li M, Lu P, Zhang D, Liu H, Wang Y. Diagnostic accuracy of imaging modalities in differentiating xanthogranulomatous cholecystitis from gallbladder cancer. *Ann Transl Med*. 2019 Nov;7(22):627.
 10. Taskesen F, Arikanoğlu Z, Uslukaya O, Oğuz A, Aliosmanoglu I, Dusak A, Turku G, Kuzu H. A rare finding during a common procedure: xanthogranulomatous cholecystitis. *Int Surg*. 2014 Sep-Oct;99(5):595-9.
 11. Feng L, You Z, Gou J, Liao E, Chen L. Xanthogranulomatous cholecystitis: experience in 100 cases. *Ann Transl Med*. 2020 Sep;8(17):1089.
 12. Kishore R, Nundy S, Mehrotra S, Metha N, Mangla V, Lalwani S. Strategies for Differentiating Gallbladder Carcinoma from Xanthogranulomatous Cholecystitis-a Tertiary Care Centre Experience. *Indian J Surg Oncol*. 2017 Dec;8(4):554-559.
 13. Hale MD, Roberts KJ, Hodson J, Scott N, Sheridan M, Toogood GJ. Xanthogranulomatous cholecystitis: a European and global perspective. *HPB (Oxford)*. 2014 May;16(5):448-58. doi: 10.1111/hpb.12152. Epub 2013 Aug 29. PMID: 23991684; PMCID: PMC4008163
 14. Rammohan A, Cherukuri SD, Sathyanesan J, Palaniappan R, Govindan M. Xanthogranulomatous cholecystitis masquerading as gallbladder cancer: can it be diagnosed preoperatively? *Gastroenterol Res Pract*. 2014;2014:253645.
 15. Yang T, Zhang BH, Zhang J, Zhang YJ, Jiang XQ, Wu MC. Surgical treatment of xanthogranulomatous cholecystitis: experience in 33 cases. *Hepatobiliary Pancreat Dis Int*. 2007 Oct;6(5):504-8. PMID: 17897914
 16. L.-F.Zhang,C.-S.Hou, J.-Y.Liuet al., "Strategies for diagnosis of xanthogranulomatous cholecystitis masquerading as gallbladder cancer," *Chinese Medical Journal*, vol. 125, no. 1, pp. 109–113, 2012.
 17. D. Sharma, R. Babu, G. Sood, G. Kapoor, R. S. Solanki, and S. Thomas, "Xanthogranulomatous cholecystitis masquerading as malignancy with liver metastasis," *ANZ Journal of Surgery*, vol. 79, no. 12, pp. 946–947, 2009.
 18. Benbow EW. Xanthogranulomatous cholecystitis. *Br J Surg*. 1990 Mar;77(3):255-6.
 19. Maeda T, Shimada M, Matsumata T, Adachi E, Taketomi A, Tashiro Y, Tsuneyoshi M, Sueishi K, Sugimachi K. Xanthogranulomatous cholecystitis masquerading as gallbladder carcinoma. *Am J Gastroenterol*. 1994 Apr;89(4):628-30. PMID: 8147372.
 20. Srinivas GN, Sinha S, Ryley N, Houghton PW. Perfidious gallbladders - a diagnostic dilemma with xanthogranulomatous cholecystitis. *Ann R Coll Surg Engl*. 2007 Mar;89(2):168-72.
 21. Saritas AG, Gul MO, Teke Z, Ulku A, Rencuzogullari A, Aydin I, Akcam AT. Xanthogranulomatous cholecystitis: a rare gallbladder pathology from a single-center perspective. *Ann Surg Treat Res*. 2020 Oct;99(4):230-23.
 22. Uchiyama K, Ozawa S, Ueno M, Hayami S, Hirono S, Ina S, Kawai M, Tani M, Yamaue H. Xanthogranulomatous cholecystitis: the use of preoperative CT findings to differentiate it from gallbladder carcinoma. *J Hepatobiliary Pancreat Surg*. 2009;16(3):333-8.
 23. Makimoto S, Takami T, Hatano K, Kataoka N, Yamaguchi T, Tomita M, Shono Y. Xanthogranulomatous cholecystitis: a review of 31 patients. *SurgEndosc*. 2020 Jul 27. doi: 10.1007/s00464-020-07828-6. Epub ahead of print. PMID: 32720174.
 24. Pandey A, Kumar D, Masood S, Chauhan S, Kumar S. Is Final Histopathological Examination the Only Diagnostic Criteria for Xanthogranulomatous Cholecystitis? *Niger J Surg*. 2019 Jul-Dec;25(2):177-182. doi: 10.4103/njs.NJS_1_19. PMID: 31579373; PMCID: PMC677118.
 25. Ros PR, Goodman ZD. Xanthogranulomatous cholecystitis versus gallbladder carcinoma. *Radiology*. 1997 Apr;203(1):10-2.