

ORIGINAL ARTICLE

XANTHOGANULOMATOUS CHOLECYSTITIS COHORT STUDY: A CLINICOPATHOLOGICAL AND INCIDENTAL FREQUENCY ANALYSIS

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ABSTRACT

Background: Xanthogranulomatous cholecystitis is a benign, uncommon, localized or diffuse inflammatory pathological condition of the gallbladder and a catastrophic distinct transformation of chronic cholecystitis. Macroscopically distinguished by multiple yellowish with lipid packed tumor like foamy masses (nodules or streaks) in the wall of the gallbladder. Microscopically, it is distinguished by a number of bubbly histiocytes with acute or chronic inflammatory cells, while in upcoming phase manifest with tremendous fibrosis. The present study was undertaken to analysis of the histopathology reports to see the frequency of incidental xanthogranulomatous cholecystitis after elective cholecystectomy.

Methods: 1522 cholecystectomies performed from January 2011 to December 2015, at tertiary care single centre Ziauddin University and Hospitals Karachi Pakistan. On Histopathology of ten gallbladder specimens after elective cholecystectomy revealed xanthogranulomatous cholecystitis. These histologically confirmed cases are identified from the retrospective analysis of patient's record.

Results: During the study period 1522 patients underwent cholecystectomy. Histopathologically confirmed xanthogranulomatous cholecystitis in ten patients (0.65% of all cholecystectomies). The mean age and standard deviation of patients with xanthogranulomatous cholecystitis was 54 ± 17.19 years (range 29-85), with male to female ratio is 1:1. The most common clinical features were abdominal pain and tenderness in the right hypochondrium. Biliary colic and acute cholecystitis were the most common preoperative diagnostic features. Ultrasonogram was performed in all patients.

Conclusion: Xanthogranulomatous cholecystitis is a scarce variant of cholecystitis with marked topographical discrepancy and preoperative clinical uncertainty and a per-operative diagnosis is a challenging task. Many times diagnosis is a histopathological revelation.

KEY WORDS: Xanthogranulomatous cholecystitis, Histopathology, Gallstones, Cohort study.

INTRODUCTION

Xanthogranulomatous cholecystitis is a scarce focal or diffuse distinct catastrophic chronic inflammatory disease of the gallbladder consisting of multiple with lipid packed yellow-brown intramural nodules or streaks that are distinguished by immense fibrosis and bubbly cells^{1,2}. In 1970, Christensen et.al; noted chronic cholecystitis with the presence of xanthoma like bubbly cells in an inflamed gallbladder so they used the descriptive name fibroxanthogranulomatous cholecystitis in a review of 180 cases³. Amazon et.al; had noted a pseudo tumor variant of chronic cholecystitis distinguished by xanthoma like bubbly cells and scarring with ceroid (wax-like)

nodules in the wall of the gallbladder. They used the name ceroid granuloma of the gallbladder⁴, but in 1981 a review of forty cases by Goodman ZD et.al; the name suggested as xanthogranulomatous cholecystitis⁵. The incidence rate of xanthogranulomatous cholecystitis among patients with symptomatic gallbladder disease ranges from 0.7 % in the United States to up to 10 % in India and Japan^{6,7}. Higher incidence frequency in sixth and seventh decades of life^{1, 2, 8,10} but it's occurrence in a very young child of two months old has also been mentioned in this study^{11,12}. With male supremacy male and female ratio is 2:1^{12,13}. One Indian study found a marked female supremacy with male to female ratio is 1:9¹⁴. The gallstones are the most important

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association of xanthogranulomatous cholecystitis seen in 80% of cases¹⁵. The relation of xanthogranulomatous cholecystitis with gallstones has been reported to be 85 to 96%^{16, 17}. It's a benign condition that may be indistinct with gallbladder malignancy¹⁸. The pathogenesis of xanthogranulomatous cholecystitis is thought to be related extravagation of the bile may be the fundamental pathway to initiate the process. Infection and certain hypersensitivity may also lead for the pathogenesis of xanthogranulomatous cholecystitis^{19, 20}.

METHODS

Ten (0.65%) histologically confirmed cases of xanthogranulomatous cholecystitis were identified from our cohort retrospective analysis of the patient's record of 1522 cholecystectomies performed during the period January 2011 to December 2015 at the tertiary care center Ziauddin University Hospital, Karachi Pakistan. The clinical, radiological, per-operative and postoperative histopathological findings of these patients have been analysed. The incidence rate of xanthogranulomatous cholecystitis was 10(0.65%) out of 1522 patients who underwent for elective cholecystectomy for gallstone disease. The statistical analysis was done on a software SPSS-21 software. Frequency and percentage tables were generated with calculation of mean and range. The appropriate statistical calculation was applied according to the data categories to identify the frequency and percentage among affected patients.

RESULTS

The incidence rate of xanthogranulomatous cholecystitis was 10 (0.65%) out of 1522 patients who underwent for elective cholecystectomy for gallstone disease, and age range was between 29 and 85 years with a mean age of 54 years (± 17.19). Five (0.32%) patients were male with mean age \pm SD (57.8 ± 20.49) years and five (0.32%) were female with mean age \pm SD (50.2 ± 14.44) years. A female to male ratio was 1:1. Chronic right upper quadrant pain was the greatest usual clinical presentation. Abdominal ultrasound scan showed marked thickening of the gallbladder wall in six cases (60%), all the ten patients had gallstones, four (40%) patients had chronic cholecystitis, and two (20%) patients had acute cholecystitis. None of the patient suspected preoperatively or per-operatively for gallbladder malignancy, but sixteen (1.05%) patients had incidental carcinoma of the gallbladder out of 1522 patients in histopathology. No significant association was observed between xanthogranulomatous cholecystitis and gallbladder malignancy. In histopathology we found focal or diffuse inflammation with massive number of bubbly histiocytes, inflammatory cells, jumbo cells and fibroblasts in a diverse part.

Table 1: Mean, median and Standard deviation of patients with Xanthogranulomatous Cholecystitis (n=1522)

	Frequency/percentage F(%)	Mean	Median	Standard deviation (\pm)
Female	5(0.32%)	50.2	50	± 14.44
Male	5(0.32%)	57.8	56	± 20.49
Total	10(0.65%)	54	53	± 17.19

Table 2: Preoperative clinical and Ultrasound findings for xanthogranulomatous cholecystitis (n=10)

	Parameters	F(%)
Clinical findings	Right upper quadrant Pain	10(100%)
	Jaundic	0(0%)
	Fever	4(40%)
	Murphy's sign	2(20%)
Ultrasound findings	Acute cholecystitis	1(10%)
	Chronic cholecystitis	4(40%)
	Thick walled gall bladder	6(60%)
	Gallstones	10(100%)

DISCUSSION

Xanthogranulomatous cholecystitis still remains inadequately comprehend, uncommon and benign disease and patient's danger being managed at a high level or managed inadequately as a result of uncertainty with or without masquerading of gallbladder malignancy. Despite its importance, the realistic incidence of this disease is still highly unrevealed with extensive variations reported in the previous studies^{21, 22}. In the current study 10(0.65%) cases manifest histopathologically for xanthogranulomatous cholecystitis from total 1522 patients. These studies propose that there may be a geographical impact upon the frequency of incidence of this disease. This has been extensively reported incidence within studies from Far East and India with the smallest number of patients undergoing cholecystectomy favor to be those reported as the appreciable incidence for xanthogranulomatous cholecystitis. It suggests that there could be reporting inclinations. A study from India reviewed 6150 gallbladder specimens in which 620 specimens of the gallbladder (10.1%) showed xanthogranulomatous cholecystitis. The male-to-female ratio is equal with little geographical impact because most commonly females underwent for cholecystectomy^{23, 24}. Some American and European studies showed less high incidence frequency of xanthogranulomatous cholecystitis as compare to India and Far East^{5, 25}. All cases of xanthogranulomatous cholecystitis exist at the same time with gallstones. These detections indicate that xanthogranulomatous cholecystitis strongly communicated with the gallstones, which is consistent

with the report of this study but not present in every patient, indicating a role for additional causative factors. All cases of xanthogranulomatous cholecystitis are related with gallstones. In this study, 33 of 42 patients communicated with gallstones, fewer than in some previous European studies reported 92%-100%^{9,25}. Several previous studies showed great communication between xanthogranulomatous cholecystitis and gallbladder malignancy^{5, 15}. But in our study, we found no communication with gallbladder malignancy.

CONCLUSION

Xanthogranulomatous cholecystitis is a universal disease with unusual and benign destructive inflammatory process, distinguished by severe fibrosis and wall thickening of the gallbladder presenting as a bubbly mass that imitate to the malignancy of gallbladder. Xanthogranulomatous cholecystitis still remains difficult to be recognized by radiologist and surgeons. It displays a marked geographical discrepancy in its incidence. Middle-aged and elderly women and men are equally affected. The pre-operative and per-operative differential diagnosis of the disease still remains a competitive situation to the surgeon and histopathological assessment of all gallbladder specimens after elective cholecystectomy for xanthogranulomatous cholecystitis is critical, and considering the infrequent existence with gallbladder malignancy.

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CONFLICT OF INTEREST The Authors declare that there is no conflict of interest.

REFERENCES

- Ueda J, Yoshida H, Arima Y, Mamada Y, Taniai N, Mineta S, et.al.; A case of xanthogranulomatous cholecystitis preoperatively diagnosed with contrast-enhanced ultrasonography. *Journal of Nippon Medical School.* 2011;78(3):194-8.
- Sharma D, Babu R, Sood G, Kapoor G, Solanki RS, Thomas S. Xanthogranulomatous cholecystitis masquerading as malignancy with liver metastasis. *ANZ journal of surgery.* 2009;79(12):946-7.
- Christensen A. Benign tumors and pseudotumors of the gallbladder. Report of 180 cases. *Arch Pathol.* 1970;90:423-32.
- Amazon K, Rywlin A. Ceroid granulomas of the gallbladder. *American journal of clinical pathology.* 1980;73(1):123-7.
- Goodman ZD, Ishak KG. Xanthogranulomatous cholecystitis. *The American journal of surgical pathology.* 1981;5(7):653-60.
- Rammohan A, Cherukuri SD, Sathyanesan J, Palaniappan R, Govindan M. Xanthogranulomatous cholecystitis masquerading as gallbladder cancer: can it be diagnosed preoperatively? *Gastroenterology research and practice.* . 2014; 2014:1-5
- Krishna RP, Kumar A, Singh RK, Sikora S, Saxena R, Kapoor VK. Xanthogranulomatous inflammatory strictures of extrahepatic biliary tract: presentation and surgical management. *Journal of Gastrointestinal Surgery.* 2008;12(5):836-41.
- Yang T, Zhang B-H, Zhang J, Zhang Y-J, Jiang X-Q, Wu M-C. Surgical treatment of xanthogranulomatous cholecystitis: experience in 33 cases. *Hepatobilary Pancreat Dis Int.* 2007;6(5):504-8.
- Parra J, Acinas O, Bueno J, Guezmes A, Fernandez M, Farinas M. Xanthogranulomatous cholecystitis: clinical, sonographic, and CT findings in 26 patients. *American Journal of Roentgenology.* 2000;174(4):979-83.
- Arora A, Mukund A. Xanthogranulomatous cholecystitis: characteristic CT findings. *Indian Journal of Gastroenterology.* 2012;31(2):85.
- Kim S-H, Kim H-Y, Jung S-E, Park K-W, Choi YH, Kim W-S, et.al.; Xanthogranulomatous cholecystitis in 2-month-old infant. *Journal of the Korean Surgical Society.* 2013;85(4):191-4.
- Guzmán-Valdivia G. Xanthogranulomatous cholecystitis in laparoscopic surgery. *Journal of gastrointestinal surgery.* 2005;9(4):494-7.
- Yabanoglu H, Aydogan C, Karakayali F, Moray G, Haberal M. Diagnosis and treatment of xanthogranulomatous cholecystitis. *Pain.* 2014;15:71-5.
- Balague C, Targarona E, Sugranyes G, Rey M, Arce Y, Viella P, et.al.; [Xanthogranulomatous cholecystitis simulating gallbladder neoplasm: therapeutic implications]. *Gastroenterología y hepatología.* 1996;19(10):503-6.
- Ros PR, Goodman ZD. Xanthogranulomatous cholecystitis versus gallbladder carcinoma. *Radiology.* 1997;203(1):10-2.
- Guzman-Valdivia G. Xanthogranulomatous cholecystitis: 15 years' experience. *World journal of surgery.* 2004;28(3):254-7.
- Kwon A-H, Matsui Y, Uemura Y. Surgical procedures and histopathologic findings for patients with xanthogranulomatous cholecystitis. *Journal of the American College of Surgeons.* 2004;199(2):204-10.
- Pinoczy J, Lange A, König C, Kaiserling E, Becker HD, Kröber SM. Xanthogranulomatous cholecystitis resembling carcinoma with extensive tumorous infiltration of the liver and colon. *Langenbeck's Archives of Surgery.* 2003;388(1):48-51.
- Mori M, Watanabe M, Sakuma M, Tsutsumi Y. Infectious etiology of xanthogranulomatous cholecystitis: immunohistochemical identification of bacterial antigens in the xanthogranulomatous lesions. *Pathology international.* 1999;49(10):849-52.
- Sawada S, Harada K, Isse K, Sato Y, Sasaki M, Kaizaki Y, et.al.; Involvement of *Escherichia coli* in pathogenesis of xanthogranulomatous cholecystitis

- with scavenger receptor class A and CXCL16–CX-CR6 interaction. *Pathology international.* 2007;57(10):652-63.
21. Fligiel S, Lewin K. Xanthogranulomatous cholecystitis: case report and review of the literature. *Archives of pathology & laboratory medicine.* 1982;106(6):302-4.
22. Solanki R, Arora H, Gaur S, Anand V, Gupta R. Xanthogranulomatous cholecystitis (XGC): a clinicopathological study of 21 cases. *Indian journal of pathology & microbiology.* 1989;32(4):256-60.
23. Duca S, Bala O, Al-Hajjar N, Iancu C, Puia I, Munteanu D, et.al.; Laparoscopic cholecystectomy: incidents and complications. A retrospective analysis of 9542 consecutive laparoscopic operations. *Hpb.* 2003;5(3):152-8.
24. Srivastava M, Sharma A, Kapoor VK, Nagana Gowda GA. Stones from cancerous and benign gallbladders are different: A proton nuclear magnetic resonance spectroscopy study. *Hepatology Research.* 2008;38(10):997-1005.
25. Karabulut Z, Besim H, Hamamci O, Bostanoglu S, Korkmaz A. Xanthogranulomatous cholecystitis. Retrospective analysis of 12 cases. *Acta Chirurgica Belgica.* 2003;103(3):297-9.