Research Article

Xanthogranulomatous cholecystitis: A pathologist perspective

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ABSTRACT

Background: Xanthogranulomatous cholecystitis (XGC) is an uncommon inflammatory disease of the gallbladder characterized by the infiltration of plasma cells, lipid-laden histiocytes, and the proliferation of fibroblasts in the gallbladder wall. Its importance lies in the fact that imaging studies and intraoperative appearance may be confused with tumors of the gallbladder. It is the name generally used to describe the lesion which results when lipids from the bile in the lumen of the gallbladder enter the wall of the organ and induce a granulomatous inflammation. The present study was undertaken to analyze histological features of XGC along with clinical features and ultrasonographic findings. **Objectives:** Correlation of XGC with clinico-radiological findings and to look for various morphological changes microscopically. **Material and Methods:** A retrospective study of 1018 patients who had undergone cholecystectomy between July 2014 and June 2016 at our hospital. Totally, 33 cases of XGC were identified among these cholecystectomies. The clinical features and radiological findings of these patients have been analyzed and compared with histologic findings. **Results:** The clinical symptoms were abdominal pain, nausea, and jaundice in 81.8%, 60.6%, and 12.12% of the patients. Preoperative ultrasonography for 33 patients revealed gallstone (90.90%) bile sludge (9.09%) and thickened wall in 30.30% of patients. **Conclusions:** XGC is difficult to diagnose pre- or intra-operatively and remains a challenge in medical practice. The definitive diagnosis depends on the histopathologic examination.

KEY WORDS: Xanthogranulomatous; Cholecystitis; Gallbladder

INTRODUCTION

Xanthogranulomatous cholecystitis (XGC) is an uncommon inflammatory disease of the gallbladder characterized by the infiltration of plasma cells, lipid-laden histiocytes, and the proliferation of fibroblasts in the gallbladder wall.[1] The term of XGC was initially proposed by Goodman and Ishak in 1981.[2] The pathogenesis of XGC is the rupture of Rokitansky-Aschoff sinuses and extravasation of bile into the muscular layer. The rupture of the serosa results in adhesion to the adjacent liver, duodenum, and transverse colon. Gallstones may have an important role in the pathogenesis since they appear to be present in most patients.[3]

Pre- and intra-operative diagnosis is difficult, and it often mimics a gallbladder carcinoma (GBC). Laparoscopic cholecystectomy is frequently unsuccessful with a high conversion rate. XGC was previously described as an uncommon form of chronic cholecystitis.[4] Christensen and Ishak initially described it as a pseudotumor with the destructive type of gallbladder inflammation, pericholecystic infiltration, hepatic involvement, and lymphadenopathy. In 1981, the term XGC was proposed in a review of 40 cases collected over a 10-year period.[2] In the literature, the incidence of XGC is reported to be 0.7% to 13.2%. A Higher incidence was reported from the Eastern countries.[5-6]

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MATERIALS AND METHODS

The cholecystectomy specimens received in the department of pathology from July 2014 to June 2016 were studied. All the specimens were subjected to histopathological examination after grossing and staining of sections by H and E stain. These sections were studied for the presence of fibrosis, giant cells, granulomas, cholesterol clefts, acute inflammation, and association with adenocarcinomas. Clinical details and radiological findings of patients were taken from the records.

RESULTS

A total of 1018 specimen of gall bladder were received during the study. Of these 33 cases were diagnosed as XGC, other cases included the cases of chronic cholecystitis (which formed the bulk), empyema and acute on chronic cholecystitis with few cases of carcinoma.

Of 33 cases, 27 patients (81.82%) patients had abdominal pain, 20 patients (60.60%) had nausea, and 4 patients (12.12%) had jaundice.

On ultrasonography, gallstones were found in 30 patients (90.90%), bile sludge seen in 3 cases (9.09%), and wall thickness was increased (more than 3 mm) in 10 (30.30%).

Out of 33 cases, 20 were females and 13 were males.

Maximum number of cases were seen in the age group of 31 to 40 years. 11 patients (33.33%) were found in this age group (Table 1).

All the cases showed the presence of lipid-laden macrophages, which in 45.45% of cases seen forming nodular aggregates, while in rest of the cases they were found in sheets. Fibrosis was found in 43.3% of cases, multinucleated giant cells were found in 3.33%, antral metaplasia was found in 27.73%, and cholesterol clefts were seen in 15.15%. In most of the cases, the inflammatory infiltrate was the mixed type. Acute on chronic cholecystitis was seen in 4 cases (12.12%) and adenocarcinoma was found in 1 case (3.03%) (Table 2 and Figures 1-5).

DISCUSSION

A total of 1018 specimen of gall bladder were received during the study. Of these 33 cases were diagnosed as XGC, other cases included the cases of chronic cholecystitis (which formed the bulk), empyema and acute on chronic cholecystitis with few cases of carcinoma. Out of 33 cases, 27 patients (81.82%) patients had abdominal pain, 20 patients (60.60%) had nausea, and 4 patients (12.12%) had jaundice. On ultrasonography, gallstones were found in 30 patients (90.90%), bile sludge seen in 3 cases (9.09%) and wall thickness was increased (more than 3 mm) in 10 (30.30%). A study done by Chauhan showed Gallbladder wall thickening on ultrasonography was in 91.9% cases, and all (100%) had cholelithiasis.[7] Out of 33 cases, 20 were females and 13 were males. Maximum number of cases were seen in the age group of 31 to 40 years. 11 patients (33.33%) were found in this age group. All the cases showed the presence of lipid-laden macrophages, which in 45.45% of cases seen forming nodular aggregates, while in rest of the cases they were found in sheets. Fibrosis was found in 43.3% of cases, multinucleated giant cells were found in 3.33%, antral metaplasia was found in 27.73%, and cholesterol clefts were seen in 15.15%. In most of the cases, the inflammatory infiltrate was the mixed type. Acute on chronic cholecystitis was seen in 4 cases (12.12%) and adenocarcinoma was found in 1 case (3.03%).

In this study, the incidence of XGC was 3.24% among 1018 patients who were operated for gall bladder stone or chronic cholecystitis, which was in similar in a study conducted by Yildirim et al.[8] XGC mostly affects middle-aged women and old persons between 60 and 70 years. In our study, mean age was 49 years, which was around 10-15 years less than the other studies.[9,10] This suggests that age must be one of the significant factors in the development of the XGC. The male to female ratio range is from 2:1 to 1:2 in other series.[8] A study from India[9] reported a 1:9 male to female ratio, while in our report male to female ratio was found 1:1.54. The different incidence of XGC may be due to

Table 1: Revealing age-wise distribution of XGC

Age in years	Number of cases (%)
21-30	2 (6.06)
31-40	11 (33.33)
41-50	4 (12.12)
51-60	9 (27.27)
61-70	5 (15.15)
71-80	2 (6.06)

XGC: Xanthogranulomatous cholecystitis

Table 2: Showing associated microscopic morphological findings

Microscopic findings	Number of cases (%)
Fibrosis	14 (42.42)
Antral metaplasia	9 (27.73)
Multinucleated giant cells	11 (33.33)
Granulomas	3 (9.09)
Cholesterol clefts	5 (15.15)
Nodular aggregates of foamy macrophages	15 (45.45)
Mixed inflammation	18 (54.55)
Acute on chronic cholecystitis	4 (12.12)
Adenocarcinoma	1 (3.03)

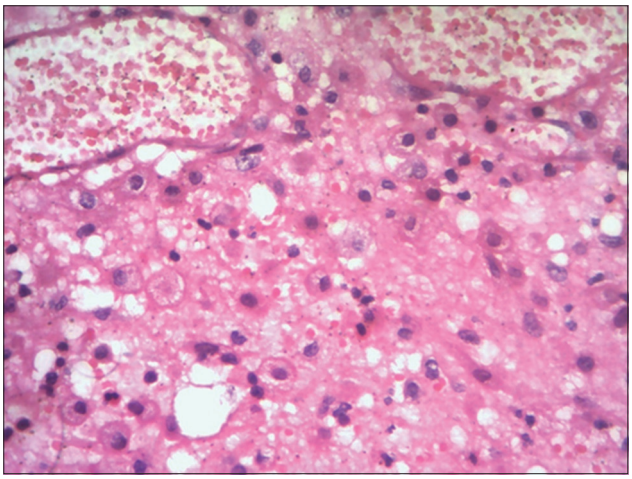

Figure 1: Sheets of lipid laden macrophages admixed with lymphocytes, plasma cells, eosinophils and polymorphs (H and E ×40)

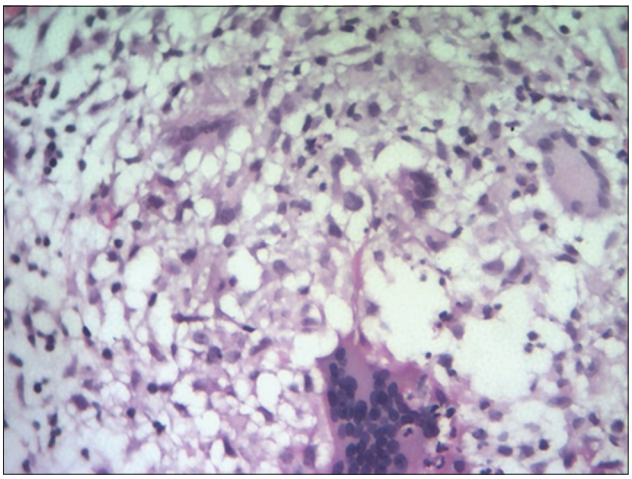

Figure 2: Areas of granulomas (H and E ×40)

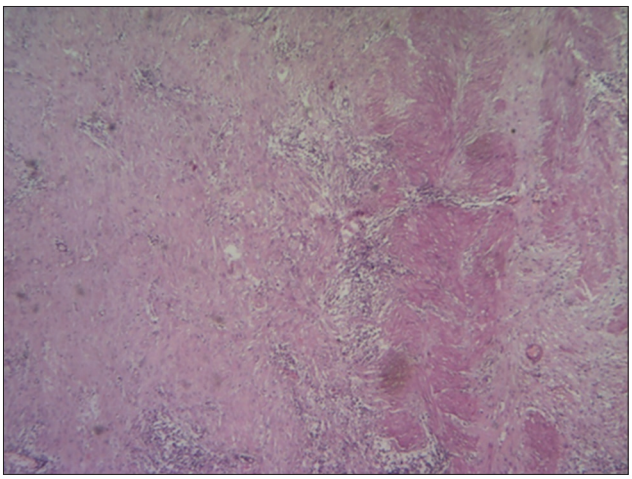

Figure 3: Dense fibrosis (H and E ×40)

misdiagnosis by clinicians. Clinically, XGC does not have a typical presentation.[11] Most of the patients in our study presented with pain in right upper quadrant, nausea, icterus and palpable mass; they are similar to acute or chronic

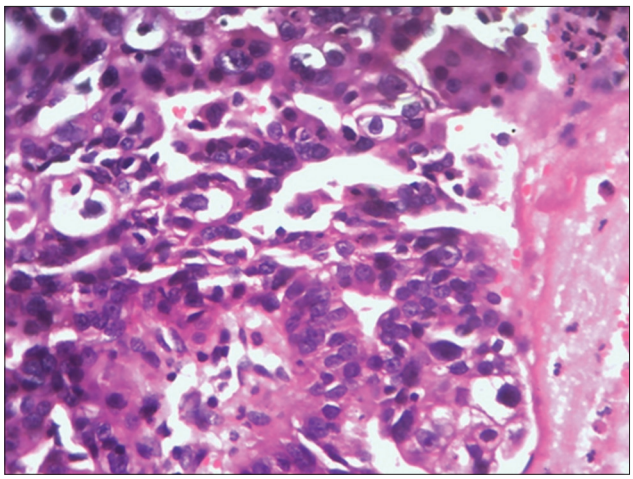

Figure 4: Area of adenocarcinoma in xanthogranulomatous cholecystitis (H and E ×40)

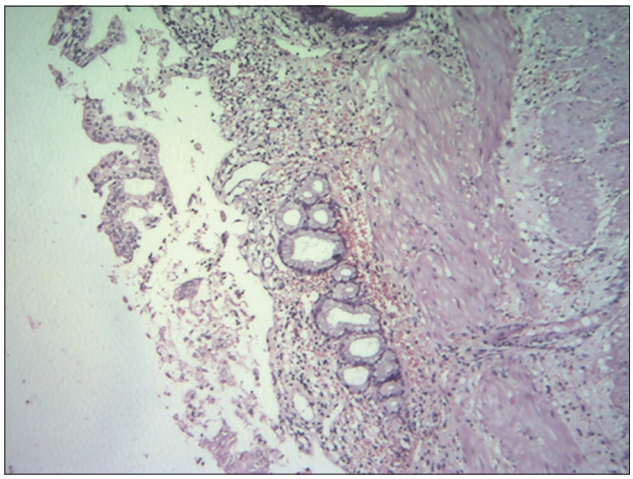

Figure 5: Antral metaplasia (H and E ×40)

cholecystitis, which was in concordance with the study by Yildirim et al.[9] These clinical features are not specific for XGC and there was no difference between the patients with cholecystitis and GBC.[6,9] it was noted that most of the patients with these symptoms required an elective surgical procedure at first presentation.

Most of the cases of XGC were identified by histopathological examination of cholecystectomy specimen. By seeing the presence of foamy macrophages, the diagnosis was confirmed. Other helpful features were marked fibrosis, cholesterol clefts, and multinucleated giant cells. None of the patients was diagnosed as XGC, and two cases were diagnosed as carcinoma of gall bladder on USG. Increasing recognition and reporting of XGC should indicate the true incidence of this condition. In this study, high misdiagnosis rate may be related to insufficient experience for imaging findings of XGC. The pathogenesis of XGC is unclear, although the role of cholesterol and bile is thought to be important.[12] Bile degradation within histiocytes as a cause of the xanthoma cells has been proposed.[12] Takahashi et al.[13]

and Goodman and Ishaks have suggested that the important event is the extravasation of bile into the gall bladder wall, either from ruptured Rokitansky-Aschoff sinuses or focal mucosal ulceration. In most cases, foci of XGC seem to be centered on Rokitansky-Aschoff sinuses. We believe that the pathogenesis of XGC is similar to that proposed by Parsons et al. for xanthogranulomatous pyelonephritis.[14] Chun et al.[15] concluded that a definitive diagnosis of GBC is not possible with only imaging findings.

CONCLUSION

The diagnosis of XGC remains challenging to clinicians and radiologists.

The presence of firm adhesions of the gallbladder to neighboring organs and tissues, thickened gallbladder wall, together with gallstone in a patient with chronic disease, is highly suggestive of XGC. The definitive diagnosis can be made by histopathological examination only.

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