A Rare Finding During a Common Procedure: Xanthogranulomatous Cholecystitis

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Xanthogranulomatous cholecystitis is a rare variant of chronic cholecystitis characterized by severe proliferative fibrosis and accumulation of lipid-laden macrophages in regions of destructive inflammation. Xanthogranulomatous cholecystitis clinically and radiologically mimics early-stage gallbladder cancer, with wall thickening on computed tomography. The study included 14 xanthogranulomatous cholecystitis patients that were identified following retrospective analysis of the records of 1248 patients that underwent cholecystectomy between 2005 and 2011. Mean age of the 5 male and 9 female patients was 56.7 years. All 14 patients had gallbladder stones; 10 had a history of acute cholecystitis, 1 had cholangitis, and 2 presented with obstructive jaundice. A right-upper quadrant mass was palpable in 2 patients. All patients underwent cholecystectomy. Open surgery was planned and performed in 6 of the 14 patients, and laparoscopic cholecystectomy was planned in 8 patients, but was converted to open surgery in 1 case. In total, 1 patient developed wound infection, 1 patient had postoperative pneumonia, and 1 patient developed intraabdominal hematoma. None of the patients in the series died. Xanthogranulomatous cholecystitis is difficult to diagnose, both preoperatively and intraoperatively, and definitive diagnosis depends exclusively on pathological examination. Xanthogranulomatous cholecystitis should be a consideration in all difficult cholecystectomy cases.

Keywords: Gallbladder – Cholecystitis – Xanthogranulomatosis

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Xanthogranulomatosis is a rare condition and arises from an unknown cause in which lipid-filled histiocytes are deposited throughout various regions of the body. Xanthogranulomatous inflammation occurs in various organs, including the skin, kidneys, retroperitoneum, intracranium, gastrointestinal tract, genital organs, and gallbladder.¹⁻³ Xanthogranulomatous cholecystitis (XGC) is a seldom-seen inflammatory disease that occurs in the gallbladder. Its primary characteristic is destructive inflammation that is local or disseminated throughout this organ. Different amounts of fibrous tissue, acute and chronic inflammatory cells, and lipid-filled macrophages are also present. The XGC regions present themselves as yellow masses within the wall of the gallbladder when examined macroscopically.⁴ The pathogenesis of XGC is unclear, but the extravasated bile conceivably originating from ruptured Rokitansky-Aschoff sinuses is purported to be the cause of this inflammatory response.^{4,5} Concomitant cholelithiasis is observed in most XGC cases. Cholelithiasis is a disease that occurs predominantly in women aged mostly 60 to 70 years. XGC accounts for 0.7 to 13.2% of all gallbladder diseases.^{6,7} A fibrotic gallbladder and dense adhesions are usually encountered during surgery, and the macroscopic appearance generally mimics gallbladder carcinoma.^{5,8} Here, we present our experience with this unusual entity.

Materials and Methods

Patient files from 2005 to 2011 at Dicle University, School of Medicine, Department of General Surgery, Diyarbakır, Turkey were retrospectively reviewed for cases of inflammatory disease of the gallbladder. Clinical data were obtained from medical charts and histopathology and operative reports, including patient demographics, clinical features, pathological findings, surgical details, and outcomes.

In total, 1248 surgically excised gallbladders were submitted for pathological examination during this period; among these, 14 cases of XGC were identified. Partial cholecystectomy can be considered the choice of procedure in cases where the gallbladder is unintentionally opened, or excessive bleeding obscures the dissection plane at the liver bed. Resection of the gallbladder at the liver bed can be performed using electrocoagulation; however, special attention should be paid to leave only the thinner layer of the gallbladder. Cauterization of the possible residual gallbladder mucosa can be a reasonable option.

Table 1 Clinical findings

Clinical features	Patients, <i>n</i>
Acute cholecystitis	10
Cholangitis	1
Abdominal pain	12
Nausea and vomiting	9
Fat intolerance	7
Abnormal physical findings	5
Right hypochondrial tenderness	4
Fever	3
Right hypochondrial mass	2

Results

XGC was observed in 14 of 1248 patients who underwent cholecystectomy between 2005 and 2011, an incidence of 1.1%. The 9 female and 5 male patients had a mean age of 56.7 ± 1.1 years (range: 35–75 years). Table 1 shows the clinical details for the 14 patients. In all, 10 of the patients (71%) had greater than or equal to one episode of acute cholecystitis, and 5 had one episode. Among the patients, 2 presented with obstructive jaundice, and a right-upper quadrant mass was palpable in 2 patients. Laboratory test results were within normal ranges, except for leukocytosis in patients with acute cholecystitis, and elevated liver function results and bilirubin levels in the jaundiced patients.

All patients underwent abdominal ultrasonography (USG), and abdominal computed tomography (CT) was performed in 6 patients. USG and CT findings are presented in Table 2. The most common finding was gallbladder stones, which was observed in all 14 patients, and the gallbladder wall was thickened in 8 (Fig. 1). Two patients underwent endoscopic retrograde cholangiopancreatography (ERCP); in these patients, a dilated common bile duct (CBD) was noted via USG and CT. Choledocholithiasis was observed in 2 patients, and the stones could be extracted in only 1 of them. All patients underwent cholecystectomy, and gallbladder stones were detected in each case. Open surgery was planned and performed in 6 patients, and preoperative ERCP was performed in 2 patients because of choledochal stones. Laparoscopic cholecystectomy was performed in the patient in whom the choledochal stone was extracted during ERCP, and open surgery was performed in the other patient in whom the choledochal stone could not be extracted during ERCP. Laparoscopic cholecystectomy was planned in 8 patients; however, the surgery was converted into open surgery in 1 patient because of severe adhesions and an inability to identify the

Table 2 Organ imaging findings

USG and CT examination findings	Patients, <i>n</i>
Gallstones	
Gallbladder	14
Bile ducts	2
Gall bladder wall thickened	8

structures at the triangle of Calot. Total cholecystectomy was performed in 9 patients, and partial cholecystectomy was performed in 5 patients.

Specimens were examined by the pathology department, and all of the patients were diagnosed with XGC (Fig. 2). The mean duration of surgery was 114.6 ± 60.3 minutes (range: 45–240 minutes); in all cases, postsurgical recovery went well. The mean duration of hospitalization was 7.3 ± 2.8 days (range: 3–13 days). The principal postoperative complications included infection of the incisional wound ($n = 1$), pneumonia ($n = 1$), and intra-abdominal hematoma ($n = 1$), all of which responded well to conservative management. None of the patients in this series died.

Discussion

The histological features of XGC can be summarized as follows: (1) chronic or acute inflammatory cell infiltration in variable degrees, (2) multitudinous macrophages that contain lipids, and (3) fibrosis at later times of disease development. Goodman and Ishak first coined the term “XGC” in 1981 when they examined 40 cases from the Armed Forces Institute of Pathology.⁹ In the present series, the incidence of XGC was 1.1% among 1248 cholecystectomies performed between 2005 and 2011. XGC is observed in a small proportion of cholecystectomy specimens,

ranging from 0.7 to 1.8% in the United States, 9.3 to 13.2% in India, and 1.2 to 10% in Japan.⁹ XGC is more prevalent in middle-aged women.^{1,7} In the presented series, there was an obvious female predominance, with a male:female ratio of 0.55.

In all, 2 patients in the present study presented with obstructive jaundice, 10 presented with acute cholecystitis, and a right-upper quadrant mass was palpable in 2 patients. All of these clinical features can be observed in acute cholecystitis, and none is characteristic of XGC. There are no XGC-specific symptoms or signs; they are similar to those observed in acute or chronic cholecystitis.¹⁰ In the present study, all 14 patients had symptoms in the right hypochondriac region, nausea, vomiting, and fever. Preoperative biochemical tests and imaging techniques such as USG and CT do not show findings characteristic of XGC. USG examination can show thickening of the gallbladder wall. Common bile duct stones, gallbladder stones, masses in the gallbladder, and pericholecystic fluid can also be detected. However, it should be noted that these findings cannot be attributed to XGC alone because they are also associated with acute cholecystitis or gallbladder carcinoma.⁷ Significant problems arise because XGC bears both a clinical and macroscopic resemblance to cancer. These problems are compounded because XGC also assumes the histological characteristics of tumors. XGC is also frequently confused with a neoplasm where there is a preponderance of spindle-shaped xanthoma cells featuring a storiform growth pattern. Nevertheless, malignant features, such as cellular atypia and pleomorphisms are not present in XGC. This disease also does not show an escalation in the number of mitotic figures, and no marked change in their shapes is observed. First, more attention must

Fig. 1 CT scan shows with xanthogranulomatous cholecystitis in a 58-year-old woman. thickened gallbladder wall (short arrows in a), and minimal pericholecystic fluid collection (arrows in a) with hypoechoic nodules (arrows in b), neck stone (arrow in c).

Fig. 2 Xanthogranulomatous inflammation of the gallbladder wall, characterized by large foam (xanthoma) cells with clear lipid-containing cytoplasm (hematoxylin and eosin, $\times 200$).

be given to this condition to mind, and a good collaboration with other clinicians must be established. To have proper interpretation of the histopathological results, clinical, imaging, and macroscopic findings should be considered also. This is particularly crucial in rapid frozen section diagnosis because small samples may increase confusion. Previous studies have shown that gallbladder cancer occurs alongside XGC in 2 to 35.4% of cases.⁴ In the present study, XGC was not associated with gallbladder carcinoma in any of the patients.

A preoperative diagnosis of XGC is difficult, and intraoperative diagnosis from a frozen section is often needed to differentiate XGC from carcinoma.^{9,11} USG results revealing the existence of hypoechoic nodules or bands in the wall of the gallbladder or CT findings showing a hypodense band around the gallbladder may be strong indications of XGC⁷; however, there were only 2 patients in the present series with such CT findings. Cholecystectomy (complete or partial) is the treatment of choice for XGC. Analysis of data from outside of China has shown that, in 65% of XGC cases, complete cholecystectomy was difficult, and 35% of cases underwent partial cholecystectomy.¹ In the present study, the mean duration of surgery was 114.6 minutes, which is longer than that for common open cholecystectomy, illustrating the difficulty of surgery in XGC patients. Complete cholecystectomy was performed in 9 patients, and partial cholecystectomy was performed in 5 patients with severe adhesions of the gallbladder to neighboring tissue.

Although XGC is a benign change in the gallbladder associated with a low mortality rate, the duration of hospitalization in patients with XGC is usually longer, and postoperative complications, including bile leakage, bile peritonitis, gallbladder bleeding, hepatic abscess, infection of the incisional wound, and cholangitic stenosis, occur more often in patients with cholecystitis who undergo cholecystectomy. This finding is largely related to the difficulty of stripping the gallbladder, mode of surgery, and physical condition of the patient.^{1,12} Complications occurred in 2 (14.2%) patients in the present study: hematoma ($n = 1$) and pneumonia ($n = 1$). None of the patients in the present study died.

In conclusion, it is sometimes difficult to distinguish between XGC and other forms of cholecystitis and gallbladder cancer because it is both clinically and radiologically nonspecific despite its typical histological features. Total cholecystectomy should be the preferred choice of treatment whenever possible because gallbladder carcinoma in conjunction with XGC occurs at a higher rate than typical cholecystitis or gallstones.

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