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Diagnosis and treatment of xanthogranulomatous cholecystitis

H. YABANOGLU, C. AYDOGAN, F. KARAKAYALI, G. MORAY, M. HABERAL

Department of Surgery, Baskent University Faculty of Medicine, Ankara, Turkey

Abstract. – BACKGROUND: The aim of this study was to review our case load of the treatment and outcomes of patients with xanthogranulomatous cholecystitis (XGC).

PATIENTS AND METHODS: Data about 21 patients were reviewed retrospectively to determine age, clinical symptoms and findings, preoperative screening, operative findings, surgical history, length of hospital stay, and postoperative complications.

RESULTS: There were 14 men and 7 women (mean age, 65 ± 11.3 yr). Preoperative ultrasonography of 17 patients showed a gallbladder stone in 14 patients, adenomyomatosis plus stones in 2 patients, and a polyp in 1 patient. There were 5 patients with acute cholecystitis and 16 patients with chronic cholecystitis. Gallbladder wall thickening was noted in 3 of the 12 patients who had abdominal computed tomography. Frozen section examinations were done in 5 patients. Radical cholecystectomy was done in 1 patient because of suspected carcinoma.

CONCLUSIONS: It is difficult to diagnose XGC preoperatively or intraoperatively, and the definitive diagnosis depends exclusively on pathologic examination.

Key Words:
Gallbladder, Gallstones, Xanthogranulomatous cholecystitis, Inflammation, Carcinoma.

Introduction

Xanthogranulomatosis is an idiopathic, rare condition that includes the accumulation of lipid-laden histiocytes in different parts of the body. Xanthogranulomatous inflammation may be found in the skin, retroperitoneum, genitals, brain, and gastrointestinal organs such as the gallbladder[1]. Xanthogranulomatous cholecystitis (XGC) is a chronic inflammatory disease of the gallbladder consisting of multiple yellow-brown intramural nodules that are characterized by extensive fibrosis and foam cells[2,3].

The disease XGC accounts for only 0.7% to 13.2% of all inflammatory disease of the gallbladder. It is usually observed in the sixth to seventh decade in life, primarily in women, and may mimic gallbladder carcinoma[1-8]. The gallbladder wall may appear irregular and thickened, with adhesions to surrounding tissue, and fistulas may develop to adjacent organs. Clinical signs and symptoms are similar to acute and chronic cholecystitis, making it difficult to differentiate XGC preoperatively. Intraoperative frozen section may be required for definitive diagnosis of XGC. If carcinoma is suspected, wide resection is needed. In addition, performing cholecystectomy is more difficult in patients with XGC than without XGC[9-12]. The purpose of this study was to review the treatment and outcomes of patients with the pathologic diagnosis of XGC after cholecystectomy in our center.

Patients and Methods

From February 1997 to May 2010, there were 21 patients with the pathologic diagnosis of XGC after cholecystectomy in our center. The clinical characteristics, imaging results, surgical findings, histopathologic characteristics, postoperative course, and surgical complications were recorded retrospectively. The demographic and clinicopathologic characteristics of 21 patients with XGC are summarized in Table I.

Results

There were 14 men (67%) and 7 women (33%). The mean age of all patients was 65 ± 11.3 years. The clinical signs and symptoms of the patients were nonspecific. There was intermittent, right upperquadrant and epigastric pain noted in 15 patients (71%), positive Murphy sign in 5 patients (24%), fever in 2 patients (10%), jaundice in 1 patient (5%), and signs of cholangitis in 1 patient (5%).

Corresponding Author: Hakan Yabanoglu, MD; e-mail: drhyabanoglu@gmail.com

Table I. Demographic and clinicopathologic characteristics of 21 patients with xanthogranulomatous cholecystitis (XGC).

Parameters	Results	%
Age (mean ± SD) (year)	67 ± 11.3	
Gender		
Male	14	66.7
Female	7	33.3
Symptoms		
Pain	15	71.5
Murphy sign	5	23.8
Jaundice	1	4.8
Fever	2	9.5
Full sign of cholangitis	1	4.8
Ultrasonographic findings		
Cholelithiasis	14	66.7
Adenomyomatosis	2	9.5
Polyp	1	4.8
Acute cholecystitis	5	23.8
Chronic cholecystitis	16	76.2
Surgical history		
Coronary bypass	4	
Total gastrectomy	1	
Nephrectomy	1	

Ultrasonography in 17 patients showed gallbladder stones in 14 patients, adenomyomatosis plus stones in 2 patients, and a polyp was in 1 patient. Acute cholecystitis was noted in 5 patients (24%) and chronic cholecystitis 16 patients (76%). Gallbladder wall thickening was noted in 3 of 12 patients who had computed tomography scans (Figures 1-3); adenomyomatosis was considered in 2 of these 3 patients, and 1 patient was suspected as having gallbladder carcinoma. There was 1 patient who had a perforated gallbladder with a stone.

Complete cholecystectomy was performed in all 21 patients (open in 13 patients and laparoscopic in 8 patients). Laparoscopic cholecystectomy was planned in 15 patients (71%), but open cholecystectomy was performed in 7 of these patients because of intra-abdominal adhesions. In the 6 other patients (29%) who initially had open cholecystectomy without laparoscopy, 2 patients had adenomyomatosis and 1 patient was suspected as having carcinoma. Intraoperative frozen section analysis showed no neoplastic cells in these 3 patients; in 2 patients, malignancy was ruled out, but in the other patient, malignancy could not be excluded and a radical cholecystectomy was performed.

The average hospital stay was 4.3 ± 2.7 days. During laparoscopic cholecystectomy, bleeding occurred intraoperatively in 1 patient (5%); hemostasis was achieved using the appropriate surgical approach. There were 2 patients (10%) who had postoperative wound infection and intra-abdominal abscess, and another 1 patient (5%) who had a wound infection without abscess. In the patients who had infection, 1 patient had perforated cholecystitis, 1 patient had a presumed diagnosis of carcinoma, and 1 patient had chronic cholecystitis with stones. All patients who developed wound infection were discharged from hospital

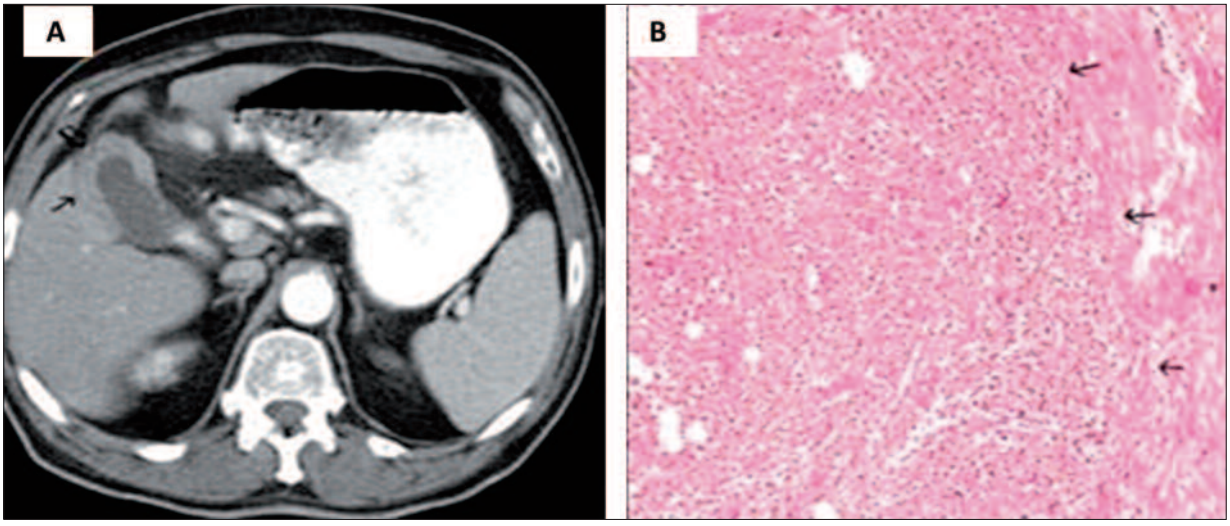

Figure 1. A 54 year-old woman who had xanthogranulomatous cholecystitis (XGC). ***A,*** The computed tomography scan shows gallbladder wall thickening, more prominent at the fundus, and an intramural nodule. ***B,*** Histopathologic findings included an intramural xanthoma in the area described as a nodule on the computed tomography scan (hematoxylin and eosin stain, original magnification ×10).

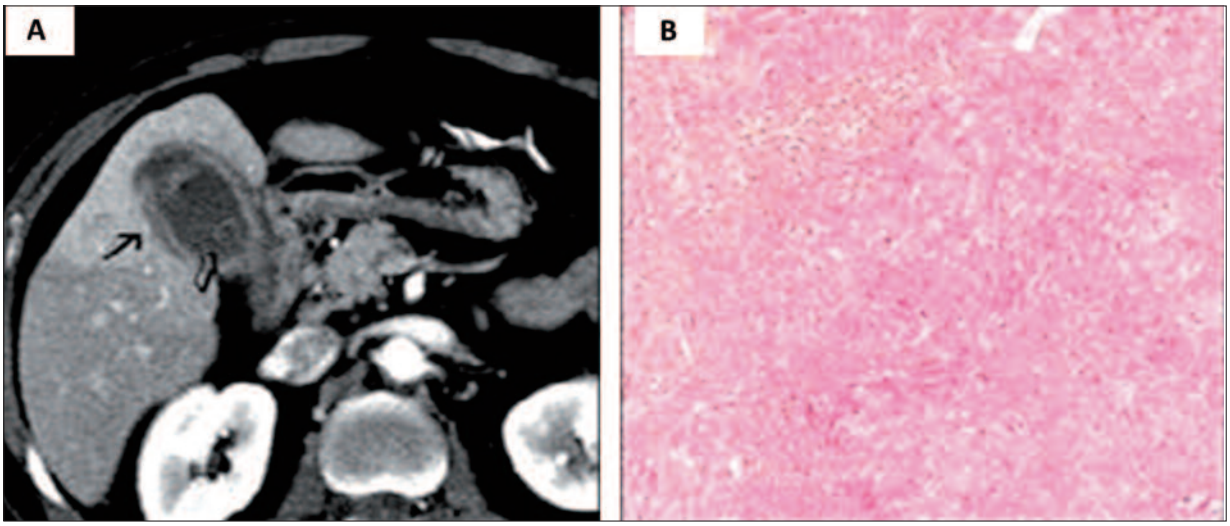

Figure 2. A 56 year-old man who had xanthogranulomatous cholecystitis (XGC). ***A,*** There was diffuse thickening of the gallbladder wall and multiple stones in the gallbladder. ***B,*** Histopathologic findings included inflammation in the gallbladder wall (hematoxylin and eosin stain, original magnification ×10).

after abscess drainage (2 patients) and antibiotic therapy. The type of operation, complications, and follow-up are summarized in Table II.

Discussion

The disease XGC is characterized by severe and chronic intramural gallbladder inflammation with fibrosis and foam cells. It was first reported in 1976 and described as a distinct pathologic condition in 1981[2,3].

The etiopathogenesis of XGC is not fully understood, but current opinion favors acute inflammation of the gallbladder because of calculous outflow obstruction. Bile enters the gallbladder wall through ruptured Rokitansky-Aschoff sinuses or mucosal ulcerations secondary to the presence of gallstones. The extravasated bile in the stroma causes an inflammatory reaction, with accumulation of histiocytes that engulf the insoluble cholesterol and bile lipids to form xanthoma cells. Microab-

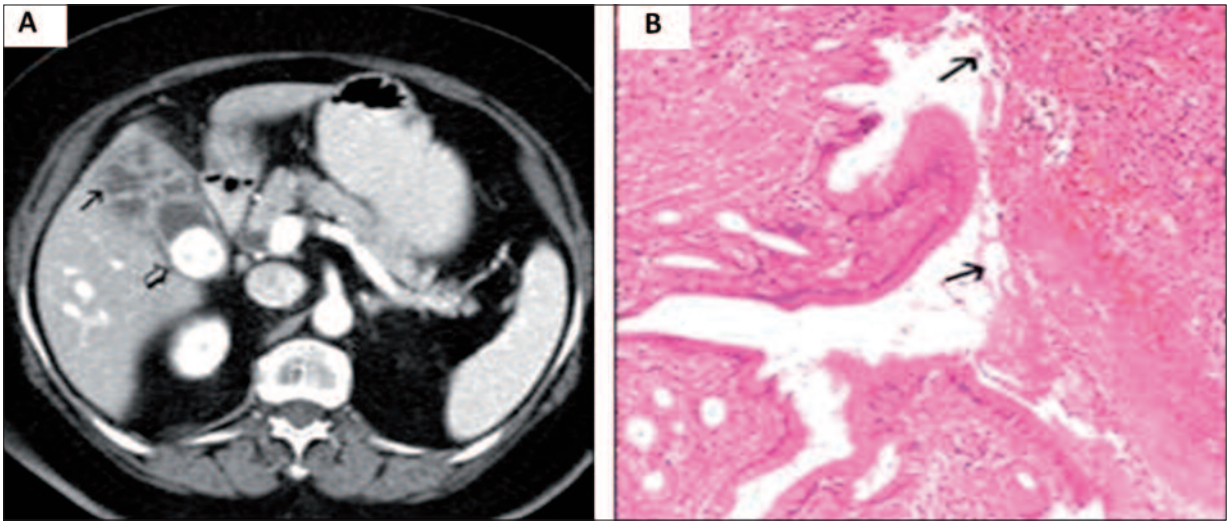

Figure 3. A 75 year-old woman who had xanthogranulomatous cholecystitis (XGC). ***A,*** There was diffuse thickening of the gallbladder wall, with multiple nodular lesions in the gallbladder wall and stones in the gallbladder. ***B***, Histopathologic findings included severe mucosal and submucosal inflammation (hematoxylin and eosin stain, original magnification ×10).

Table II. Surgical treatment, postoperative complications, and follow-up information in 21 patients with xanthogranulomatous cholecystitis (XGC).

Surgical approach and outcomes	Results	%
Open cholecystectomy	6	28.6
Carcinoma suspect	3	
Acute cholecystitis	1	
Previous surgery	2	
Laparoscopy converted to open surgery	7	33.3
Severe adhesions to surrounding tissues	5	
Anatomic ambiguity	2	
Laparoscopic cholecystectomy	8	38.0
Complications	4	
Intra-abdominal bleeding	1	
Superficial wound infection	2	
Deep surgical area infection	1	
Hospital stay (d)	4.3 ± 2.7	
Mortality	0	0.0

scesses can form in the gallbladder wall, resulting in xanthogranulomata. A fibrous reaction follows, resulting in scarring[2,3,6].

The disease XGC is more frequently seen in older patients, as in the present study[1-3,13]. Although XGC usually is more common in women, most of the present patients were men. The association between XGC and cholelithiasis has been noted in 92% to 100% cases[2,3], but cholelithiasis was noted only in 16 of 17 patients (94%) who had ultrasonography in the present study.

It is difficult to differentiate XGC from other gallbladder problems by physical examination, clinical studies, laboratory tests, and radiographic findings. Gallstones and gallbladder wall thickening are common ultrasonographic findings in patients with XGC, but these are not specific. Furthermore, XGC is similar clinically to cholecystitis and may present with nausea, vomiting, right upper quadrant pain, leukocytosis, and a positive sonographic Murphy sign[4,6]. These symptoms and signs are similar to those noted with acute and chronic cholecystitis. There is no specific clinical finding for XGC. Biliary sludge is reported in 35% to 50% patients who have XGC. Although it has been reported that bands in the gallbladder wall and hypoechoic nodules may be characteristic findings, and computed tomography may show gallbladder wall thickening and homogeneous contrast enhancement of the bladder mucosa, these findings are not specific to XGC[4,6,8]. The sensitivity of imaging methods used in the diagnosis of XGC is low; in a study of 33 patients with XGC, initial diagnosis of gallbladder carcinoma was made preoperatively with abdominal ultrasonography in 7 patients (21%) and computed tomography in 5 patients (15%), but the pathologic results were compatible with XGC[1].

Although imaging features of XGC and gallbladder carcinoma can overlap substantially, recent reports have shown that specific computed tomography and magnetic resonance imaging findings, if present, can provide excellent accuracy for the differentiation of XGC and gallbladder cancer[14,15].

Gallbladder cancer has been reported concomitantly in patients with XGC[16,17]. Ghosh et al[17] showed that 6% patients with XGC had associated gallbladder cancer, but the expression of p53, proliferating cell nuclear antigen, and beta-catenin in the areas showing XGC-like morphology were the same as in other patients with XGC. Another report showed that 12% patients had coexisting XGC and gallbladder cancer[16,17].

Preoperative complications of XGC have been reported in 32% of patients. The most common preoperative complications were perforation, abscess, and fistula formation. Chronic inflammation can cause the gallbladder to have wall thickness, and in some cases, can cause Mirizzi syndrome[9,18]. Although adhesions were common, fistula formation and Mirizzi syndrome were not observed in the present patients. However, there were 12 patients (57%) who had adhesions between the gallbladder and surrounding tissues; adhesions were noted intraoperatively in 1 patient who had laparoscopic surgery alone, 4 patients who had open cholecystectomy alone, and 7 patients who had surgery that started with laparoscopy but was completed with open cholecystectomy. Previous studies have reported adhesions in 88% patients[1].

Treatment of choice for XGC is cholecystectomy, either partial or complete. The duration of surgery usually is longer than cholecystectomy for other disorders[1,19,20] because of difficulties in surgical dissection due to surgical adhesions and other concomitant pathology in patients who have XGC. We achieved complete cholecystectomy in all patients. In patients with invasion of the liver bed by the gallbladder or tight adhesions to adjacent structures, the gallbladder wall should be excised as much as possible. When the mucosa cannot be completely excised, the walls of the sac may be cauterized, or iodine may be used to devitalize the sample. Vigorous dissection is avoided to minimize the risk of injury to adjacent organs.

Frozen section examination may be done intraoperatively in patients with suspected carcinoma, and surgery may be modified according to the result. Frozen section examination is not a routine procedure for gallbladder carcinoma because accurate histopathologic results may not be available with a frozen section. In 3 patients with suspicion of carcinoma in our study, intraoperative frozen sections were examined. In 2 patients, malignancy was ruled out, while in the other case, malignancy was present exclusion failed, and a radical cholecystectomy was necessary to be performed. In a previous study, 9 patients had intraoperative suspicion of carcinoma based on appearance of the gallbladder but a wider resection was avoided because of a negative frozen section examination[1]. However, in Japan and the United States, frozen section examinations have shown 10% concomitant occurrence of XGC and carcinoma. This relation is important because carcinoma can be missed when XGC is present concomitantly, and incorrect evaluation of the extent of tumor may result in inadequate surgical resection[2,21].

Although XGC is a benign disease with low mortality, it may cause prolonged hospital stay and may be associated with an increased risk of postoperative complications such as bile leak, biliary peritonitis, wound infection, intra-abdominal abscess, bleeding, and cholangitic stenosis[1,18]. In our study, the average hospital stay was 4.3 ± 2.7 days. No major complications occurred in our patients. Intraoperatively, in 1 patient (4.7%), bleeding occurred during laparoscopic cholecystectomy which was controlled intraoperatively. In 2 (9.5%) patients, wound infection occurred postoperatively. Intra-abdominal abscess was also observed in one of these whereas in one patient (4.7%) only wound infection was seen. Perforated cholecystitis developed in one of these patients, one patient had a presumed diagnosis of carcinoma, and one patient had chronic cholecystitis with stones. All patients were discharged after appropriate drainage and antibiotic therapy.

Conclusions

In summary, XGC is a rare disease that can mimic gallbladder carcinoma. Therefore, gallbladder carcinoma must be excluded as a diagnosis. Intraoperative frozen section specimens must be evaluated by experienced pathologists, and when a suspicious finding is observed, the pathologist may guide the surgeon to perform an adequate resection.

Conflict of Interest

The Authors declare that there is no conflict of interest.

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