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Case Report

Xanthogranulomatous Cholecystitis Masquerading As Gallbladder Cancer: A Diagnostic Dilemma

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Abstract

Xanthogranulomatous cholecystitis is an uncommon variant of chronic cholecystitis, characterized by marked thickening of the gallbladder wall and dense local adhesions that may be confused with a malignant process. In this paper, the authors report a new case of xanthogranulomatous cholecystitis in a 63-year-old female patient that was misdiagnosed per-operatively as gallbladder cancer and treated with extensive excision. The common imaging techniques are not always able to differentiate xanthogranulomatous cholecystitis from gallbladder cancer and the final diagnosis is usually established by histological examination of the resected specimen. This entity should be kept in mind in difficult cholecystectomy cases.

INTRODUCTION

Xanthogranulomatous cholecystitis (XGC) is an uncommon form of chronic cholecystitis characterized by a focal or diffuse destructive inflammatory process, with varying proportions of fibrous tissue, acute and chronic inflammatory cells and accumulation of lipid-laden macrophages in areas of inflammation. It often mimics a gallbladder carcinoma, leading to a diagnostic dilemma [1]. Pre- and intra-operatively, it is difficult to diagnose this entity and the final diagnosis is usually based on histological examination of the resected specimen. In this paper, the authors report a new case of XGC in a 63-year-old woman that was misdiagnosed intra-operatively as gallbladder cancer and treated with extensive excision.

CASE REPORT

A 63 year-old female patient with a medical history of hypertension, was admitted for repeated attacks of right hypochondriac pain. Upon admission, the patient's temperature was 37.5ºC. On physical examination, palpation of the abdomen revealed tenderness in the right upper quadrant and a palpable mass in gallbladder region. In addition, the Murphy's sign was positive. Laboratory findings were within normal range. Abdominal ultrasonographic examination showed multiple gallstones with evidence of gallbladder wall thickening (6 mm) (Figure 1). The preoperative diagnosis was cholecystitis. Initially, a laparoscopic approach was utilized, but adhesions of the gallbladder to the transverse colon and to the liver necessitated conversion to an open procedure. At laparotomy, the gallbladder was suspicious to harbour a malignant tumour as it was firmly adherent to the liver and seemed to invade the transverse colon. The gallbladder was excised by cholecystectomy with adjacent liver wedge resection and right hemicolectomy. Macroscopically, the gallbladder specimen measured 13 x 8 cm and was adherent to the colon (Figure 2). The cut section findings of the gallbladder showed some gallstones with a markedly thickened wall suspicious of malignancy.

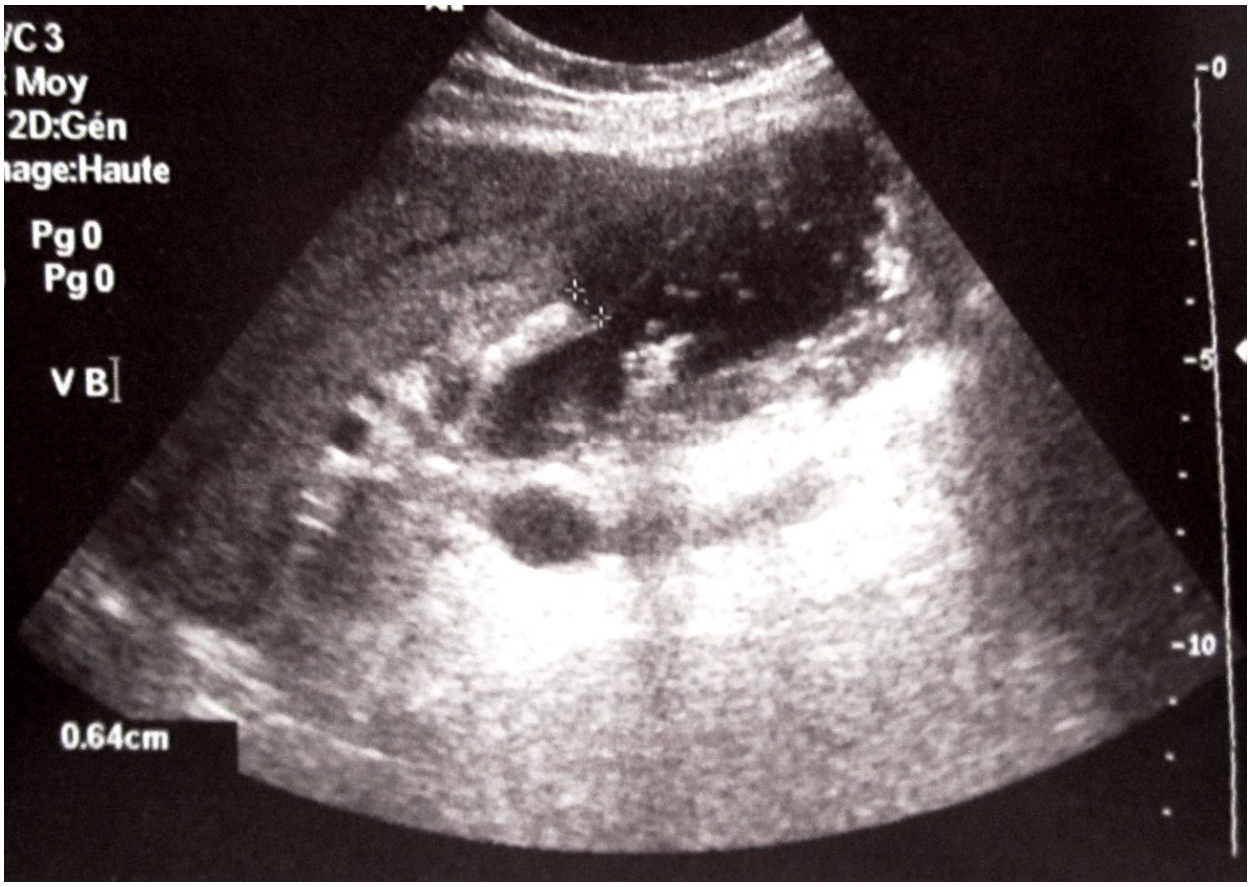

Figure 1. Abdominal ultrasonographic examination displaying multiple gallstones with evidence of gallbladder wall thickening (6,4 mm).

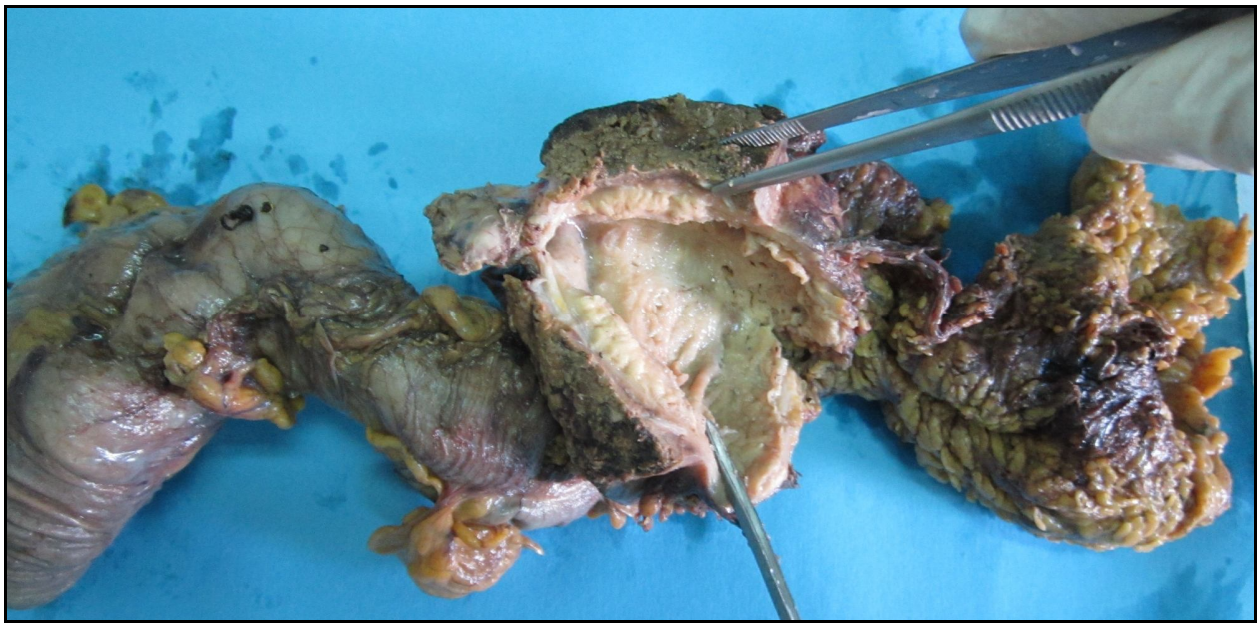

Figure 2. Macroscopic examination revealed that the gallbladder was firmly bound to the colon by dense fibrous adhesions.

Histological examination of the gallbladder specimen revealed focal ulceration of the mucosa with severe chronic inflammation of the lamina propria and submucosa, associated with mild fibrosis and muscular hypertrophy (Figure 3). Numerous foamy macrophages and scattered multinucleated giant cells were also present, along with occasional cholesterol clefts (Figures 4 and 5). This inflammatory infiltrate extended to the colonic submucosa (Figure 6). Immunohistochemical study showed intense and diffuse positive immunostaining of macrophages for CD 68 (Figure 7). The final pathological diagnosis was XGC. Postoperative course was unremarkable. The patient was well after a two-month follow-up period.

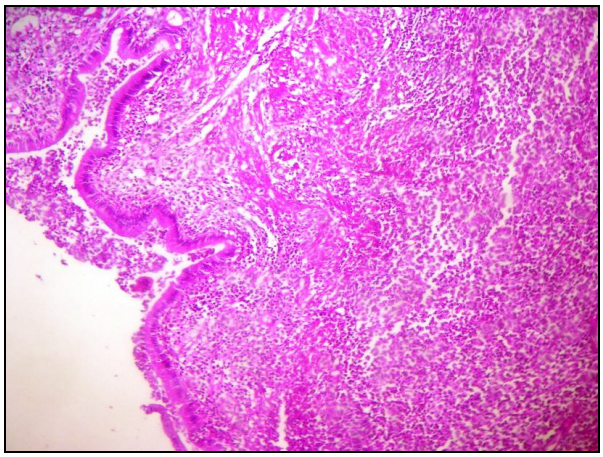

Figure 3. Photomicrograph showing thickening of the gallbladder wall that harbours a dense and polymorphous inflammatory infiltrate (H&E, original magnification; x 200).

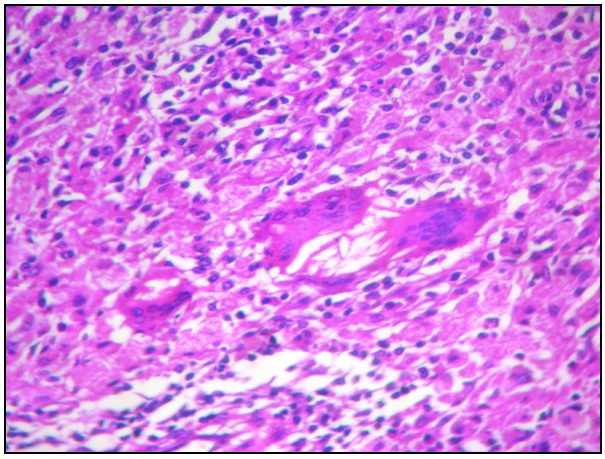

Figure 4. Multinucleated giant cells admixed with foamy histiocytes and chronic inflammatory cells (H&E, original magnification; x 400).

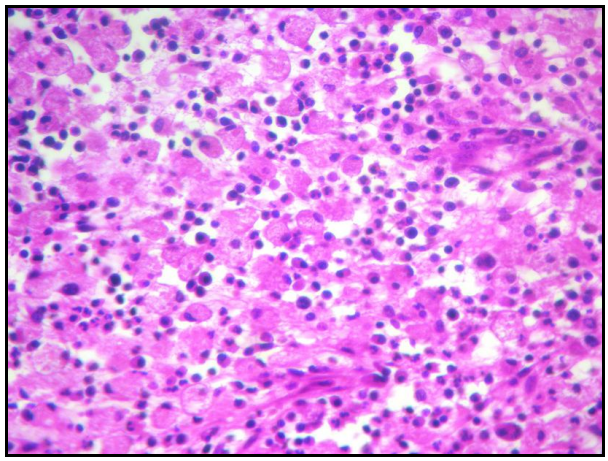

Figure 5. Foamy histiocytes are present with plasma cells and neutrophils (H&E, original magnification; x 400).

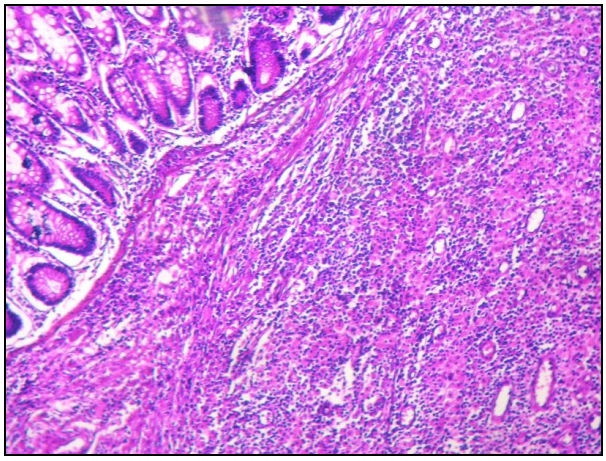

Figure 6. The inflammatory process extended to the submucosa of the colon (H&E, original magnification; x 200).

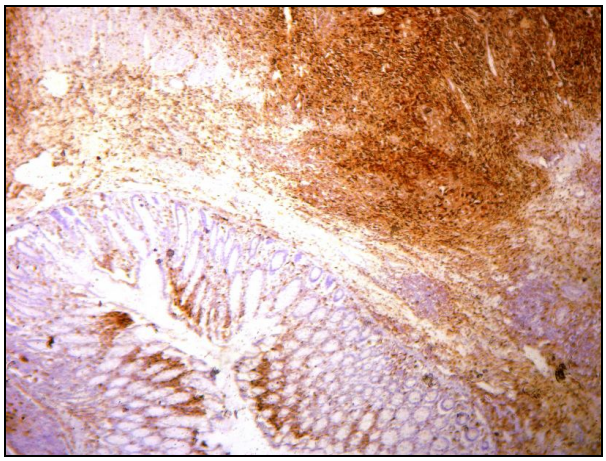

Figure 7. Foamy histiocytes of the colonic submucosa showed intense and diffuse positive immunostaining with CD 68 (Immunohistochemistry, original magnification; x 100).

DISCUSSION

Xanthogranulomatous cholecystitis is an uncommon form of chronic cholecystitis, representing between 0.7% and 13.2% of gallbladder disease [2]. There is an association with obesity and diabetes in some series, and most patients present in the sixth and seventh decades of life [3, 4]. Our patient was 63 years old. Clinically, no symptoms and signs are specific for XGC and they are similar to those of acute and chronic cholecystitis. On examination, less than one-half of patients have a palpable right upper quadrant mass as it was the case in our patient [4]. The preoperative diagnosis of XGC with imaging techniques is difficult; however, the presence of hypo-echoic nodules or bands in a thickened gallbladder wall together with stone on ultrasonography or a hypo-dense band around the gallbladder on CT is highly suggestive of the disease [3, 4, 5]. The pathogenesis of XGC is not entirely clear, but attention has focused on the role of mucosal ulceration and rupture of Rokitansky-Aschoff sinuses, with extravasation of bile into the interstitium and secondary mixed inflammatory response. Rupture of the gallbladder serosa may occur, with extension of the disease process to the adjacent liver and bowel. A significant localized fibrous reaction may also occur [2, 4-7]. Operative strategy of XGC varies from the subtotal cholecystectomy to extended cholecystectomy, including all the adjacent xanthogranulomatous tissue. In the radical approach, a possible association of XGC with adenocarcinoma of the gallbladder is taken into account. The adhesions, which are commonly present, often increase the complication rate and the operating room time [3]. According to some authors, preoperative fine needle aspiration biopsy and intra-operative frozen section are valuable tools for differential diagnosis when there is no invasion of adjacent organs, otherwise they would not influence the surgical strategy [8, 15]. In our case, neither fine needle aspiration biopsy nor intra-operative frozen section was performed. To the best of our knowledge, only seven cases of extended surgical resections for XGC have been reported so far (Table 1).

Table 1: Characteristics of the patients with XGC who underwent extended surgical resections: Literature review

Author/year	Age/sex	Symptoms	Tumor markers	Involvement	Performed resection	Follow-up
Okamoto (1990) [9]	70 / F	Fever, general malaise	CA19.9 ↑, CEA normal	Liver, bile duct, transverse colon	Cholecystectomy, local atypical liver resection, bile duct resection and transverse colectomy	Uncomplicated postoperative course, alive 6 months after surgery
Maeda (1994) [10]	75 / F	No complaints	CA19.9↑, CEA normal	Liver bed and transverse colon	Cholecystectomy with local atypical liver resection and transverse colectomy	Uncomplicated postoperative course, follow-up not reported
Furuta (1996) [11]	46 / M	Epigastric pain	CA19.9 and CEA normal	Liver, bile duct, duodenum, right hepatic artery, right portal vein	Right hepatectomy and pancreatoduodenectomy	-
Natori (1997) [12]	55 / M	No complaints	CA19.9 normal, CEA↑	Liver (gallbladder bed) and bile duct	Cholecystectomy with local atypical liver resection and bile duct resection	-
Enomoto (2003) [13]	64 / M	High fever , hypochondralgia	CA19.9 and CEA normal	Liver, bile duct, duodenum, transverse colon, right hepatic artery and right portal vein	Right hepatectomy, pancreatoduodenectomy and transverse colectomy	Uncomplicated postoperative course, alive 4 years after surgery
Pinocy (2003) [14]	64 / M	Hypochondralgia, fever	-	Right colonic flexure	Cholecystectomy and resection of the right colonic flexure	-
Spinelli (2006) [15]	46 / F	Epigastric pain, sense of fullness, jaundice	CA19.9↑, CEA normal	Right liver, right colonic flexure, second duodenal portion	Right hepatectomy, partial duodenectomy and right hemicolectomy	Uncomplicated postoperative course, alive 1 year after surgery
Present case (2012)	63 / F	Right hypochondriac pain	-	Liver bed and transverse colon	Cholecystectomy,Liver (gallbladder bed) and right hemicolectomy	Uncomplicated postoperative course

In these cases, additional procedures such as bile duct resections, segmental resections of colon or duodenum, partial pancreatoduodenectomies have been performed. It can be discussed if such extended surgical procedures could be avoided in presence of a benign disease. Our patient exhibited severe, destructive, tumour-like xanthogranulomatous inflammation, with extensive invasion of adjacent organs (right lobe of the liver, colon). On gross examination of the gallbladder in XGC, stones are identified in most cases, along with irregular wall thickening and poorly demarcated yellow or brown nodules of varying sizes associated with mucosal ulceration. The lesion may be extensive, with formation of fistulas from the gallbladder to the duodenum or skin. Culture of fluid obtained from the gallbladder lumen may yield growth of E. coli, Klebsiella and Enterococcus [3, 5, 6]. Histologically there is a mixture of different cells, but the predominant cells are foamy histiocytes. Lypmphocytes and plasma cells are also present. Sometimes multinucleated giant cells are present, along with occasional cholesterol clefts. Histiocytes may contain bile or ceroid pigment. There is often some fibrosis, and plump spindle cells may align in a vague storiform arrangement. It has been reported that gallbladder carcinoma can be seen as a coexistent lesion with XGC in 2% to 35.4% of the cases [2, 5].

In summary, a case of XGC is reported along with pathological findings. Pre- and intra-operatively, it is difficult to diagnose this entity but it should be kept in mind in difficult cholecystectomy cases. Because of its overlapping clinical, radiological and macroscopic findings with gallbladder cancer, definitive diagnosis of XGC relies on extensive sampling and thorough microscopic examination coupled with immunohistochemical investigation to exclude the possibility of coexisting tumour.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article is reported.

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