

A case report of Xanthogranulomatous Cholecystitis – A Rare Entity

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Abstract

Xanthogranulomatous cholecystitis is a benign, uncommon type of chronic cholecystitis manifested by focal or diffuse severe inflammatory process of the gallbladder (GB). It is inflammatory disease of the gallbladder characterized by the infiltrations of plasma cells, lipid-laden histiocytes, and the fibroblasts proliferation in GB wall. Gallstones are present in all patients, and like most symptomatic gallbladder diseases, there is a female predominance. It is an active inflammatory process which could leads to significant morbidity. The term Xanthogranulomatous cholecystitis was initially proposed by Goodman and Ishak in 1981. 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. Macroscopically, it appears like yellowish masses in the wall of the GB. Radiologically it is an important mimic of gallbladder carcinoma.

Key words: Xanthogranulomatous cholecystitis, gallbladder MRI, GB carcinoma, Chronic cholecystitis.

Introduction:

Xanthogranulomatous cholecystitis (XGC) is a rare and chronic inflammatory condition of the gallbladder, a unique entity first described by Christensen and Ishak in 1970. [1]

It is characterized by destructive inflammation, the formation of xanthogranulomas, lipid-laden macrophages, multinucleated giant cells, and fibrosis. [1, 2]

The pathogenesis of XGC remains unclear but is thought to involve gallbladder obstruction, infection, and subsequent bile extravasation, leading to a chronic inflammatory response. Clinically and radiologically, XGC often mimics gallbladder carcinoma, presenting with nonspecific symptoms such as right upper quadrant pain, jaundice, and a palpable mass. [3]

Imaging findings, including thickened gallbladder walls and mass-like lesions, further complicate the differentiation between XGC and malignancy. This diagnostic overlap frequently results in the need for surgical intervention to confirm the diagnosis.[4, 5]

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Case presentation

Our case is a 69-year-old male with recurrent attacks of upper abdominal pain for more than 10 yrs. There is also history of weight loss of 9 kg over 2 months, loss of appetite, decreased activity and generalized weakness. No history of jaundice or fever. On examination there is suspected mass in the RUQ which is tender on palpation. Patient did US abdomen in private clinic that showed GB wall thickening.

Investigations.

IMAGING: MRI Abdomen and MRCP:



Figure 1 Shows distended GB with thickened wall and high signals intramural pockets.

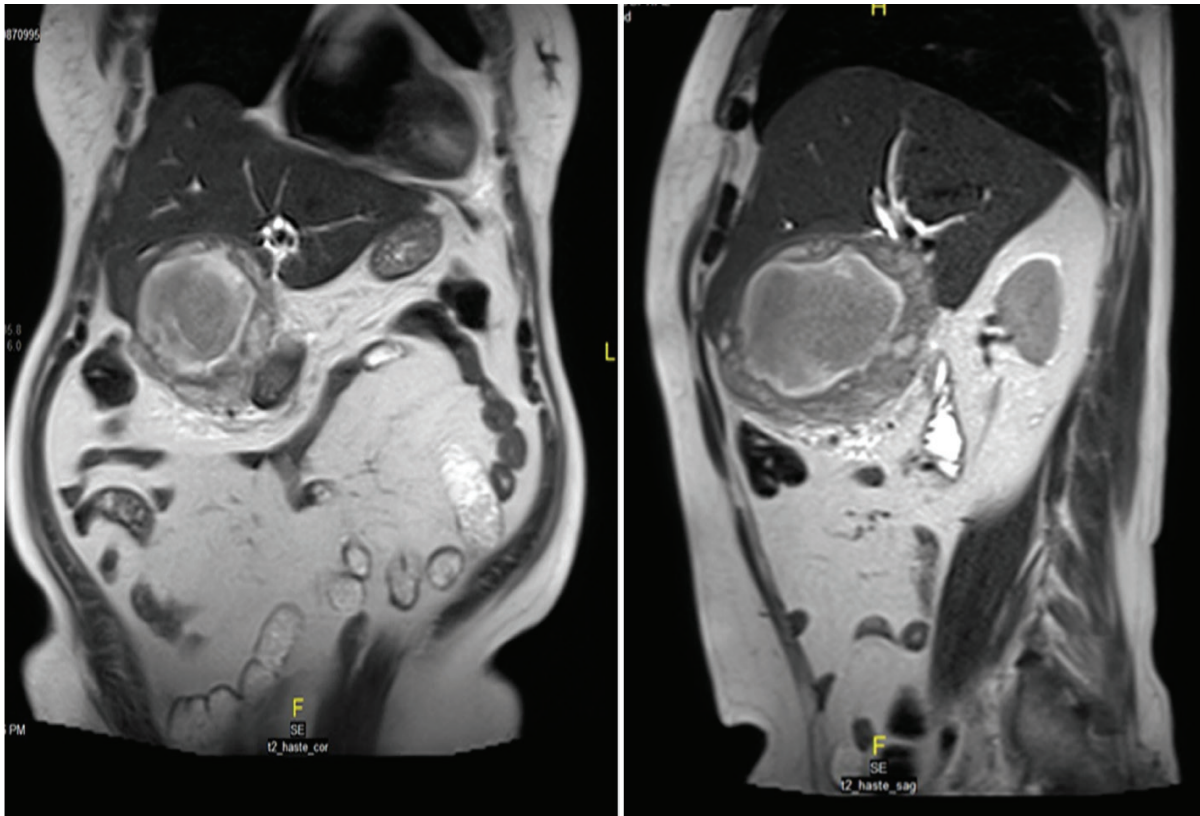


Figure 2 T2 WI Coronal and Sagittal, re-demonstration of distended, thick G.B wall with high signal intramural pockets. Blurring of interface between GB and liver. Pericholecystic edema and fat stranding. Mild intrahepatic biliary radicles dilatation.

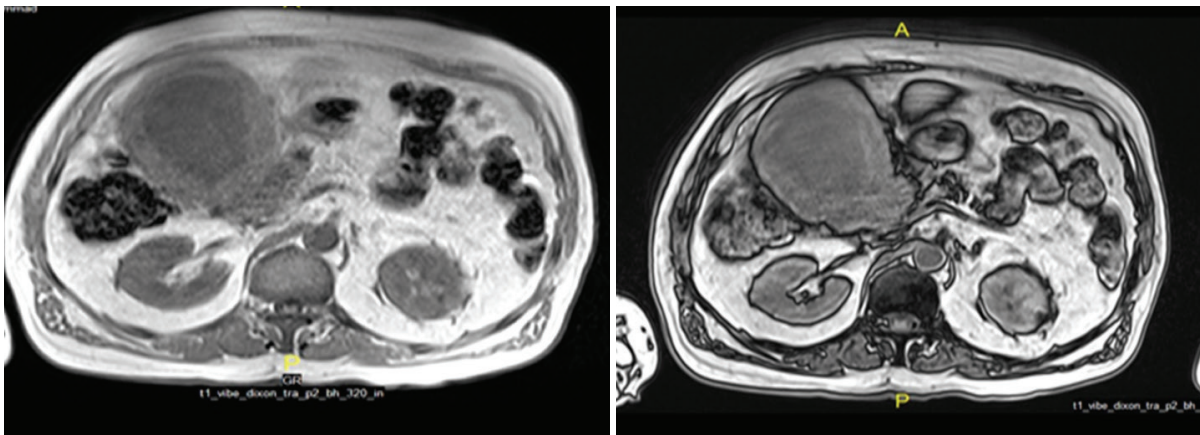


Figure 3 IN and OUT phase revealed absence of fat contents.

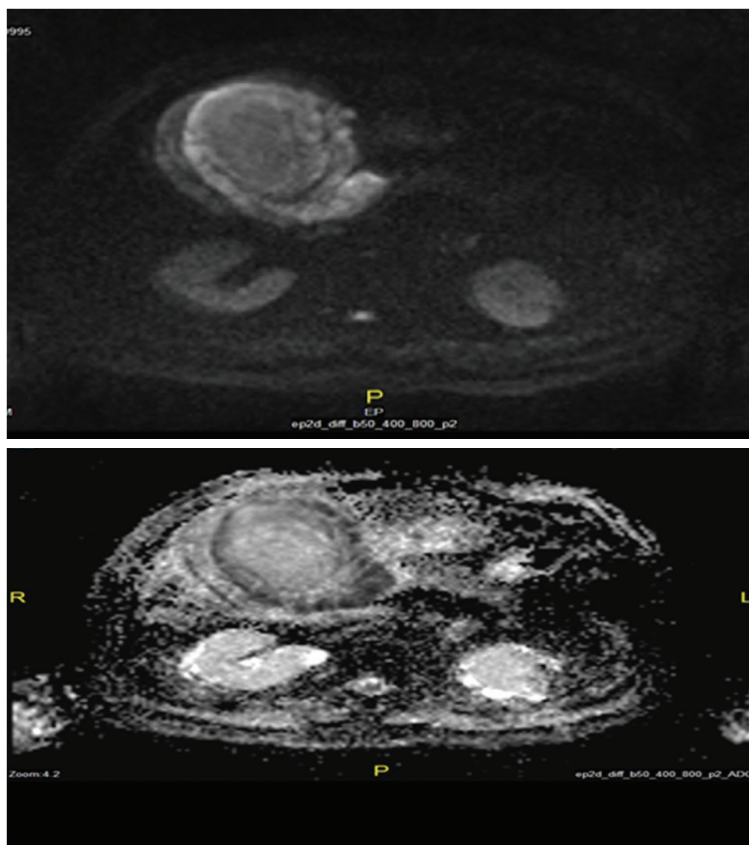


Figure 4 DWI and ADC revealed restricted diffusion of the pockets (abscesses) without restriction of septae between it.

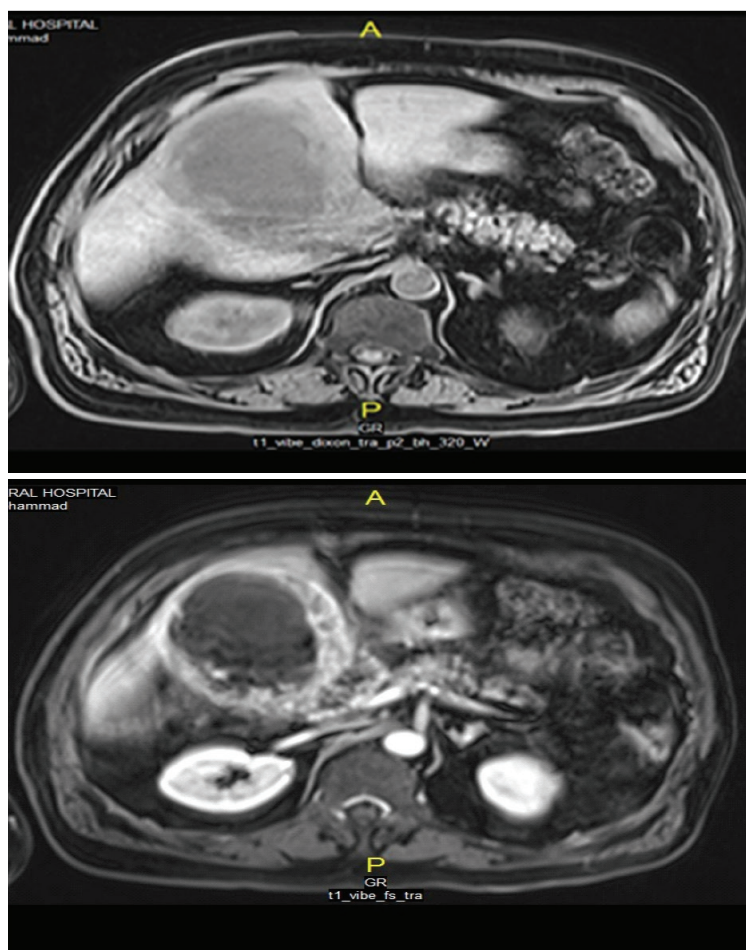


Figure 5 Pre and Post contrast revealed enhancement of the gall bladder wall without washout. The pockets are not enhanced.

LABS: Laboratory investigations were normal except elevated liver function tests (LFTs) that showed aspartate aminotransferase 54 UI/L, alanine aminotransferase 39 UI/L, total bilirubin 45.7 $\mu\text{mol/L}$, direct bilirubin 17.4 $\mu\text{mol/L}$.

Differential diagnosis

Primary GB carcinoma was the main concerning differential.

Acute or chronic cholecystitis and acute cholangitis.

Treatment

Laparoscopic cholecystectomy was converted to an open cholecystectomy with liver resection due to extensive adhesions.

Outcome

Surgical pathology revealed

- Acute suppurative and hemorrhagic cholecystitis on top of Xanthogranulomatous cholecystitis.
- Benign hepatic tissue is identified, shows steatosis.
- Negative for dysplasia or malignancy.

Discussion

This patient presented with intermittent RUQ pain with tender palpable mass. However, there was no jaundice or fever. Only 20% of patients with Xanthogranulomatous cholecystitis (XGC) manifested with obstructive jaundice which is not a frequent presentation [1]. XGC is an uncommon variant of chronic cholecystitis characterized by xanthogranulomatous inflammatory changes of the GB. Intramural accumulation of lipid-laden macrophages, acute and chronic inflammatory cells is the main features [1]. XGC could be severe and spill over to the adjacent organs as liver, bowel and stomach resulting in dense adhesions, perforation, abscesses, fistulous communication with adjacent bowel. XGC is an uncommon, focal, or diffuse destructive inflammatory process of the GB. This issue was first described in 1970 by Christen and Ishak as fibroxanthogranulomatous inflammation [2]. Recently, these terms, as ceroid granuloma, ceroid-like histiocytic granuloma of the GB [3] and biliary granulomatous cholecystitis [4], have been abandoned in favor of XGC, a descriptive term first used by McCoy et al [5]. McCoy et al [6] in 1976 though it was first described in 1970 by Christensen et al [7]. Christensen et al [7] and Amazon et al [8] had observed a pseudo tumoral expression of chronic cholecystitis which was specified by the xanthoma-like foam cells, scarring and contained ceroid (wax-like) nodules in an inflamed GB wall. XGC is manifested by irregular GB wall thickening with formation of yellowish nodules which composed of lipid-laden macrophages, inflammatory cells, and fibroblasts. The pathogenesis is chronic inflammation and gallstones are present in most of the patients. XGC

could mimic GB cancer or results in complications such as perforation, abscess, and fistula.

In 78–98% of XGC cases, gallstones are noted [11], obesity and/or diabetes mellitus are common [10]. The pathogenesis of XGC could suggested that the extravasation of bile into the GB wall, either from ruptured Rokitansky-Aschoff sinuses or focal mucosal ulceration [3,9]. Gallstones obstruction and intraluminal bile stasis also involved [12].

Patients can present with features of acute cholecystitis (22%), chronic cholecystitis (88%), pain (95%), obstructive jaundice (22%), cholangitis (2%) and palpable mass (5%) [13]. On examination, a palpable mass or positive Murphy's sign could be localized. However, these clinical features are not specific for XGC and often no clinical difference between XGC and GB carcinoma [14].

Complications in about 32% of cases including perforation, abscess formation, fistulous tracts to the duodenum or skin, and extension of the inflammation to the liver, colon, or surrounding soft tissues [15]. Yu et al [16] stated that elevation of tumor biomarkers could happened in XGC which added further confusion in differentiating XGC with GB carcinoma.

XGC is connected with GB carcinoma in 8.5% - 30.5% of cases [17].

Possibility of coexisting infection has also been proposed. Howard et al [21] have stated that intraoperative cultures of the bile and GB was positive for *Escherichia coli*, *Klebsiella*, *Enterococcus* and, less frequently, *Pseudomonas*, *Serratia* and *Staphylococcus aureus*.

Parra et al [22] observed that the wall thickening was hyperechoic in comparison to the liver in 100% of patients examined by ultrasound. The presence of hypoechoic nodules or bands in the thickened GB wall could be seen. The sonographic hypoechoic nodules were reported in 15% and 73% cases by Parra et al [22] and Kim et al [23] respectively. Hypoechoic band was reported in 19% of cases [22,24]. Hypoechoic bands could be result from generalized involvement of the mucosa [22]. Complications as perforation, abscess and hepatic infiltration could be assessed on ultrasound [22,23].

CT findings of patients presenting with acute symptoms and patients presenting with chronic symptoms are usually not much different [25]. CT findings including diffuse or focal wall thickening, luminal surface enhancement (LSE) with continuous mucosal lines or mucosal lines with focal breach and intramural hypoattenuating nodules in the thickened walls. Cholelithiasis and choledocholithiasis are often found.

GB thickened wall from 4.0 mm to 18.5 mm and is usually diffuse [25]. Diffuse GB wall thickening has been seen in 88.9% and 87.8% of patients by Goshima et al [26] and Zhao et al [25] respectively. Focal thickening is less common in XGC, and is more with GB carcinoma. Diffuse thickening is usually symmetrical but diffuse asymmetrical thickening has also been found in 22.2% cases [25,26].

The intramural nodules (85.7% and 61.1%) by Zhao et al [25] and Goshima et al [26] respectively) are either xanthogranulomas or abscesses. A large area of the thickened GB wall by intramural nodules is highly associated with XGC [27]. XGC is more often revealed on imaging than abscesses as the abscess results in more complications [19].

A continuous mucosal lining is more seen with XGC (66.7% of cases) in comparison with disrupted mucosal line (33.3%) [26]. XGC is abnormalities of GB wall and hence mucosal surface is intact or only focally denuded. On the other hand, GB carcinoma arises from the GB epithelium and induces mucosal disruption in most of the cases. Mucosal disruption was observed in 82.2% cases of GB carcinoma. Mucosal disruption in XGC is only seen with diffuse thickening of the GB wall and patients with disrupted mucosal lining are more prone to have complications [25].

The infiltration of adjacent structure scan manifest as pericholecystic fat strandings, blurring of interface between liver and GB, early enhancement of liver (or transient hepatic attenuation difference), infiltration of bowel (duodenum/colon), infiltration of stomach and invasion of abdominal wall. While pericholecystic fat stranding and blurring of interface between liver and GB are common, the other findings are less appreciated.

Hepatic infiltration appears as an early parenchymal enhancement in 40% of cases [25]. Other complications are GB perforation, abscesses or fistulations. Inflammation of the biliary tree (xanthogranulomatous cholechochitis) could be seen [29]. However, lack of dilated intrahepatic biliary is more seen in XGC and it could differentiate it from GB carcinoma.

Lymphadenopathy (> 10 mm short axis diameter) has been mentioned by different studies. Zhao et al [25] stated an incidence of 10.2%, Goshima et al [26] stated an incidence of 90%. However, both studies stated that regional lymphadenopathy could be useful in differentiation from GB carcinoma. 41% patients with GB cancer showed homogeneous enhancement of enlarged lymph nodes in comparison to 100% of XGC [26].

MRI, In-phase and out-of-phase chemical shift imaging demonstrating fat within the thickened gallbladder wall in XGC [20]. Zhao et al [25] subjected intramural nodules to chemical shift imaging. 77.7% of XGC nodules displayed reduction of signal intensity on opposed -phase images. This variability of the intramural nodule on MRI could be due to the presence of different contents as foamy histiocytes, lymphocytes, plasma cells, polymorphonuclear leucocytes, fibrosis, giant cells, micro abscess and necrosis within these nodules [26].

Areas of iso- to mildly high signal on T2 WI, displaying mild enhancement in early phase and intense enhancement in delayed phase, consistent with areas of excessive of xanthogranulomas [28]. Areas with very high signal intensity on T2 WI without enhancement matched with necrosis and/or abscesses [28].

Enhanced areas in the liver bed in early phase on CT and MR images could be associated with XGC which consistent with accumulation of inflammatory cells and extensive fibrosis [28].

A study by Binit Sureka, et al, 2017, stated that the majority of cases (73.3%) showed discontinuous mucosa. 75% were found with thickened wall 3–10 mm and 0% normal wall thickness ($p=0.03$). Diffuse thickened wall in 76.7%, focal thickening in 10% and polypoidal thickened wall in 6.7% cases. Intramural nodules with discontinuous mucosal lining in 87.5%.

The study concluded that, discontinuous mucosal lining is evident in XGC. Diffuse thickened wall, intramural nodules, continuous or discontinuous mucosa and Gall stones could suggest XGC rather than GB cancer [30].

Kang et al [43] have showed the value of diffusion-weighted magnetic resonance imaging (DWI) in differentiating XGC from GB wall-thickening type of cancer. DWI restriction was founded in GB cancer (68%) and in XGC (7%). Also, the mean ADC value of XGC was higher than GB cancer wall-thickening type with statistical significance ($1.637 \times 10^{-3} \text{ mm}^2/\text{s}$ vs $1.076 \times 10^{-3} \text{ mm}^2/\text{s}$ respectively, $P = 0.005$) [31]. The study concluded that DWI in addition to routine MRI improves differentiation between XGC and wall-thickening of gallbladder cancer.

It was concluded that coexisting of diffuse gallbladder wall thickening, low-attenuated intramural nodules, continuous mucosal line, mucosal enhancement and gallbladder stone highly suggest XGC. XGC commonly infiltrating the liver and surrounding fat. Chemical-shift MRI helps classifying intramural nodules in the gallbladder wall.

Abbreviations; US – Ultrasound; RUQ - Right Upper Quadrant; GB – Gallbladder; MRI - Magnetic Resonance Imaging; MRCP - Magnetic Resonance Cholangiopancreatography; LFTs - Liver Function Tests; LABS- Laboratory; RUQ - Right Upper Quadrant; XGC - Xanthogranulomatous Cholecystitis;

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