

Xanthogranulomatous cholecystitis: A malignant mimicker

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ABSTRACT

Xanthogranulomatous cholecystitis (XGC) is a rare, chronic inflammatory disease of the gallbladder (GB) that often mimics GB carcinoma clinically, radiologically, and intraoperatively. Its accurate diagnosis is critical to avoid unnecessary extensive surgery. A 71-year-old female presented with diffuse abdominal pain and intermittent fever for 2 months. Imaging (magnetic resonance cholangiopancreatography and contrast-enhanced computed tomography) revealed irregular thickening of the GB wall with a rent in the fundus and pericholecystic collection, suggesting a neoplastic etiology. A diagnostic laparoscopy with radical cholecystectomy was performed due to high suspicion of carcinoma. Gross examination showed a thickened, ragged GB wall infiltrating into the liver. Histopathology revealed mucosal denudation, subepithelial fibrosis, foamy histiocytes, and chronic inflammatory infiltrates, confirming the diagnosis of XGC. No malignancy was identified. The patient recovered uneventfully and remained asymptomatic at 9-month follow-up. XGC is a benign but aggressive inflammatory condition that can closely resemble GB cancer. Histopathological examination remains the gold standard for diagnosis. Awareness of this entity is essential to guide appropriate surgical management and avoid overtreatment.

Key words: Carcinoma, Cholecystitis, Gallbladder, Xanthogranulomatous

Xanthogranulomatous cholecystitis (XGC) was first described as a benign pseudotumor of the gallbladder (GB) in 1970 by Christensen and Ishak [1]. The term XGC was proposed by McCoy *et al.* in 1976 [2]. XGC is a rare inflammatory disease of the GB characterized by abnormal wall thickening and severe proliferative fibrosis with the formation of multiple yellow–brown intramural nodules. The incidence ranges from 0.7 to 10% of all the cholecystectomy specimens, with predominance in the elderly age group of 60–70 years, with a male-to-female ratio of 2:1 [3]. Due to the thickening, extensive fibrosis, and adherence to surrounding structures, it is often difficult to differentiate XGC from carcinoma of the GB and poses a diagnostic dilemma.


Here, we present the case of a 71-year-old female with XGC who was managed with laparoscopic cholecystectomy as a mimicker of carcinoma GB. This case is presented for its rarity and to emphasise the importance of a high degree of suspicion of XGC in a radiologically and clinically suspicious case of carcinoma GB, and to highlight the importance of histopathology as the gold standard for diagnosis.

CASE REPORT

A 71-year-old female presented with diffuse abdominal pain for 2 months to the surgical outpatient department. The pain was dull, moderate in intensity, and continuous in nature in the right upper quadrant (RUQ) with radiation to the back. The pain did not have any aggravating or relieving factors. There was also a history of intermittent fever during this period, which was relieved by medication. There was no past history of hypertension, diabetes mellitus, immunocompromised state, or other comorbid conditions. There was no relevant history of drug usage.

On examination, the patient had a body mass index of 22.5 with a pulse of 82/min, blood pressure of 130/50 mm Hg, and a Spo₂ of 98%. On per abdominal examination, a mass was palpated in the right hypochondrium.

Ultrasonography revealed diffuse thickening of the GB wall, suggesting a neoplastic cause. Magnetic resonance cholangiopancreatography revealed a thickened and irregular GB wall with altered signal intensity at the fundus and neck regions, with a possibility of neoplastic etiology. A contrast-enhanced computed tomography was done, which showed a rent in the GB at the fundus and body with adjacent non-enhancing hypodense collection

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and pericholecystic mesenteric fat stranding and focal suspicious wall thickening in the neck of the GB, and suggested a carcinoma of the GB.

With this diagnosis, a diagnostic laparoscopy along with radical cholecystectomy was planned. Intraoperatively, the GB wall thickness of 1.8 cm was noted with yellowish nodules on the wall. No gallstones were noted. There were dense adhesions to the adjacent structures, including the liver.

A cholecystectomy specimen with attached liver was received for histopathological examination. The GB measured $8 \times 5 \times 2.5$ cm, and the adherent liver measured $7 \times 5 \times 1.5$ cm. The surface of the GB was ragged with attached fat, yellow nodules, and necrotic tissue (Fig. 1a). On the cut section, the wall was irregularly thickened with a maximum thickness of 1.7 cm (Fig. 1b). The wall appeared to be infiltrating into the liver parenchyma. The lumen was filled with solidified mucoid material. The liver appeared grossly normal. A single lymph node was identified at the neck of the GB and measured $1 \times 0.6 \times 0.5$ cm with a gray–white cut surface.

On histopathological examination, sections studied from the GB showed focal denudation of mucosa with extensive subepithelial fibrosis (Fig. 2a) and sheets of foamy histiocytes admixed with chronic inflammatory cell infiltrate composed of lymphocytes and plasma cells (Fig. 2b). Fibrosis was seen extending into the hepatic parenchyma. The rest of the liver appeared unremarkable. Sections studied from the lymph node revealed reactive lymphadenitis. Based on these findings, a final diagnosis of XGC was offered. Nine months after surgery, the patient was asymptomatic and in good health.



Figure 1: (a) Gross image of the gallbladder shows a thickened wall with yellowish nodules and attached liver, (b) Cut section shows thickened gallbladder wall along with attached liver parenchyma

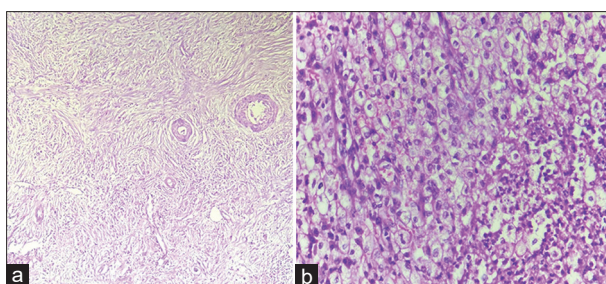


Figure 2: Microscopic image shows (a) gallbladder wall with extensive areas of fibrosis ($\times 40$, H&E), (b) sheets of foamy macrophages within the wall of the gallbladder ($\times 40$, H&E)

DISCUSSION

Cholecystectomy is one of the most common surgical specimens received for histopathological examination. The most common indication is cholecystitis secondary to cholelithiasis, with a global incidence of 6% [4] and an incidence of 4% in India [5]. India is also a high-incidence area for GB cancer (GBC) and contributes to about 10% of the global GBC burden [6]. XGC is an inflammatory disease of the GB characterized by obliterative fibrosis and the presence of foam cells. The prevalence of XGC ranges from 1.3 to 1.9% in Europe and the Americas and soars up to 8.8% in India [7]. The exact etiology of XGC is not known, though it is widely attributed to gallstones and bile leakage into the GB wall. The disease presents with features of acute or chronic cholecystitis with RUQ pain, nausea, vomiting, jaundice, and anorexia, though none are specific for it. The standard treatment of XGC involves open cholecystectomy because of dense fibrous adhesions, excessive inflammation, and risk of concurrent malignancy [8]. Pandey *et al.* suggested in 2019 that all asymmetrically thickened GB walls be treated as suspicious unless proved otherwise [9].

XGC is a mimicker of carcinoma of the GB clinically as well as radiologically. The clinical presentation of carcinoma is similar to XGC. Due to the non-specific nature of symptoms, diagnosis often relies on imaging studies and histopathological diagnosis. However, there are no definite radiological or serological markers to distinguish between the two entities with certainty. Fine needle aspiration cytology or intraoperative frozen section may be of some value, but the spillage in case of carcinoma GB remains a major risk, and there is also a 2% chance of coexistence of the two pathologies [8]. Therefore, distinguishing the two conditions is challenging, and histopathological diagnosis is paramount. The clinicoradiological differential diagnosis of XGC, besides carcinoma GB, may include acute cholecystitis, chronic cholecystitis, or cholangitis adenomyomatosis [10].

Feng *et al.* [8] in their study of 50,005 cholecystectomies found 100 cases of XGC. Clinically, patients most frequently presented with chronic and acute cholecystitis. Within these 56% presented with RUQ pain, 27% with hyperpyrexia, and a RUQ mass was found in 6% of the cases, and an elevated WBC count in 30% similar to our case. Lei Deng *et al.* also found pain in the RUQ to be the most common presentation [11]. The GB wall thickness of 5–9 mm has been suggested in various studies, and this point toward a chronic etiology. Choleliths are generally present in XGC but were not seen in our case, as also reported by Rahman *et al* [12].

The etiopathogenesis in XGC suggests obstruction to bile flow by gallstones. Cholestasis results in extravasations of bile into the GB wall. This starts an inflammatory process, with the involvement of Rokitsky–Aschoff sinuses, leading to the formation of submucosal abscesses or xanthogranulomas. This leads

to fibrous reaction and dense scarring from the healing of the inflammatory reaction. The inflammatory reaction may be associated with the development of a fistula between the GB and adjoining structures [13].

Grossly, the GB is thickened with fibrous adhesions and yellow nodules or streaks. The thickness of the GB is a consistent feature as found in most studies, including ours [7, 11, 12]. Pre-operative differentiation of XGC from other inflammatory or malignant conditions based on clinical presentation, serological factors, or radiological findings remains difficult. Hence, XGC is a histopathological diagnosis. Diagnostic features on microscopic evaluation are lipid-laden macrophages and the presence of fibroblasts, in the absence of dysplastic cells [3].

In a study of 6783 cases with 131 XGC cases over 10 years in a single center by Torun *et al.* [14], laparoscopic surgery was the treatment of choice. There were no post-operative complications in 84% of the patients, whereas surgical site infections were seen in 5.3%. The days of hospital stay ranged from 0 to 26 days, with a mean of 5.27 ± 4.59 days and a median of 4 days. This was in accordance with the uneventful post-surgical recovery of our patient. The differential diagnosis of XGC on histopathology includes GB adenocarcinoma with signet cell features, where immunohistochemistry with cytokeratin may be helpful, and malakoplakia, which may be distinguished with special stains such as periodic Schiff stain and Von Kossa for Michaelis-Gutmann bodies [15].

CONCLUSION

XGC is a rare, benign disease that is often confused with GBC, with no characteristic radiological or clinical findings before histological analysis. XGC can be managed with laparoscopic cholecystectomy with minimal post-operative complications. A high degree of suspicion and histopathological confirmation must be included in the diagnosis. There is a need for further studies for pre-operative differentiation of XGC from other GB pathologies.

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