XANTHOGRANULOMATOUS CHOLECYSTITIS - A DIAGNOSTIC DILEMMA: REVIEW OF LITERATURE WITH TWO CASE REPORTS

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ABSTRACT

BACKGROUND
Xanthogranulomatous cholecystitis (XGC) is a destructive pathological process of gallbladder. Preoperative imaging techniques may assist in diagnosis of XGC. It exhibits similar/overlapping imaging and intraoperative findings as those of gallbladder cancer, leading to its frequent misdiagnosis. Definitive diagnosis in such cases depends on histopathological examination. We report two cases of XGC.

CONCLUSION
Pre-operative diagnosis of XGC should be done to avoid extended surgery.

KEYWORDS
Cholecystectomy, Xanthogranulomatous Cholecystitis, Ceroid Granulomas.


BACKGROUND
Xanthogranulomatous is an idiopathic, rare process in which lipid-laden foamy histiocytes are deposited at various locations in the body. Xanthogranulomatous inflammation occurs in various sites such as the skin, kidney, retroperitoneum, intracranial, gastrointestinal tract, genital organs and gallbladder. XGC is a rare variant of inflammatory disease of the gallbladder, characterised by focal or diffuse infiltration by inflammatory cell (acute and chronic), lipid laden macrophages, multinucleate giant cells with varying proportions of fibrous tissue and often mimics macroscopically as a gallbladder carcinoma, leading to a diagnostic dilemma.¹ XGC has been known by synonyms such as ceroid granuloma, ceroid-like histiocytosis and fibroxanthogranulomatous inflammation in 1970.²³ The nomenclature was done by McCoy et al in 1976 and described as a distinct pathological condition by Goodman and Ishak in 1981.⁴ The prevalence of XGC among patients with symptomatic gallbladder disease ranges from 0.7% in the United States to up to 10% in India and Japan.¹

Here, we report two cases diagnosed as XGC based on histopathological examination which were intraoperatively and radiologically confusing.

CASE REPORT
Case 1
A 45-year-old female patient was presented with acute abdomen with pain in right hypochondrium, vomiting and fever. No history of weight loss and anorexia. Laboratory tests showed neutrophilic leucocytosis. USG-abdomen revealed multiple gallstones, diffuse thickening of the gallbladder wall with one nodule, hypoechoic area in fundus. No evidence of enlarged lymph node. Considering clinical presentation and USG finding, diagnosis of the carcinoma gallbladder was offered. Cholecystectomy was done and gallbladder specimen sent for histopathology. On gross examination, size was 5.5 x 2.5 x 2 cm, outer surface rough with fibroed area, wall thickness (0.3-0.5 cm) and one area in fundus (2 x 1.5 cm) (Figure-1) with multiple gallstones was identified.

Case 2
A 50-year-old female patient was presented with abdominal pain in right hypochondrium, vomiting, fever and positive Murphy's sign. No history of weight loss or anorexia. Routine tests were within normal ranges, except neutrophilic leucocytosis. Abdominal ultrasonography revealed single stone and variable thickening of the gallbladder wall with multiple intramural hypoechoic nodules. No evidence of enlarged lymph node was seen. Based on imaging and clinical features, a diagnosis of the XGC? carcinoma gallbladder was made. Cholecystectomy was done and sample sent for histopathology. Grossly, the gallbladder was 7 x 3 x 2.4 cm in size, outer surface rough and wall thickness varying (0.3-0.7 cm), multiple intramural nodules in the fundus and body which were yellow in colour. (Figure-2). Single gallstone was identified.

Multiple sections taken from both the gallbladder specimens showed foamy macrophages, plasma cell, lymphocytes, neutrophils, foreign body type and Touton-type giant cells and cholesterol defts infiltrating transmurally (mucosa, muscle layer and adventitia of gallbladder) (Figure-3). No evidence of malignancy was found in both the cases.
Figure 1. Gross: Size of gallbladder 5.5 x 2.5 x 2 cm, wall thickness (0.3-0.5 cm) and one growth in fundus area (2 x 1.5 cm.)

Figure 2. Grossly, the gallbladder was 7 x 3 x 2.4 cm in size and wall thickness varying (0.3-0.7 cm), multiple intramural nodules in the fundus and body.

Figure 3A

Figure 3B

Figure 3C

Figure 3D

Figure 3. Microscopic examination - Chronic inflammatory cell with multinucleated giant cell (A-scanner, B-10x); Cholesterol cleft (C-scanner); Cholesterol cleft, giant cells, foamy histiocytes and inflammatory cell (D-40x)
DISCUSSION

XGC is a destructive pathological process that can spread to adjacent structures leading to adhesion and the case may be confused with gallbladder carcinoma and required extended radical surgery. Role of preoperative FNA, tumour marker and preoperative frozen section can be a great help to take decision for surgical procedure in OT.

Clinically, XGC does not have a typical presentation and may be difficult to distinguish from other inflammatory/neoplastic gallbladder pathology. The pathogenesis of XGC is uncertain, but it is agreed upon to be an inflammatory response to extravasated bile, possibly from ruptured Rokitansky-Aschoff sinuses or by mucosal ulceration. This causes a granulation reaction that leads to the formation of intramural nodules. In addition, the inflammation causes the lecithin in the bile to react with free fatty acids, thus producing lyssolecithin. This results in further damage to the gallbladder.

The event incites an inflammatory reaction in the interstitial tissue, whereby fibroblasts and macrophages phagocytose the biliary lipids in bile, such as cholesterol and phospholipids leading to the formation of xanthoma cells mixed with chronic and acute inflammatory cells. The rupture of the serosa results in adhesion to the adjacent liver, duodenum and transverse colon. Fligiel and Lewin made the analogy to xanthogranulomatous pyelonephritis, where obstruction with stasis is an important aetiological factor and suggested a role for gallstones in causing obstruction in XGC. Christensen et al and Amazon et al had noted a pseudotumoural form of chronic cholecystitis that was characterised by the presence of xanthoma-like foam cells and scarring and that contained ceroid (wax-like) nodules in an inflamed gallbladder. They used the terms fibroxanthogranulomatous inflammation and ceroid granulomas of gallbladder, respectively, which are now known as synonyms of XGC. From a mechanical point of view, the physical presence of stones within the gallbladder might impede the viscous evacuation of bile and cause inflammatory changes of the gallbladder wall, such as fibrosis and muscular atrophy.

Radiological features Studies to Differentiate XGC from CA are

1. Continuity of mucosal line (Continuous-XGC/Disrupted-CA)
2. Thickness and patterns of gallbladder wall (Diffuse-XGC/Focal-CA)
3. Luminal surface enhancement or enhancement characteristic of mucosa (More apparent-XGC/Less apparent-CA)
4. Submucosal attenuated or echoic nodules or bands (Hypoechogenic-XGC/Hyperattenuated or hyperechoic-CA)
5. Intrahepatic biliary duct dilation (Absence-XGC/Present-CA)
6. Homogenous enhancement of enlarge lymph node (Absence-XGC/ Presence-CA) at least one of these findings was noted in 68.7% (11/16) cases with XGC by Rammohan A et al. Kim et al also reported that the combination of USG findings of diffuse wall thickening and intramural hypoechogenic nodules suggest diagnosis of XGC. Uchiyama et al reported that an enhanced continuous mucosal line with gallstone on CT image was highly suggestive of XGC.

Although well defined pathologically, XGC is difficult for the radiologist to recognise because some of the sonographic features of the disease such as gallbladder wall thickening and calculi are nonspecific and closely mimic malignancy. The presence of diffuse wall thickening of the gallbladder with intramural hypoechogenic nodules or bands are identified on sonography. Preoperative imaging techniques do not have characteristic finding for XGC. In our study, in one case with thickening of gallbladder wall, gallbladder stones, a hypoechogenic nodule in fundus had findings on ultrasound examination suggestive of carcinoma of the gallbladder and second case with presence of multiple intramural hypoechogenic nodules and degree of enhancement of the gallbladder wall had findings on ultrasound examination suggestive of XGC? carcinoma of the gallbladder. Xanthogranulomatous cholecystitis exhibits similar/overlapping imaging (by conventional imaging techniques of USG, CT, MRI, diffusion-weighted magnetic resonance imaging (DWI) and FDG-PET) and intraoperative findings as those of gallbladder cancer, leading to its frequent misdiagnosis. However, it is often difficult to distinguish XGC from gallbladder carcinoma.

Role of serum tumour marker, FNAC, frozen section and immunohistochemistry must be considered in such cases to confirm preoperative diagnosis, so as to avoid extended surgery.

Kim et al reported that intramural nodules were seen histologically in all patients with XGC, but radiologically in only 53% (10/19). Definitive diagnosis in such cases finally depends on histopathological examination. Multiple section from variable thickness of gallbladder wall must be examined to avoid coexisting gallbladder carcinoma, to which it strongly simulates.

CONCLUSIONS

Xanthogranulomatous cholecystitis can be a diagnostic dilemma and a correct pre-operative diagnosis should be done to avoid extended surgery. The combination of clinical, radiological finding (USG, CT, MRI and FDG-PET) combined with serum tumour marker (CEA and CA19-9), FNAC, Frozen section and Immunohistochemistry (CD68) can help in diagnosis and management of XGC.

REFERENCES