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XANTHOGRANULOMATOUS CHOLECYSTITIS: DIFFICULTY IN DIFFERENTIATING FROM GALLBLADDER CANCER

General Surgery

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KEYWORDS

INTRODUCTION:

Xanthogranulomatous cholecystitis (XGC) is a benign, rare form of chronic cholecystitis characterized by focal or diffuse inflammation of the gallbladder. Its incidence varies in different subjects from 1.2% to 8.9%. It is often misdiagnosed as a carcinoma GB in many cases in clinical and radiological diagnoses, and sometimes even in histopathological tests. XGC was first described by Christensen and Ishak, as Fibroxanthogranulomatous inflammation in the 1970s. This condition was later described as ceroid as histiocytic granuloma of the gall bladder (GB) and biliary granulomatous cholecystitis. It is characterized by focal or diffuse destructive inflammatory process that mainly involves endothelial cells, fibrous tissues and lipid-laden macrophages. In particular it shows brownish-yellow spots with unusual irregular and asymmetrical thickening of the bladder wall. Its pathogenesis is unclear. It is thought to begin as biliary obstruction with severe or chronic cholelithiasis and an increase in intra-gallbladder pressure.

This pressure causes rupture of Rokitansky-Aschoff (RA) sinuses or mucosal ulcers by releasing bile and consequent Xanthogra nulomatous inflammation. The inflammatory process usually develops and may spread to nearby organs that form dense adhesions and huge mass of inflammatory tissue around the GB.

Clinical Features And Laboratory Marks

Patients may show symptoms of pain (95%), chronic cholecystitis (88%), obstructive jaundice (22%), acute cholecystitis (22%), cholangitis (2%) and palpable mass (5%). On examination, a palpable mass or positive Murphy's sign can be localised. However, these clinical features are not specific to XGC and generally no clinical differences between patients with carcinoma gallbladder and XGC can be detected.

Leukocytosis has been detected even though no specific biochemical testing or liver function abnormalities have been detected in XGC diagnosis. Elevated tumor biomarkers are common in XGC which further creates confusion in distinguishing this disease from gallbladder carcinoma.

METHODS AND MATERIALS

The retrospective study was conducted on data collected from a patients who had undergone surgery in our department of General Surgery for diagnosis of cholecystitis / carcinoma gall bladder from January 2017 to January 2020 . A total of 52 patients were used for the study during this period. Of these, 44 patients were diagnosed with Xanthogranulomatous cholecystitis and 8 were diagnosed with Ca GB. We have studied various histomorphological changes in these specific cases. Special stress was given by mucosal ulceration, thickening of the wall, fibrosis, evidence of epithelial dysplasia and serosal changes. We also reviewed radiological findings and patient clinical data including age, gender, symptoms and signs.

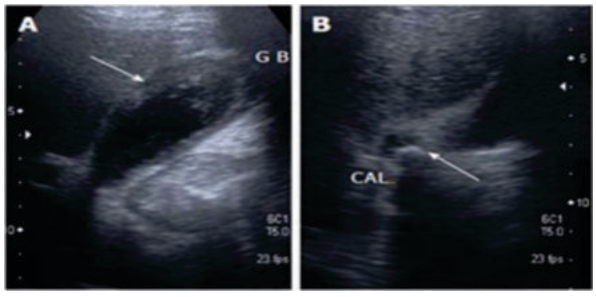
All gallbladder specimens were formalin fixed. They were opened longitudinally and sections were taken from the neck, body and region of the fundus that had been stained with H&E stain and then examined with a microscope.

RADIOLOGICAL RESULTS

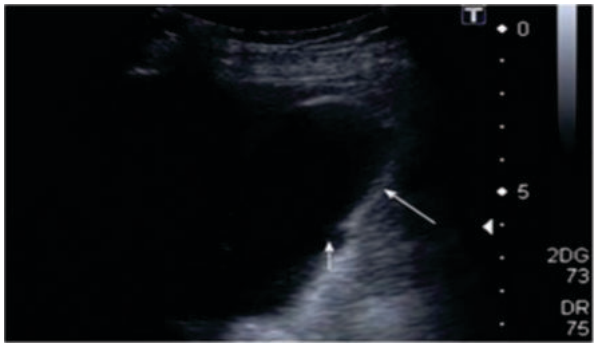
Ultrasonography

The sonographic findings include the presence of gallstones or sludge and moderate to marked focal or diffuse thickening of the gallbladder wall. Wall thickening was hyperechoic. The presence of hypoechoic nodules or bands on a thickened wall can be detected from time to time, their presence being considered a characteristic feature . Hypoechoic lesions on sonography were detected in 73% of cases. Hypoechoic band was detected in about 19% of XGC cases. Xanthogranulomatous nodules behave as hypoechoic sites that are well defined in sonography. Hypoechoic bands may be caused by more generalized involvement of the mucosa.

USG whole abdomen suggestive of ?GB mass, ?XGC, ?Ca GB underwent CT and MRI for further diagnosis



Ultrasound image showing a well distended gallbladder. The diffuse hyperechoic wall thickening (arrow, A) and obstructive calculus in gallbladder neck region (arrow, B). GB: Gallbladder.

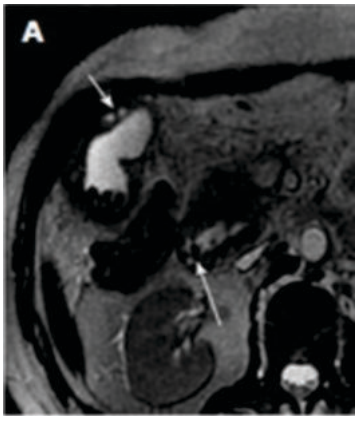


A well distended gallbladder showing diffuse hyperechoic wall thickening (long arrow). Note is made of a small mucosal defect (short arrow) with a small hypoechoic collection in thickened gallbladder wall.

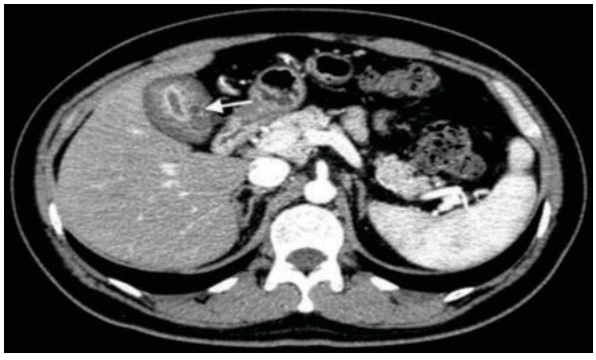
Computed tomography

Computed tomography (CT) findings of patients presenting with acute symptoms and patients presenting with chronic symptoms are usually not much different. CT findings include - diffuse or focal wall thickening, intramural hypoattenuating nodules in thickened walls, luminal surface enhancement (LSE) with continuous mucosal lines or mucosal lines with focal breach. Cholelithiasis and choledocho lithiasis are often seen associated with XGC.

Xanthogranulomas are more often revealed on imaging than abscesses though the later cause more clinical complications. In acute inflammatory phase intramural nodules were abscesses in contrast to xanthogranulomas in the latter phase LSE is defined as enhancement of the gallbladder wall predominantly at the luminal surface. LSE noted in XGC is more apparent in the portal venous phase and represents preservation of the epithelial layer. This further points towards the intramural location of the disease process with an intact overlying mucosa as opposed to the disrupted mucosa in gallbladder carcinoma.

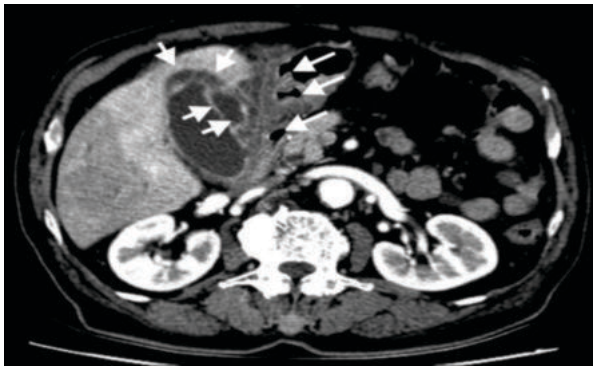


Axial T2W image (A) showing multiple gallbladder calculi with a diffusely thickened wall showing multiple intramural nodules (short arrow). Note is also made of a small filling defect involving the ampullary common duct (long arrow)



A 42-year-old woman with XGC. The contrast-enhanced computed tomography image shows severe, diffuse wall thickness and a continuous mucosal line. An intramural hypoattenuated nodule is also seen (arrow).

XGC- xanthogranulomatous cholecystitis.

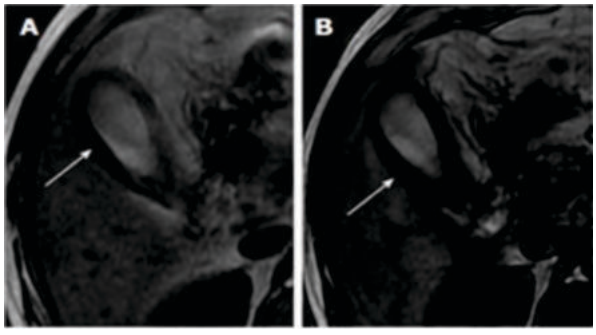


An 87-year-old man with XGC. The contrast-enhanced computed tomography image shows diffuse wall thickness, distension, and multiple intramural hypoattenuated nodules (short arrows). The interface between the gallbladder wall and the liver is not apparent, suggesting spread of inflammation into the liver; infiltration to the duodenum and stomach was also seen (long arrows). XGC, xanthogranulomatous cholecystitis.

CT findings showed significant difference between XGC and carcinoma of gallbladder. These findings were diffuse gallbladder wall thickening, continuous mucosal lining, intramural hypo-attenuating nodules in the thickened walls, absence of macroscopic hepatic invasion and absence of intrahepatic bile duct dilatation[22]. They reported that the diagnostic accuracy of XGC increases with the presence of three or more of the above mentioned findings. Besides, presence of regional lymphadenopathy is more prevalent in carcinoma compared to XGC. While 58.9% cases with gallbladder carcinoma had retroperitoneal lymph nodes enlargement, only 10.2% cases of XGC had mild lymph node enlargement (1-1.5 cm in diameter)

Magnetic resonance imaging

In-phase and opposed-phase chemical shift imaging is helpful in demonstrating fat within the thickened gallbladder wall in patients with XGC. Patients were subjected intramural nodules to chemical shift imaging. Seventy-seven point seven percent of XGC nodules showed reduced signal intensity on out-of-phase images. This variable nature of the intramural nodule on magnetic resonance imaging (MRI) can be attributed to the presence of diverse contents like foamy histiocytes, lymphocytes, plasma cells, polymorphonuclear leucocytes, fibrosis, giant cells, microabscess and necrosis within these nodules. The researchers also observed that few nodules (2 out of 11) were detected only on CT and not seen on MRI and attributed this to a lower spatial resolution of MRI. Areas of iso- to slightly high signal intensity on T2-weighted images, showing slight enhancement at early phase and strong enhancement during delayed phase of dynamic study, corresponded with areas of abundant xantho granulomas. Areas with very high signal intensity on T2-weighted images without enhancement corresponded with necrosis and/or abscesses



3.0 T magnetic resonance axial chemical shift imaging using in-phase (A) and out-phase sequences (B). Presence of intramural fat is markedly evident in the form of loss of signal from gallbladder wall on out of phase imaging (arrow) compared to in-phase image (arrow).

MANAGEMENT

Patients diagnosed with XGC underwent radical cholecystectomy and patients suspicious of Ca GB underwent extended cholecystectomy.

In surgery, XGC may appear to have advanced gallbladder carcinoma due to wall thickness and the destructive localization spread of inflammation. Carcinoma may be covered with severe inflammation. An investigation of the frozen phase within surgery or FNAC was suggested to confirm the diagnosis. In cases where there is no invasion of nearby organs these tools are indicated because they may change the surgical strategy (e.g., simple cholecystectomy vs associated liver resection).

DISCUSSION

XGC is a rare form of cholecystitis. The incidence of Xantho granulomatous cholecystitis was 1.76% in our study. There were 20 women and 2 male XGC male patient in our study showing the preponderance of women with the disease. It shows an increase in the incidence of gallstones in women.

Although radiology is helpful in detecting abnormal gallbladder, they often fail to distinguish between gallbladder cancer and XGC. Radiological changes observed in XGC are abnormal wall thickness, severe proliferative fibrosis and scars, formation of multiple brown-yellow intramural nodules and extensive involvement of adjacent organs. These changes may mimic malignancy. It is often associated with gallstones with XGC.

The presence of gallstones, diffuse thickening, and collapsed lumen are autonomously connected with XGC on ultrasound. However,

these findings can also be found in adenomyosis and gallbladder carcinoma. XGC characterstics such as, adhesion, gallbladder wall thickening, and pericholecystic fat infiltration can mimic Gallbladder carcinoma. Microscopic examination is the basis for XGC identification and shows a wide range of foamy histocyte, giant cells, and fibrosis with dysplastic.

In our study, we observed various histopathological changes of XGC in the gall bladder. It is often difficult to distinguish XGC from carcinoma, especially those situations with the involvement of surrounding structures. A study by KM Roberts reported various histomorphological changes in XGC. They described two types of xanthoma cells - round cells and spindle cells with long nuclei. These spindle-shaped cells are arranged in a storiform pattern. These spindle-shaped cells raise suspicion of malignancy, which was also found in our study.

RESULTS:

The study was conducted on data that was collected from patients who had undergone surgery in our department from January 2017 to January 2020 Patients showed a variety of clinical symptoms, ultrasonography was performed on all patients , CT and MRI was done before surgery in patients suspicious of XGC and Ca GB (52), but none of the patients were previously diagnosed. Radical cholecystectomy was performed on patients suspicious of XGC and extended cholecystectomy was done for Ca GB suspected patients. Intraoperative findings of the surgery included cholecystolithiasis, choledocholithiasis, thick gallbladder wall, lesions penetrating nearby tissues, abnormal anatomy of Calot's triangle, enlarged regional lymph nodes and internal gallbladder fistula. Histopathological examination of all the resected gallbladders were done in which out of 52, 8 were diagnosed as Ca GB and 44 cases were diagnosed as XGC.

In 52 cases, 44 cases were diagnosed as Xanthogranulomatous cholecystitis after pathology, 43 were diagnosed as XGC on CT. There were 40 female patients and 4 male patients showing female dominance for the disease. Patients' age ranged from 26 to 60 years of age with mean age of 43 years And 8 were diagnosed with Ca GB post pathology, and 9 were diagnosed as Ca GB post CT .

CONCLUSIONS

XGC is difficult to diagnose before or through surgery and remains a challenge in clinical practice. The exact diagnosis is based on histopathologic examination. However, diagnosing atypical conditions may be difficult, but recognizing the pathological changes found in the disease and the frequency of imaging can be important information provided by pathologists and radiologists. CT is 98% specific for XGC and Ca GB.

Purpose:

To compare cases of xanthogranulomatous cholecystitis (XGC) with carcinoma GB.