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Preoperative Diagnosis of Xanthogranulomatous Cholecystitis

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Introduction

A sixty-one years old man, known case of hypertension presented to the hepatobiliary surgery clinic, Royal Hospital, Muscat, Oman, in December 2020 with a history of right upper quadrant pain associated with nausea, vomiting, loss of appetite and jaundice for the past two months. On examination, tenderness and fullness were present over the right upper quadrant. Laboratory investigations showed deranged liver function test with elevated liver enzymes and bilirubin level. The total count of white blood cells and neutrophils were normal. Cancer Antigen 19-9 (CA 19-9) was elevated reaching 2364 U/mL and Carcinoembryonic Antigen (CEA) was negative. Computerized Tomography (CT) and Magnetic Resonance Imaging (MRI) of abdomen were performed. CT revealed irregular diffuse mural wall thickening of the gallbladder along with few hypoattenuating mural nodules, multiple hyperdense calculi and pericholecystic fluid collection. Poor fat plane to the adjacent liver parenchyma was seen and common bile duct (CBD) was mildly dilated with multiple calculi noted within it. MRI showed a diffusely thickened gallbladder along with few non enhancing mural nodules within the thickened wall which showed iso- to slightly hypointense signal on both T1 and T2-wieghted images and some of them demonstrated reduced signal in opposed images (OP) denoting microscopic fat depositions of xanthogranuloma In post contrast images, smooth luminal surface enhancement along with focal area of early enhancement of adjacent liver parenchyma were noted. The

diagnosis of Xanthogranulomatous Cholecystitis (XGC) was raised. Endoscopic Retrograde Cholangiopancreatography (ERCP) was performed for biliary decompression and CBD stone extraction and stent insertion. Later, total radical cholecystectomy with resection of segment 4B/5 of liver and portahepatis and celiac lymph node dissection were done and showed a gallbladder mass with surrounding greater omental adhesions extending to adjacent liver parenchyma and hepatic flexure with no evidence of liver or peritoneal metastasis. The postoperative period was uneventful. The histopathology report revealed XGC with no evidence of malignancy. XGC is uncommon inflammatory condition of the gallbladder in which the diagnosis can be challenging on both imaging and histopathology due to overlapping features with other serious conditions like carcinoma of the gallbladder. We report the CT and MRI findings of XGC with a literature review.

Informed patient consent of publication was obtained.

Comment

XGC is a rare type of chronic cholecystitis that was first reported by Christensen et al in 1970.[1] The underlying pathophysiology is still unclear, although many hypotheses attributed this condition to a bile leak into the gallbladder wall which occurs secondary to Rokitansky sinuses rupture or mucosal injury in long standing high intraluminal pressure of the gallbladder due to obstructing stones. Subsequently, this leads to an inflammatory reaction that will attract more foamy cells and macrophages resulting in chronic infiltrative granulomatous inflammation and fibrosis which may extend to involve the adjacent structures.[1,2] The histopathology reveals an ill-defined infiltrative yellow mass of thickened gallbladder wall.[2] Half of the XGC cases are associated with pericholecystic fat infiltration and hepatic extension. 36% of the cases are associated with biliary obstruction and reactive lymphadenopathy.[2,3,4] Microscopically, XGC shows a mixture of xanthogranuloma with foamy histiocytes, macrophages and fibroblasts.[2] XGC is an uncommon disease with estimated prevalence rate of 0.7-10%.[1] It is predominantly seen among elderly women in their sixth to eighth decades of life.[1,2] 80% of XGC cases are associated with gallbladder calculi. The association between XGC and gallbladder carcinoma is doubtful, although some studies in the literature reported gallbladder carcinoma in 8.5% to 30.5% of XGC cases.[1] Accompanying bacterial infections can also be identified and commonly

isolated organisms are Escherichia coli, Klebsiella and Enterococcus.[2] One third of XGC cases are associated with complications such as perforation, abscess and fistula formation, inflammatory infiltration to adjacent structures including the liver, colon and abdominal wall.[1,2] The clinical presentation of XGC is variable and non-specific.[1] Majority of the patients present with right upper quadrant pain and features of chronic cholecystitis. On examination, right upper quadrant tenderness and palpable mass can be seen. No specific laboratory test is available for XGC.[2] Elevated leukocytes level is usually present. Some XGC cases may show elevated tumor marker levels like CA 19-9 and CEA.[2,4]

Radiological images play a key role in the diagnosis of XGC, although sometimes the radiological diagnosis of XGC can be difficult due to overlapping features with other conditions.[2,4] Ultrasound (US) examination may show significant focal or diffuse gallbladder wall thickening with associated calculi or sludge.[1,3] Presence of hypoechoic nodules within thickened wall is a typical finding which favors the diagnosis of XGC.[1] Rana et al studied features of GB wall thickening in US which help to differentiate between XGC and gall bladder carcinoma. Presence of focal wall thickening, wall disruption and indistinct liver margin favors underlying neoplastic process compared to diffuse wall thickening or intramural features including echogenic foci and hypoechoic nodules which favors benign process like XGC.[8] The most common CT finding of XGC is diffuse gallbladder wall thickening with presence of intramural hypodense nodules or bands and luminal surface enhancement with continuous mucosal line.[3,4,5] Goshima et al found that five CT findings improve the sensitivity and diagnostic accuracy for XGC which help to differentiate it from gallbladder carcinoma.[5] Those include the above-mentioned CT findings in addition to absence of intrahepatic bile duct dilatation and hepatic invasion.[1,5] Kobayashi et al developed a scoring system of five CT components to improve the diagnostic sensitivity and specificity of XGC. It includes diffuse wall thickening of gallbladder, presence of intramural nodules or bands, absence of polypoid lesions, pericholecystic infiltration and pericholecystic abscess. They concluded that presence of three or more findings have high specificity of 94% and sensitivity of 77% for the diagnosis of XGC.[4] CT may also show associated findings like cholelithiasis and choledocholithiasis along witwall h possible associated previously mentioned complications.[3,4,6] CT findings of the current patient (Figure 1) show comparable findings including irregular diffuse gallbladder mural thickening

along with few hypoattenuating mural nodules, multiple hyperdense calculi, pericholecystic fluid collection and choledocholithiasis. Poor fat planes to the adjacent liver parenchyma is also noted.

MRI usually demonstrates findings similar to the CT scan.[1] Signal drop-out in In-phase and Opposed-phase chemical shift imaging denoting the presence of microscopic fat within the thickened gallbladder wall is considered a characteristic finding of XGC.[3] Diffusion weighted imaging has an additive value which helps to further discriminate between XGC and gallbladder carcinoma. Majority of gallbladder carcinomas show diffusion restriction compared to only 7% of XGC cases.[3,5,7] MRI of the current patient (figure 2) shows a diffusely thickened gallbladder wall along with few mural nodules within the thickened wall some of which demonstrate signal drop-out in opposed-phase images (OP) denoting microscopic fat depositions of xanthogranuloma. In postcontrast images, smooth luminal surface enhancement and focal area of early enhancement of adjacent liver parenchyma is noted. No evidence of diffusion restriction was seen.

Carcinoma of the gallbladder and gallbladder actinomycosis are the most challenging differential diagnosis for XGC and the radiological diagnosis can be difficult due to overlapping features.[1,2] Fine needle aspiration cytology (FNAC) or biopsy can be helpful preoperatively for further differentiation.[2] The systemic review shows that FNAC was an efficient and safe method for diagnosis of gallbladder carcinoma with high sensitivity, specifity and low complication rate. Percutaneous biopsy is un common minimally invasive procedure which can be helpful to diagnose the unresectable cases, however it can be rarely associated with such complications like hemorrhage, bacteremia, bile leakage and peritonitis and tumor seeding. False negative results can occurred especially in small sized lesion.[1,2] Adenomyomatosis is another differential diagnosis which is characterized by intramural foci of cholesterol crystals with characteristic reverberation comet tail artefacts on US and “pearl necklace sign” On T2-weighted images.[1,3]

Cholecystectomy is the treatment of choice for XGC.[2] However, complete removal can be challenging due to extensive adhesions and local inflammatory infiltration.[1] A recently published systemic review showed that half of XGC cases required open cholecystectomy and conversion

rate was reaching 35%. Although majority of these surgeries were complex, the mortality and complication rates were low and found to be 0.3% and 2-6% respectively.[9]

XGC is a rare variant of chronic cholecystitis and the diagnosis can be suspected on pre-operative imaging in the presence of typical characteristic imaging findings. However, some cases can be misleading due to overlapping features with other conditions. Sometimes, FNAC is helpful in pre-operative diagnosis.

Authors' Contribution

AH collected the clinical and radiological data, reviewed literature and drafted the manuscript. IS supervised the work, selected the representative images and reviewed the manuscript. AK created the idea and reviewed the manuscript. All authors approved the final version of the manuscript.

References

1. Singh VP, Rajesh S, Bihari C, Desai SN, Pargewar SS, Arora A. Xanthogranulomatous cholecystitis: What every radiologist should know. World J Radiol. 2016;8(2):183-191. doi:10.4329/wjr.v8.i2.183
2. Rammohan A, Cherukuri SD, Sathyanesan J, Palaniappan R, Govindan M. Xanthogranulomatous cholecystitis masquerading as gallbladder cancer: can it be diagnosed preoperatively?. Gastroenterol Res Pract. 2014;2014:253645. doi:10.1155/2014/253645
3. Zhao F, Lu PX, Yan SX, Wang GF, Yuan J, Zhang SZ, Wang YX. CT and MR features of xanthogranulomatous cholecystitis: an analysis of consecutive 49 cases. Eur J Radiol. 2013;82(9):1391-1397. doi:10.1016/j.ejrad.2013.04.026
4. R, Kobayashi T, Ogasawara G, Kono Y, Mori K, Kawasaki S. A scoring system based on computed tomography for the correct diagnosis of xanthogranulomatous cholecystitis. (2020) Acta radiologica open. 9 (4):2058460120918237. doi:10.1177/2058460120918237

5. Goshima S, Chang S, Wang JH, Kanematsu M, Bae KT, Federle MP. Xanthogranulomatous cholecystitis: diagnostic performance of CT to differentiate from gallbladder cancer. Eur J Radiol. 2010;74(3):e79-e83. doi:10.1016/j.ejrad.2009.04.017
6. Bo X, Chen E, Wang J, et al. Diagnostic accuracy of imaging modalities in differentiating xanthogranulomatous cholecystitis from gallbladder cancer. Ann Transl Med. 2019;7(22):627. doi:10.21037/atm.2019.11.35
7. Feng L, You Z, Gou J, Liao E, Chen L. Xanthogranulomatous cholecystitis: experience in 100 cases. Ann Transl Med. 2020;8(17):1089. doi:10.21037/atm-20-5836
8. Rana P, Gupta P, Kalage D, Soundararajan R, Kumar-M P, Dutta U. Grayscale ultrasonography findings for characterization of gallbladder wall thickening in non-acute setting: a systematic review and meta-analysis. Expert Rev Gastroenterol Hepatol. 2022;16(1):59-71. doi:10.1080/17474124.2021.2011210
9. Frountzas M, Schizas D, Liatsou E, et al. Presentation and surgical management of xanthogranulomatous cholecystitis. Hepatobiliary Pancreat Dis Int. 2021;20(2):117-127. doi:10.1016/j.hbpd.2021.01.002

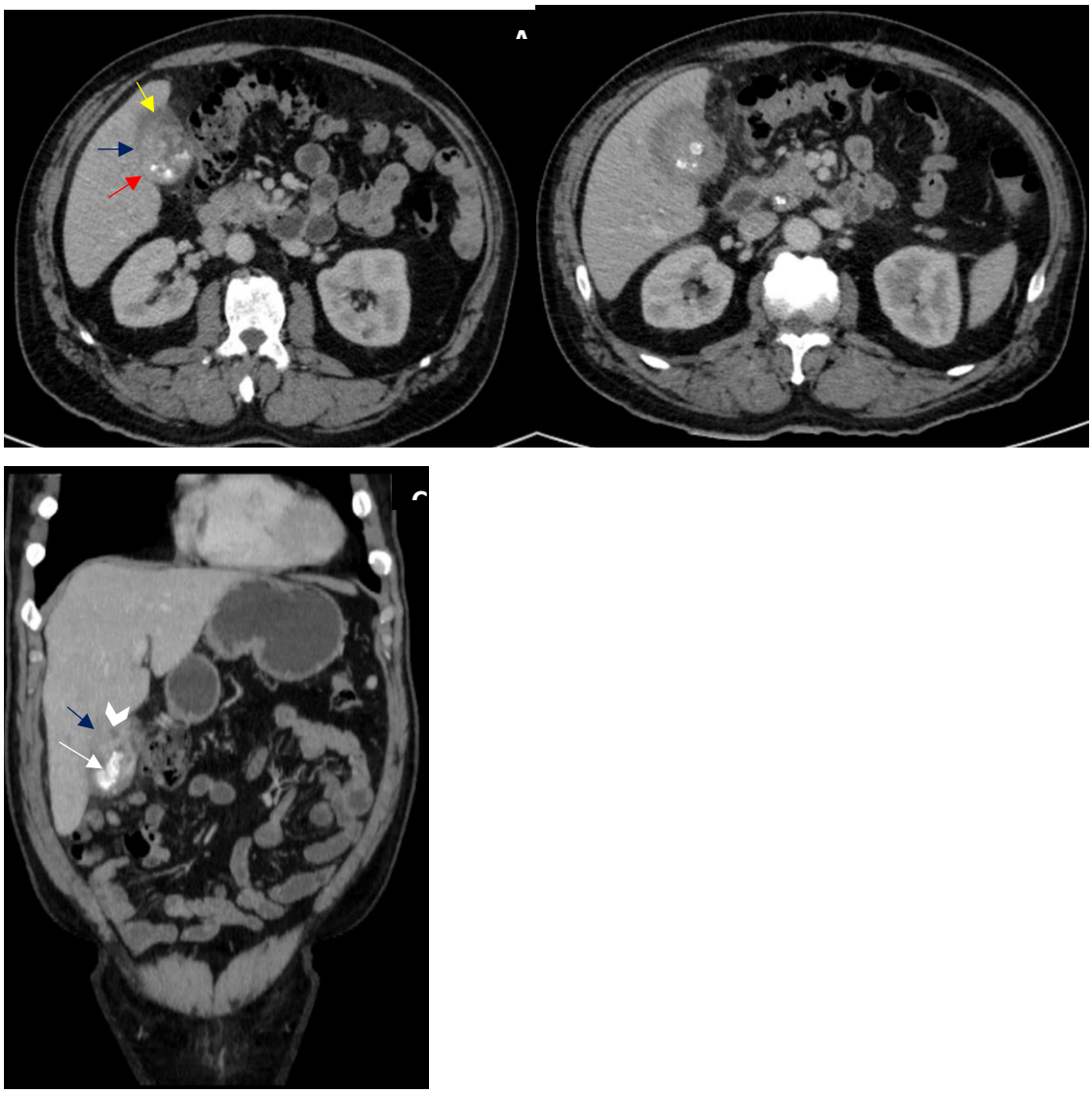

Figure 1: Contrast enhanced Computed Tomography (CT) scans of the abdomen in axial and coronal views from **(A–C)** demonstrate irregular diffuse gallbladder mural thickening (red arrows) along with few hypoattenuating mural nodules (white head arrows). Multiple hyperdense calculi (white arrows) and pericholecystic fluid collection (yellow arrows) are seen. Poor fat planes to the adjacent liver parenchyma is noted (blue arrows).

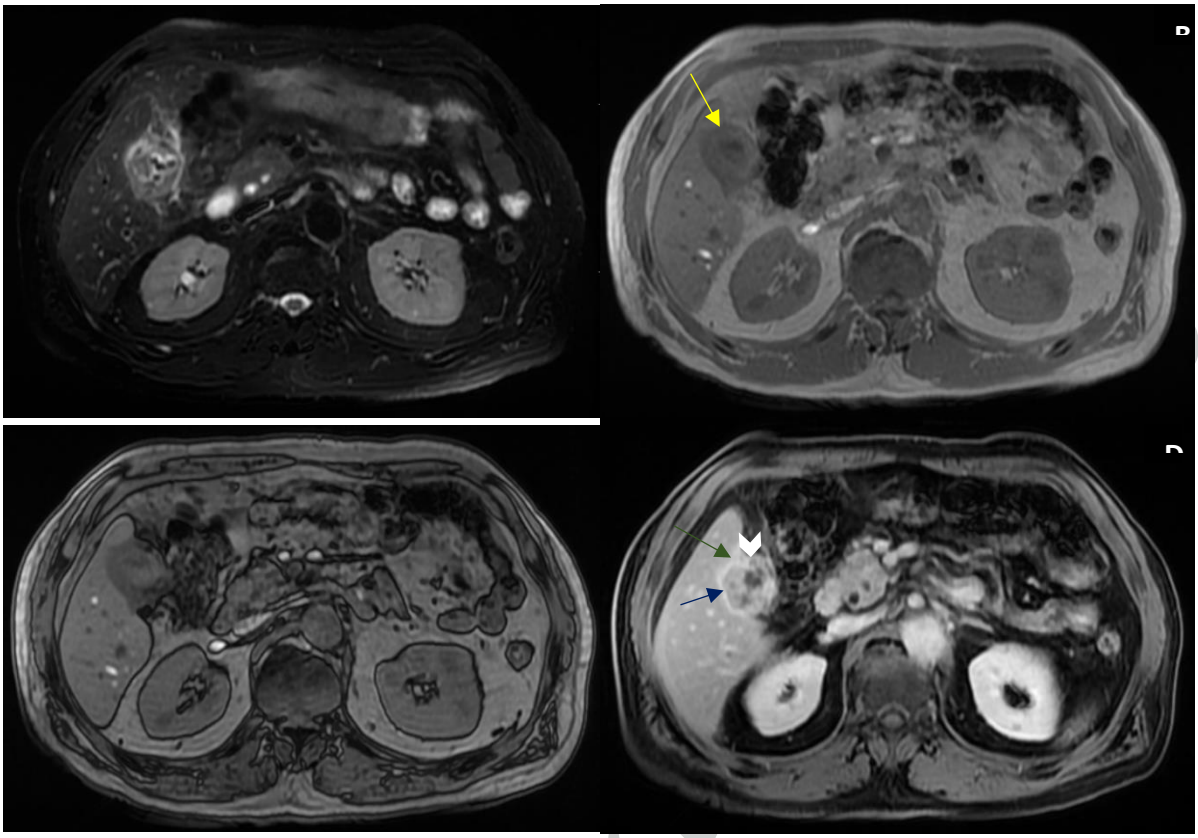

Figure 2: Magnetic Resonance imaging (MRI) of the abdomen from (A–D) including T2W image **(A)**, In-phase (IP) **(B)**, Opposed-phase (OP) chemical shift imaging **(C)**, T1WI post contrast images in axial **(D)** show a diffusely thickened gallbladder wall along with few non enhancing mural nodules within the thickened wall which showed iso- to slightly hypointense signal on both T1 and T2-wieghted images and (white head arrows) some of which demonstrate reduced signal in opposed images (OP) denoting microscopic fat depositions of xanthogranuloma (red arrows). Minimal pericholecystic fluid. smooth luminal surface enhancement is noted in post contrast images (blue arrows). Focal area of early enhancement of adjacent liver parenchyma is seen (green arrows).