CASE REPORT

Xanthogranulomatous cholecystitis mimicking gallbladder cancer

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SUMMARY

Xanthogranulomatous cholecystitis (XGC) is a benign, uncommon variant of chronic cholecystitis characterised by focal or diffuse destructive inflammatory process of the gallbladder (GB). Macroscopically, it appears like yellowish tumour-like masses in the wall of the GB. This article reports on a 74-year-old woman with XGC mimicking GB cancer.

BACKGROUND

Xanthogranulomatous cholecystitis (XGC) is a rare, chronic granulomatous inflammation of the gallbladder (GB) first described by Christensen and Ishak¹ in 1970 as 'fibroxanthogranulomatous inflammation' and later in 1976 as XGC by McCoy *et al.*² It is believed to be a variant of chronic cholecystitis with invasive features to surrounding structures that can be destructive and cause significant morbidity. It is predominantly seen in the Japanese or South Asian population with age of presentation between 44 and 63 years.^{3 4} The prevalence ranges from 0.7% in the USA to 10% in India^{5–8} with no clear gender differences.^{3 4 8 9} It is usually difficult to clinically distinguish XGC from GB carcinoma due to their similar modes of presentation as shown in our case.

CASE PRESENTATION

A 74-year-old Caucasian woman presented with painless obstructive jaundice. She had no history of GB disease, smoking or alcohol intake. She had no symptoms of fever, nausea, vomiting, abdominal pain, weight loss or changes in bowel habits. Physical examination revealed generalised icterus with excoriation marks. The abdomen was non-distended with positive bowel sounds. Tenderness was noted in the right upper quadrant with positive Murphy's sign.

INVESTIGATIONS

Laboratory investigations were normal except elevated liver function tests (LFTs) that showed aspartate aminotransferase 93 IU/L, alanine aminotransferase 74 IU/L, total bilirubin 7.0 mg/dL, direct bilirubin 4.1 mg/dL, indirect bilirubin 2.9 mg/dL and alkaline phosphatase 1050 IU/L. Carbohydrate antigen 19-9 (CA19-9) level was in the normal range.

Abdominal ultrasound showed an irregularly thickened GB with mild dilation of the extrahepatic bile duct (figure 1). CT (figure 2) and MR cholangiopancreatography of the abdomen revealed a markedly thickened contracted GB with submucosal hypoattenuated nodules. Endoscopic retrograde

cholangiopancreatography (ERCP) revealed opacification of the biliary tree and cystic duct with no common bile duct (CBD) dilation, mucosal irregularity, filling defect or stricture. The attached radiological images show non-specific features that are not pathognomonic to XGC or GB cancer.

DIFFERENTIAL DIAGNOSIS

- Primary GB carcinoma was the main concerning differential.
- Acute or chronic cholecystitis and acute cholangitis were lower on the list.

TREATMENT

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

OUTCOME AND FOLLOW-UP

Surgical pathology revealed subacute cholecystitis with xanthogranulomatous inflammation without evidence of malignancy as shown in figure 3. Following surgery, the patient's symptoms and LFTs improved dramatically and she was discharged to follow-up with her primary care physician.

DISCUSSION

Our elderly patient presented with obstructive jaundice and radiological investigations revealed a thickened GB which raised the possibility of GB cancer. Only about 20% of patients with XGC present with obstructive jaundice as seen in this case which supports the fact that it is not a frequent form of presentation. When it occurs, it is usually due to cholestasis from spread of XGC causing CBD stenosis or strictures or due to Mirizzi syndrome that has been associated in up to 12.8% of cases though not seen in this case.^{6 10 11} About 96% of patients

Figure 1 Abdominal ultrasound showing an irregularly thickened gallbladder with mild dilation of the extrahepatic bile duct.

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Figure 2 CT of the abdomen revealed a markedly thickened contracted gallbladder with submucosal hypoattenuated nodules.

may present with abdominal pain likely due to acute cholecystitis⁶ with positive Murphy's sign as noted in our case. Several studies have shown the strong association between gallstones and XGC.^{3 4 11} Over time, gall stones may lead to stasis and rupture of Rokitansky-Aschoff sinuses or mucosal ulceration leading to extravasation of bile into the GB wall which incites a host of inflammatory cascade with phagocytosis of biliary lipids by macrophages and fibroblasts leading to the formation of xanthoma cells.^{9 12} Other clinical features may be nausea, vomiting, anorexia, weight loss or abdominal mass.

Studies from the UK, USA, Japan and India have shown possible coexistence of XGC with GB cancer with estimates ranging from 0.2% to 12.5%.^{3 9 13 14} A recent study showed that XGC may be associated with a precancerous lesion of GB cancer probably due to its distribution of macrophages as well as upregulation of oncogenes and tumour marker expression.¹⁵ Patients with coexisting GB cancer are more likely to present with weight loss, anorexia, jaundice and a palpable mass.¹⁶ The main difficulty in studying the precancerous lesions of GB is the fact that it is impossible to perform a follow-up because the diagnosis is established after the cholecystectomy. Therefore, evidence relating these lesions to cancer is determined indirectly.

Macroscopically, the GB is thickened with yellow nodules formed of inflammatory foci extending to adjacent structures

Figure 3 Histological tissue sample highlighting granulomatous giant cells (arrows), lymphocytes and lipid-laden macrophages.

like the liver, duodenum, transverse colon and omentum.⁴ Histology usually reveals granulomatous giant cells, lymphocytes, fibroblasts, histiocytes, mucosal ulceration, cholesterol clefts, haemosiderin deposits and lipid-laden macrophages which could be rounded, foamy macrophages or spindle-shaped cells with granular cytoplasm and elongated cells⁴ (figure 3).

Laboratory tests often show non-specific derangements as shown in our patient with predominant cholestatic pattern. The CA19-9 tumour marker has been shown to be unreliable in differentiating XGC from GB cancer as it can be high in both the conditions.¹¹ Likewise CA19-9 can be elevated in various benign hepatobiliary conditions like bacterial cholangitis, biliary obstruction, acute or chronic pancreatitis and cystic fibrosis and liver cirrhosis. F-fluorodeoxyglucose-positron emission tomography has shown some promising results in differentiating between benign and malignant lesions with sensitivity and specificity ranging from 75% to 78% and 82% to 100%, respectively, for the detection of GB cancer.¹⁷⁻¹⁹ However, several cases of false-positive results have undermined its utility mainly because inflammatory cells as seen in XGC also have high rates of glucose metabolism similar to malignant cells and can also be picked up.²⁰⁻²²

Ultrasound and CT scan may show non-specific GB wall thickening, cholelithiasis and GB wall hypoechoic nodules or bands²³ but only a CT scan showing intramural hypoattenuated nodules occupying more than 60% of the GB wall thickness has significant specificity for the differentiation of XGC from GB cancer.²⁴ The presence of diffuse GB wall thickening, continuous mucosal line, intramural hypoattenuated nodules, absence of macroscopic hepatic invasion and lack of intrahepatic biliary dilation on CT scan could help differentiate XGC from GB cancer with sensitivity and specificity of 83% and 100%, respectively, when three of these five findings are observed.²⁵

ERCP with brush cytology has a high specificity but a low sensitivity for detecting biliary malignancies and often requires transpapillary cholangioscopy and endoscopic ultrasound-guided fine-needle aspiration to increase diagnostic yield.^{26 27} Fine-needle aspiration and cytology has shown to be useful in differentiating XGC from GB cancer with a sensitivity of 90.6% and a specificity of 94.7% in detecting GB cancer.²⁸ Surgery is the preferred treatment option and up to 80% of laparoscopic procedures are converted to open surgery mainly due to extensive adhesions, dense fibrosis and concerns for possible malignancy.^{8 29} Generally, surgical difficulties are often encountered during laparoscopic cholecystectomy leading to suggestions that XGC may be a risk factor for conversion to open surgery in patients undergoing laparoscopic cholecystectomy.³⁰ Intraoperative frozen section can be helpful if the inflammation is confined to the GB.³¹ However, frozen sections rarely influence the intraoperative decision to do extensive dissection if the inflammation has spread beyond the GB.^{16 30} Moreover frozen sections have been shown to have high false-negative results.^{20 31 32} Postoperative prognosis is usually very good and patients tend to make full recovery. Complications include fistulae from GB to the skin or duodenum and a high rate of postoperative infection.⁴

In conclusion, XGC is a rare, benign, chronic inflammation of the GB that closely mimics GB cancer in its clinical, biochemical, radiological and intraoperative features and only histopathology can definitively differentiate the two conditions.

Learning points

- Xanthogranulomatous cholecystitis (XGC) is a rare, chronic granulomatous inflammation of the gallbladder (GB) that can mimic a GB carcinoma (through clinical features, radiological imaging and operative findings).
- Knowledge of this pathology is important when managing elderly patients with obstructive jaundice so that appropriate counselling can be given to the patients and their families about possible therapeutic options and outcomes.
- Treatment is surgical and most laparoscopic cases are converted to open cholecystectomy due to extensive adhesions.
- Only pathology can definitively differentiate XGC from GB carcinoma.
- Prognosis of this condition is very good compared with a GB carcinoma.

Competing interests None.

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REFERENCES

- Christensen AH, Ishak KG. Benign tumors and pseudotumors of the gallbladder. Report of 180 cases. *Arch Pathol* 1970;90:423–32.
- McCoy JJ Jr, Vila R, Petrossian G, et al. Xanthogranulomatous cholecystitis. Report of two cases. *J S C Med Assoc* 1976;72:78–9.
- Dixit VK, Prakash A, Gupta A, et al. Xanthogranulomatous cholecystitis. *Dig Dis Sci* 1998;43:940–2.
- Roberts KM, Parsons MA. Xanthogranulomatous cholecystitis: clinicopathological study of 13 cases. *J Clin Pathol* 1987;40:412–17.
- Hanada K, Nakata H, Nakayama T, et al. Radiologic findings in xanthogranulomatous cholecystitis. *AJR Am J Roentgenol* 1987;148:727–30.
- Krishna RP, Kumar A, Singh RK, et al. Xanthogranulomatous inflammatory strictures of extrahepatic biliary tract: presentation and surgical management. *J Gastrointest Surg* 2008;12:836–41.
- Reyes CV, Jablolkow VR, Reid R. Xanthogranulomatous cholecystitis: report of seven cases. *Am Surg* 1981;47:322–5.
- Guzman-Valdivia G. Xanthogranulomatous cholecystitis: 15 years' experience. *World J Surg* 2004;28:254–7.
- Goodman ZD, Ishak KG. Xanthogranulomatous cholecystitis. *Am J Surg Pathol* 1981;5:653–9.
- Kawate S, Ohwada S, Ikota H, et al. Xanthogranulomatous cholangitis causing obstructive jaundice: a case report. *World J Gastroenterol* 2006;12:4428–30.
- Han SH, Chen YL. Diagnosis and treatment of xanthogranulomatous cholecystitis: a report of 39 cases. *Cell Biochem Biophys* 2012;64:131–5.
- Takahashi K, Oka K, Hakozaki H, et al. Ceroid-like histiocytic granuloma of gall-bladder—a previously undescribed lesion. *Acta Pathol Jpn* 1976;26:25–46.
- Houston JP, Collins MC, Cameron I, et al. Xanthogranulomatous cholecystitis. *Br J Surg* 1994;81:1030–2.
- Kwon AH, Sakaida N. Simultaneous presence of xanthogranulomatous cholecystitis and gallbladder cancer. *J Gastroenterol* 2007;42:703–4.
- Zhuang PY, Zhu MJ, Wang JD, et al. Xanthogranulomatous cholecystitis: a clinicopathological study of its association with gallbladder carcinoma. *J Dig Dis* 2013;14:45–50.
- Rao RV, Kumar A, Sikora SS, et al. Xanthogranulomatous cholecystitis: differentiation from associated gall bladder carcinoma. *Trop Gastroenterol* 2005;26:31–3.
- Anderson CD, Rice MH, Pinson CW, et al. Fluorodeoxyglucose PET imaging in the evaluation of gallbladder carcinoma and cholangiocarcinoma. *J Gastrointest Surg* 2004;8:90–7.
- Oe A, Kawabe J, Torii K, et al. Distinguishing benign from malignant gallbladder wall thickening using FDG-PET. *Ann Nucl Med* 2006;20:699–703.
- Ramos-Font C, Gomez Rio M, Rodriguez-Fernandez A, et al. Positron tomography with 18F-fluorodeoxyglucose in the preoperative evaluation of gall bladder lesions suspicious of malignancy. Diagnostic utility and clinical impact. *Rev Esp Med Nucl* 2011;30:267–75.
- Spinelli A, Schumacher G, Pascher A, et al. Extended surgical resection for xanthogranulomatous cholecystitis mimicking advanced gallbladder carcinoma: a case report and review of literature. *World J Gastroenterol* 2006;12:2293–6.
- Sawada S, Shimada Y, Sekine S, et al. Expression of GLUT-1 and GLUT-3 in xanthogranulomatous cholecystitis induced a positive result on (18)F-FDG PET: report of a case. *Int Surg* 2013;98:372–8.
- Koh T, Taniguchi H, Yamaguchi A, et al. Differential diagnosis of gallbladder cancer using positron emission tomography with fluorine-18-labeled fluoro-deoxyglucose (FDG-PET). *J Surg Oncol* 2003;84:74–81.
- Shetty GS, Abbey P, Prabhu SM, et al. Xanthogranulomatous cholecystitis: sonographic and CT features and differentiation from gallbladder carcinoma: a pictorial essay. *Jpn J Radiol* 2012;30:480–5.
- Chun KA, Ha HK, Yu ES, et al. Xanthogranulomatous cholecystitis: CT features with emphasis on differentiation from gallbladder carcinoma. *Radiology* 1997;203:93–7.
- Goshima S, Chang S, Wang JH, et al. Xanthogranulomatous cholecystitis: diagnostic performance of CT to differentiate from gallbladder cancer. *Eur J Radiol* 2010;74:e79–83.
- DeWitt J, Misra VL, Leblanc JS, et al. EUS-guided FNA of proximal biliary strictures after negative ERCP brush cytology results. *Gastrointest Endosc* 2006;64:325–33.
- Singh V, Bhasin S, Nain CK, et al. Brush cytology in malignant biliary obstruction. *Indian J Pathol Microbiol* 2003;46:197–200.
- Krishnani N, Shukla S, Jain M, et al. Fine needle aspiration cytology in xanthogranulomatous cholecystitis, gallbladder adenocarcinoma and coexistent lesions. *Acta Cytol* 2000;44:508–14.
- Guzman-Valdivia G. Xanthogranulomatous cholecystitis in laparoscopic surgery. *J Gastrointest Surg* 2005;9:494–7.
- Parra JA, Acinas O, Bueno J, et al. Xanthogranulomatous cholecystitis: clinical, sonographic, and CT findings in 26 patients. *AJR Am J Roentgenol* 2000;174:979–83.
- Rastogi A, Singh DK, Sakhuja P, et al. Florid xanthogranulomatous cholecystitis masquerading as invasive gallbladder cancer leading to extensive surgical resection. *Indian J Pathol Microbiol* 2010;53:144–7.
- Agarwal AK, Kalayarsan R, Javed A, et al. Mass-forming xanthogranulomatous cholecystitis masquerading as gallbladder cancer. *J Gastrointest Surg* 2013;17:1257–64.

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