

◆ CASO CLÍNICO

Xanthogranulomatous cholecystitis: case series in a rural area, clinicopathological study and review of literature

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Summary

Xanthogranulomatous cholecystitis is a destructive inflammatory disease of the gallbladder, rarely involving adjacent organs and mimicking an advanced gallbladder carcinoma. The diagnosis is usually possible only after pathological examination. We are reporting two of such rare cases in female patients attending our institute. In both patients xanthogranulomatous cholecystitis was diagnosed on histopathology.

Key words. Cholecystitis, xanthogranulomatous, laparoscopy.

Colecistitis xantogranulomatosa: serie de casos en un área rural, estudio clínico-patológico y revisión de la literatura

Resumen

La colecistitis xantogranulomatosa es una enfermedad inflamatoria destructiva de la vesícula que raramente compromete a los órganos adyacentes y simula un carcinoma avanzado de la vesícula. Habitualmente el diagnóstico solo es posible después del examen patológico. Comunicamos dos de estos raros casos en pacientes de sexo femenino que se atendieron en nuestro instituto. En ambas pacientes la colecistitis xantogranulomatosa fue diagnosticada por la histopatología.

Palabras claves. Colecistitis, xantogranulomatosa, laparoscopia.

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The term xanthogranulomatous cholecystitis (XGC) describes a rare inflammatory lesion of the gallbladder, characterized by marked proliferative fibrosis, infiltration of macrophages and foam cells involving the wall of the gallbladder.¹ In this pathology, the gallbladder is thickened and irregular with extension of yellow xanthogranulomatous inflammation to adjacent organs. This condition is extremely difficult to suspect before the surgery because macroscopically resembles a carcinoma of the gallbladder. We would like to report two of these unusual cases studied at our institute.

Case 1

A 42-year-old female came with complaints of abdominal pain mainly in the right upper quadrant for 15 days. There was also a history of fever along with chills at night, associated with vomiting. She had a history of passing high-colored urine but stool colour was normal. Her vital parameters were normal. On abdominal examination, guarding and tenderness was present in the right hypochondrium region and no mass was felt. Bowel sounds were present and per-rectal examination was normal. On laboratory exams, hemoglobin was 11.5 g/dL, white blood cell count 8200 per mm³, total bilirubin 2.7 mg/dL, aspartate aminotransferase (AST) 65 IU/L, alanine aminotransferase (ALT) 85 IU/L and alkaline phosphatase 186 IU/L. Ultrasonography (USG) of the abdomen and pelvis showed a thick walled gallbladder with multiple gall stones and pericholecystic fluid. Common bile duct (CBD) and pancreas were normal. Patient was hydrated and started on third generation antibiotics, along with injection of vitamin-K for 3 days. Repeated liver function

tests showed normal values: bilirubin 0.7 mg/dL, AST 37 IU/L, ALT 56 IU/L and alkaline phosphatase 180 IU/L. Laparoscopic cholecystectomy was done easily and operative findings revealed a small contracted intrahepatic gall bladder, with multiple yellow gallstones, and thickened and indurated wall. On gross pathology, the external surface was hemorrhagic. The cut section revealed multiple yellowish green stones in the fundus. Mucosa was slightly atrophied. On microscopy, multiple sections revealed flattened atrophied mucosal epithelium showing band like infiltrate of foamy histiocytes having eosinophilic and vacuolated cytoplasm with eccentric nuclei (Figures 1 and 2). There was no evidence of dysplasia, malignancy or tuberculosis. The diagnostic impression was xanthogranulomatous calculous cholecystitis.

Figure 1. Microphotograph showing normal mucosa, hypertrophied muscle layers and small focus of foamy macrophages (H & E, X-40).

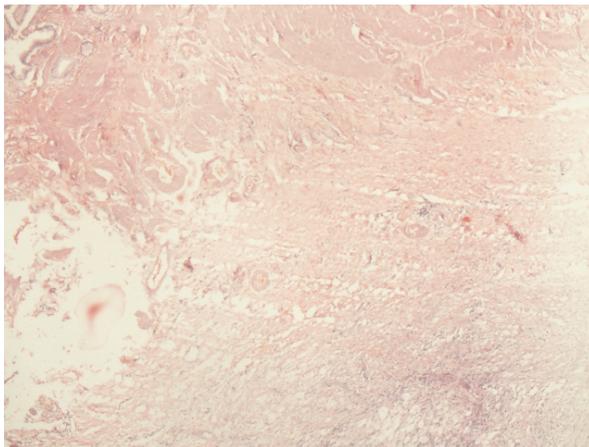
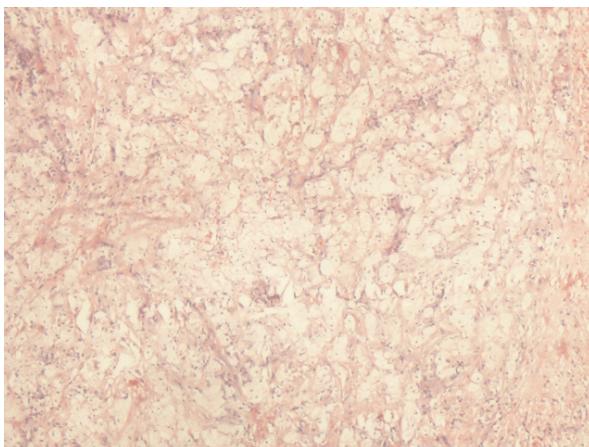


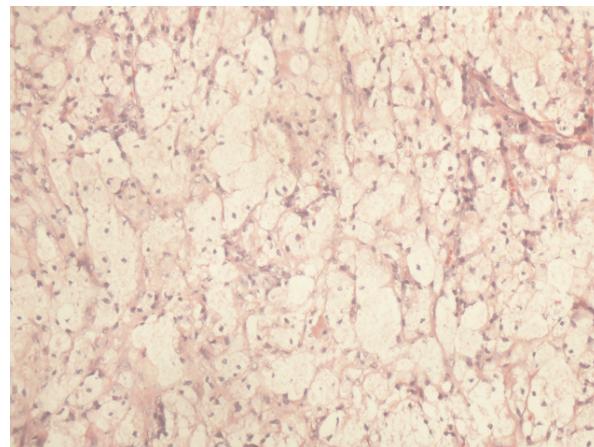
Figure 2. Low power view showing sheaths of macrophages fat laden (H & E, X-10).



Case 2

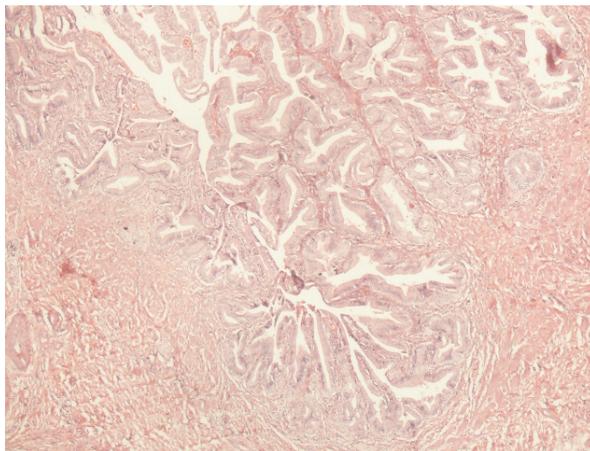
A 51-year-old female presented with acute abdominal pain of sudden onset. Pain was present since one month ago in right upper abdomen and was associated with vomiting and fever. Fever was present for 10 days without any chills and rigors. There was a history of loss of weight and appetite, without jaundice. On examination, patient was febrile with a pulse rate of 110 per min. Per-abdomen examination revealed tenderness and guarding in right hypochondrium and umbilical region, without any palpable lump. Laboratory tests revealed: hemoglobin 10.5 g/dL, white blood cell counts 27,100 per mm³, total bilirubin 1.5 mg/dL, AST 27 IU/L, ALT 46 IU/L and alkaline phosphatase 156 IU/L. USG showed a thickened gall bladder wall with multiple gallstones and pericholecystic fluid. CBD was dilated, multiple stones were present and pancreas was normal. Endoscopic retrograde cholangio-pancreatography (ERCP) was done, CBD stones were removed and a 7 French stent was put. She was diagnosed as having acute cholecystitis and responded to conservative management. Patient was regularly followed up and was admitted for cholecystectomy. Repeated USG showed a thick walled gallbladder with multiple gallstones and CBD stent in situ, without any CBD stone. Patient underwent open cholecystectomy and operative findings revealed dense adhesions between the gall bladder, the liver and the omentum. Gallbladder was inflamed and distended and CBD was normal. Bile culture was normal. On gross examination, gall bladder was 9 cm in length and thick walled with multiple calculi and inflammation. External surface was blackish and irregular.

Figure 3. Papillary infolding of gallbladder mucosa (villous adenoma) (H & E, X-20).



Microscopic examination revealed hypertrophic mucosal epithelium with papillary infoldings (Figures 3 and 4). There were numerous Rokitansky–Aschoff sinuses along with muscular hypertrophy. There was a diffuse as well as nodular collection of foamy macrophages. Mucosa was infiltrated by chronic inflammatory cells. A diagnosis of XGC with papillary adenoma was made. Patient was discharged on 10th post-operative day in a satisfactory condition.

Figure 4. Papillary infolding of gallbladder mucosa (villous adenoma) (H & E, X-40).



Discussion

XGC is an uncommon variant of chronic cholecystitis characterized by the presence of greyish yellow nodules or streaks in the gallbladder wall, mainly caused by lipid-laden macrophages.² XGC was first reported and named by McCoy et al³ and was initially thought to be a malignant disease process, but many studies now show that this disease behaves in a similar fashion to xanthogranulomatous pyelonephritis, another benign disorder. It is characterized histologically by varying degree of chronic or acute inflammatory cell infiltration, many macrophages containing lipids and fibrosis during the later stages.⁴ XGC is an uncommon form of chronic cholecystitis, representing between 0.7% and 13.2% of gallbladder disease.^{5,6} Pre-operative diagnosis is rarely made. It can be diagnosed on USG and mainly confirmed on histopathology. Frequently, these patients are misdiagnosed as either having only cholelithiasis or gallbladder cancer.

Christensen and Ishak first coined the pathological diagnosis of XGC, describing seven patients with pseudotumor of gallbladder.⁷ Many other

pseudonyms, such as ceroid granulomas, ceroid-like histiocytosis and fibroxanthogranulomatous inflammation, existed before the Armed Forces Institute of Pathology formally characterized XGC.⁸ Some authors suggest that if aetiology is unknown, XGC results from the extravasation of bile into the gallbladder wall, in the presence of gallstones, obstruction, and cholestasis. With involvement of Rokitansky–Aschoff sinuses,⁹ the process is supposed to start as an initial inflammatory process, followed by a granulomatous reaction, similarly to the etiopathogenesis of xanthogranulomatous pyelonephritis. In this entity, chronic infection and calculi are common findings as seen in our cases.

When the tension of the distended gall bladder exceeds its normal compliance, these sinuses rupture, spreading inflammation to the adjacent tissues. The inflammation causes the lecithin in the bile to react with free fatty acids, thus producing lysolecithin. This results in further damage to gall-bladder mucosa, initiating a destructive cascade. The degradation of bile to the tissues results in infection and inflammation, where histiocytes accumulate and phagocytose the bile pigment, haemosiderin and cholesterol, thus giving the characteristic XGC appearance of macrophage-laden foamy cells (histiocytes) mixed with chronic and acute inflammatory cells.^{10,11} XGC is characterized by formation of multiple yellowish nodules within the gallbladder wall.

Clinical manifestations of XGC are usually those of acute or chronic cholecystitis, but some patients present anorexia, nausea, vomiting, right upper quadrant pain and mass, suggesting gallbladder cancer. Although imaging modalities such as CT scan, USG, ERCP and percutaneous transhepatic cholangiography (PTC) help to diagnose the pre-operative complications and only histologically the exact diagnosis of XGC can be made. It may be difficult to distinguish XGC clinically from acute or chronic cholecystitis and radiologically from gallbladder cancer. XGC is commonly associated with complications like gallbladder perforation, hepatic abscess, biliary stricture, biliary obstruction, ascending cholangitis and biliary fistulas.¹²

Since dissection at Calot's triangle is extremely difficult due to dense adhesions, laparoscopic surgery is rarely successful in XGC but in our first case we were able to perform laparoscopic cholecystectomy. Some have advocated a subtotal cholecystectomy with drainage of the subhepatic space to decrease the likelihood of iatrogenic injury at the

CBD level. Due to the high prevalence of primary fistulas, cholecystectomy along with excision of all the surrounding xanthogranulomatous tissue is required to assure the complete prevention of fistulas and future recurrence of XGC.

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