Follicular Cholecystitis Mimicking Xanthogranulomatous Cholecystitis and Malignancy: A Case Report

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Abstract
Chronic follicular cholecystitis (CFC) is a rare pathology characterized by prominent lymphoid follicles in the lamina propria distributed throughout the gallbladder wall. It has also been mentioned in the literature as lymphoid hyperplasia and pseudolymphoma. CFC represents less than 2% of cholecystectomies. Its etiopathology is mostly unknown. Most reports are based on histopathological findings, with little or no imaging analysis. We describe a case involving a 66-year-old man radiologically diagnosed as xanthogranulomatous cholecystitis (XGC) versus malignancy, revealing CFC with surrounding inflammatory changes in the cholecystectomy specimen.

Keywords
- follicular cholecystitis
- magnetic resonance imaging
- xanthogranulomatous cholecystitis

Introduction
Chronic follicular cholecystitis (CFC) is a rare entity that represents less than 2% of cholecystectomies. All reported cases have been managed surgically with the diagnosis made postoperatively based on histological findings.¹ To the best of our knowledge, there are no magnetic resonance imaging (MRI) reports about this pathology. We present a case of CFC and describe and illustrate the imaging findings. For the first time, we report the presence of surrounding inflammatory changes.

Case Presentation
A 66-year-old man was referred to our hospital for having right-sided abdominal pain and dyspepsia. The patient’s symptoms had started 4 months ago. The patient’s medical history was unremarkable except for the presence of high blood pressure. The physical abdominal examination was unremarkable. The laboratory findings showed elevated erythrocyte sedimentation rates (45 mm), normal leukocytes count (8900/mL) with 65% of segmented neutrophils, an elevated carbohydrate antigen 19–9 (CA 19–9) of 531.9 UI/L, and normal carcinoembryonic antigen (CEA) of 1.8 UI/L.

Abdominal ultrasound (US) was performed, which showed a heterogeneous thickening of the gallbladder fundus wall with low resistance flow on power Doppler and hypoechoic intramural nodules (► Fig. 1). The MRI revealed intramural nodules with elevated T2WI signal intensity (► Fig. 2) and heterogeneous signal intensity and contrast-enhancement of the thickened fundus wall (► Fig. 3). Diffusion-weighted imaging (DWI) showed an increase in signal intensity on successively higher-b-value DWI images and low signal intensity on the corresponding apparent diffusion coefficient (ADC) map, with a value of 0. 9 × 10⁻³ mm²/s (► Fig. 4). The surrounding gallbladder and liver parenchyma had inflammatory changes.

A presumptive diagnosis of xanthogranulomatous cholecystitis (XGC) versus gallbladder carcinoma was made and surgery was performed. No preoperative fine-needle aspiration or biopsy was made because suspicion of gallbladder carcinoma was suggested. The cholecystectomy specimen revealed CFC with surrounding inflammatory changes.
cancer was high due to the size of the lesion and the high values of CA 19–9. The gallbladder was found adhered to the adjacent omentum, transverse colon, and liver parenchyma. Cholecystectomy, atypical hepatic segmentectomy of segments IVb, and V, and segmentary resection of the transverse colon were done due to adhesions between the gallbladder and surrounding organs. The specimen was sent to the department of pathology for histopathological examination.

The hematoxylin and eosin (H&E)-stained section from the gallbladder showed proliferating or reactive lymphoid follicles with prominent germinal centers along with chronic inflammatory infiltrate comprising lymphocytes, histiocytes, eosinophils, and plasma cells underlying the lamina propria throughout the thickness of the gallbladder wall. There was no necrosis, atypical cells, and xanthomized histiocytes. This tissue infiltrated the liver parenchyma and adjacent colonic wall. Extensive areas of fibrosis were recognized, forming dense septa that dissected and intermingled with the infiltrate areas. Liver parenchyma showed portal spaces with chronic mononuclear inflammatory infiltrate and stromal fibrosis. Pathological diagnosis of CFC of the gallbladder with the liver and colon involvement was made.

The postoperative course was uneventful and the patient was discharged 10 days after surgery.
Discussion

CFC is a very rare benign entity with only a few cases published in the literature.\(^2,3\) It represents less than 2% of cholecystectomies.\(^1,4\) CFC has been mentioned as lymphoid hyperplasia, pseudolymphoma, and chronic cholecystitis with lymphoid hyperplasia. It was first described on cholecystograms by Estrada et al\(^5\) in 1960. Being a highly uncommon pathology, the literature reports different opinions about this entity.\(^6\) It is characterized by hyperplastic lymphoid follicles with germinal centers consisting of polymorphous lymphoid populations.\(^7,8\) For the diagnosis, an increase in the number of intraepithelial lymphocytes per 100 biliary cells above the normal proportion of three to four lymphocytes is needed.\(^9\)

The pathogenesis of CFC is unclear although it may be caused by an immune reaction to luminal agents of the gallbladder.\(^10\) Other theories include an autoimmune-mediated disorder in other areas of the gastrointestinal tract or gram-negative bacterial infection that induce a lymphocytic reaction, such as *E. coli*, *K. pneumoniae*, or *S. typhi*.\(^2,3,9-11\) This inflammatory pattern can be encountered in other parts of the gastrointestinal tract such as the esophagus, stomach, duodenum and colon, and in the orbits and lungs.\(^8\)

Risk factors for developing CFC are unclear because there are uncertain causal associations. It seems to affect more frequently middle-aged or elderly females, and other conditions such as chronic hepatitis, thyroiditis, or primary biliary cirrhosis can coexist.\(^8\) Differential diagnoses arise mainly between XGC and gallbladder carcinoma. XGC is an unusual variant of chronic cholecystitis that is characterized by a lipid-laden inflammatory process that can invade neighboring structures and can be blended with cancer. Moreover, it is a challenging diagnosis as there are imaging similarities between XGC and gallbladder cancer such as the enhancing and thickened wall, and the tendency to involve neighboring organs.

Findings such as intramural hypoattenuated nodules occupying 60% of the area of the thickened wall, intact enhancing mucosal lining, absence of biliary tract dilatation, no large masses, and absence of lymph nodes suggest a diagnosis of XGC instead of cancer.\(^12\)

In our case, the gallbladder had diffuse parietal thickening, intramural nodules with elevated T2WI signal intensity, and preservation of linear mucosal enhancement, similar to an XGC. However, the intramural nodules did not show signal fall on opposed-phase images as in XGC. It must be taken into account that although they share epidemiological characteristics regarding age and sex, XGC does not present a clear association with gallbladder cancer,\(^13\) even though metaplastic changes can be found in up to 75% of patients with CFC. However, its relationship with gallbladder carcinogenesis is unclear too.\(^1\) In our case, no metaplastic changes were found.

We found no report regarding the adhesions and fibrosis to the liver and colon in CFC. As CFC is thought to be caused by an immune reaction, chronic gallbladder inflammation may induce a progressively irreversible fibrotic response that can affect surrounding tissues. The surrounding fatty tissue had a high signal intensity on the T2-weighted and fat-suppressed images, and the liver parenchyma adjacent to the gallbladder showed enhancement at the arterial phase, both representing the inflammatory changes. We had no previous imaging examinations to determine when these changes started.

Sometimes, the difficulty to distinguish XGC from gallbladder carcinoma derives from extensive surgical resections. It is important to consider CFC as a differential diagnosis, and in some cases perform a frozen section of the gallbladder to arrive at a correct diagnosis and avoid wider surgical resections.

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Conflicts of Interest

There are no conflicts of interest.
References

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