Radiology Case Reports 18 (2023) 3513–3521

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/radcr

Case Report

Xanthogranulomatous cholecystitis in a patient with ulcerative colitis and primary sclerosing cholangitis: A case report ☆,☆☆

Mohammad Kazem Tarzamni, MD[a,b], Homa Aminzadeh Ghavifekr, MD[c], Hadise Zeynalkhani, MD[b], Masoud Shirmohamadi, MD[d], Elham Eghbali, MD[a,b], Ali Jafarizadeh, MD, MPH[c], Seyed Siavash Ghareghoran, MD[b], Seyedeh Elnaz Hashemizadeh, MD[e], Masih Falahatian, MD[b,]*

[a] *Department of Radiology, Emam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran*
[b] *Medical Radiation Sciences Research Group, Tabriz University of Medical Sciences, Tabriz, Iran*
[c] *Research Center for Evidence–Based Medicine, Iranian EBM Centre: A Joanna Briggs Institute Affiliated Group, Tabriz University of Medical Sciences, Tabriz, Iran*
[d] *Liver and Gastrointestinal Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran*
[e] *Department of Surgical and Clinical Pathology, Emam Reza Hospital, Tabriz University of Medical Sciences, Tabriz, Iran*

ARTICLE INFO

Article history:
Received 10 May 2023
Revised 6 July 2023
Accepted 10 July 2023

ABSTRACT

Chronic gallbladder disease due to xanthogranulomatous cholecystitis is uncommon, and its symptoms are generally vague. While there is no firm evidence to link xanthogranulomatous cholecystitis to primary sclerosing cholangitis or ulcerative colitis.

The patient is a 41-year-old male with a history of ulcerative colitis, primary sclerosing cholangitis, and biliary stenting who complained of symptoms of anorexia, jaundice, and pruritus. In the initial ultrasound exam, there was evidence of intrahepatic and extrahepatic bile duct dilation along with a significant and mass-like circumferential thickening of the gallbladder wall. Magnetic resonance cholangiopancreatography was performed for further evaluation, which indicated increased gallbladder wall thickness, containing mul-

List of abbreviations: ADC, Apparent diffusion coefficient; CBD, common bile duct; CCA, cholangiocarcinoma; CT, Computed tomography; DWI, Diffusion Weighted Images; ERCP, endoscopic retrograde cholangiopancreatography; ESR, Erythrocyte sedimentation rate; IBD, inflammatory bowel disease; IgG4, immunoglobulin G4; IgG4-SC, IgG4-related sclerosing cholangitis; LSE, luminal surface enhancement; MRCP, Magnetic resonance cholangiopancreatography; MRI, Magnetic resonance imaging; PSC, primary sclerosing cholangitis; UC, ulcerative colitis; UDCA, ursodeoxycholic acid; XGC, Xanthogranulomatous cholecystitis.

☆ Acknowledgments: We thank the radiology department and the endoscopy department of Imam Reza Hospital, Tabriz University of Medical Sciences.

☆☆ Competing Interests: The authors have declared that no competing interests exist.

* Corresponding author.
E-mail address: Masih.falahatian@gmail.com (M. Falahatian).

https://doi.org/10.1016/j.radcr.2023.07.024

Keywords:
Xanthogranulomatous cholecystitis
Primary sclerosing cholangitis
Ulcerative colitis
Magnetic resonance cholangiopancreatography
Gallbladder wall thickening
Case report

tiple T2 hyper-signal nodules while the mucosal layer was intact. There was also a filling defect in the common bile duct's distal portion. These findings matched a xanthogranulomatous cholecystitis diagnosis and a possibly malignant lesion in the distal of the common bile duct. The patient ultimately had a cholecystectomy, and pathology findings confirmed the diagnosis of xanthogranulomatous cholecystitis. Biopsy specimens obtained from the distal of the common bile duct lesion were microscopically identified as intramucosal adenocarcinoma.

In patients with a history of primary sclerosing cholangitis who present with nonspecific symptoms suggesting chronic gallbladder disease and radiologic evidence of circumferential gallbladder wall thickening containing intramural nodules and intact mucosa, xanthogranulomatous cholecystitis should be kept in mind.

Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) of unknown etiology with an estimated incidence and prevalence of 1.2-20.3 and 7.6-245 cases per 100,000 persons/y, respectively [1]. Clinically, UC is most commonly associated with constitutional symptoms and bloody diarrhea, along with a characteristic continuous mucosal inflammation of varying degrees extending proximally from the rectum in colonoscopic evaluation [2].

Extraintestinal manifestations and complications of UC are well-recognized clinical entities that include primary sclerosing cholangitis (PSC), cholangiocarcinoma (CCA), colonic cancer, and articular involvement [3]. PSC is a chronic cholestatic liver disease most commonly affecting young male patients with UC that is associated with symptoms of pruritus, fatigue, abdominal pain, and jaundice [4]. It is well-established that patients with PSC, either with or without concomitant ulcerative colitis, have a higher likelihood of developing complications like cholangiocarcinoma (CCA) and liver failure [4]. CCA occurs with an annual incidence of 0.5%-1.5% in patients with recognized PSC [5].

Xanthogranulomatous cholecystitis (XGC) is an uncommon form of cholecystitis that was first described by Christensen et al. in 1970 and later by McAvoy et al. in 1976 as a form of chronic cholecystitis that closely resembled tumors with microscopic features of xanthoma-like foam cells and scarring with ceroid (wax-like) nodules in an inflamed gallbladder wall, often with extensive fibrosis [6,7]. It has been documented that XGC can occur simultaneously with gallstones (86.1%), cancer of the gallbladder (5.2%-5.9%), choledocholithiasis, Mirizzi syndrome, cholangitis, and chronic pancreatitis [8,9].

While xanthogranulomatous cholangiopathy has been reported in PSC patients and sometimes occurs simultaneously with XGC in patients presumed to have a malignant process, to the best of our knowledge, there has been no report on an association between PSC, either with or without UC, and the development of XGC.

Here we report a rare condition of concomitant XGC and intraductal adenocarcinoma of the common bile duct (CBD) in a patient with a history of UC and PSC.

Case presentation

Our patient is a 41-year-old male with a history of ulcerative colitis and primary sclerosing cholangitis. The patient was diagnosed as a case of ulcerative colitis via biopsy specimens obtained during colonoscopy and as a case of PSC by magnetic resonance cholangiopancreatography (MRCP) 5 and 1.5 years prior to his current complaint, respectively. He was being treated for these conditions with ursodeoxycholic acid (UDCA), prednisolone, and mesalazine. He developed symptoms of significant weight loss, pruritus, jaundice, fever, and anorexia over 6 months. Due to these symptoms, ultrasonography of the liver and the gallbladder was conducted, which indicated a mild dilation of the common bile duct (CBD) and a slightly thickened gallbladder wall.

The patient subsequently underwent MRCP for further assessment of the biliary tract. MRCP demonstrated evidence of asymmetric thickening as well as luminal narrowing in the middle and distal portion of CBD, which were consistent with chronic cholangiopathy due to PSC/IgG4 disease or cholangiocarcinoma (Fig. 1). Simultaneously the patient's records were significant for an IgG4 level of 1522, alkaline phosphatase level of 1009, bilirubin (total bilirubin: 12.2 – with direct component accounting for 8.55), and an ESR of 51. Our patient underwent a stenting procedure by endoscopic retrograde cholangiopancreatography (ERCP) due to incomplete biliary drainage. The ERCP report included a description of diffuse intrahepatic bile duct irregularity as well as severe stenosis at the distal portion of the CBD due to a suspicious filling defect (Fig. 2). Biopsy specimens were obtained from this lesion which was later diagnosed as an intramucosal adenocarcinoma (Fig. 3). However, the patient refused to undergo surgery.

Eight months later, in his current admission, the patient complained of anorexia and jaundice; he was therefore hospitalized with suspicion of the stent's malfunction. Initial ultrasonography of the liver and gallbladder showed intrahepatic and extra-hepatic bile duct dilation along with a significant and mass-like circumferential wall thickening of the gallbladder. The severely thickened gallbladder wall contained multiple hypoechoic nodules which were separated from each other with vascular septations. According to these findings, xanthogranulomatous cholecystitis and neoplastic infiltration of

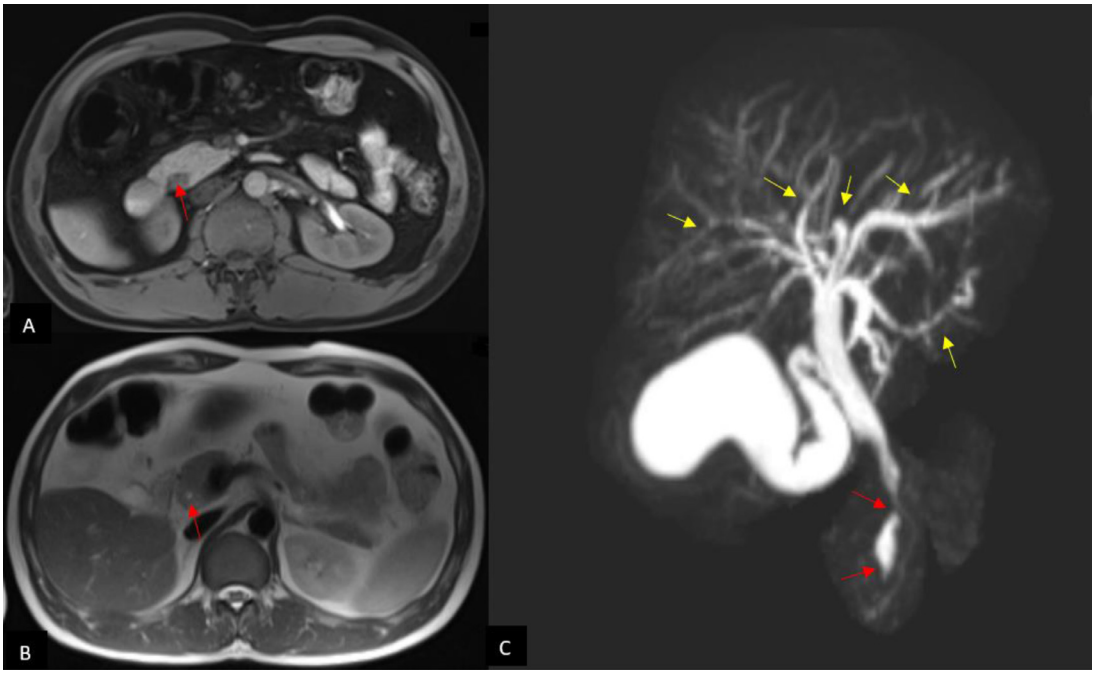

Fig. 1 – Axial T1 noncontrast (A) and T2 (B) weighted MRI images showing a suspicious lesion in distal of the CBD (shown by red arrowheads). MRCP (C) displaying an irregularity in the middle and distal portion of the CBD due to asymmetrical wall thickening (shown by red arrows). Note: the mild irregularities with a beaded appearance (shown by yellow arrows) in the intrahepatic biliary tree (C).

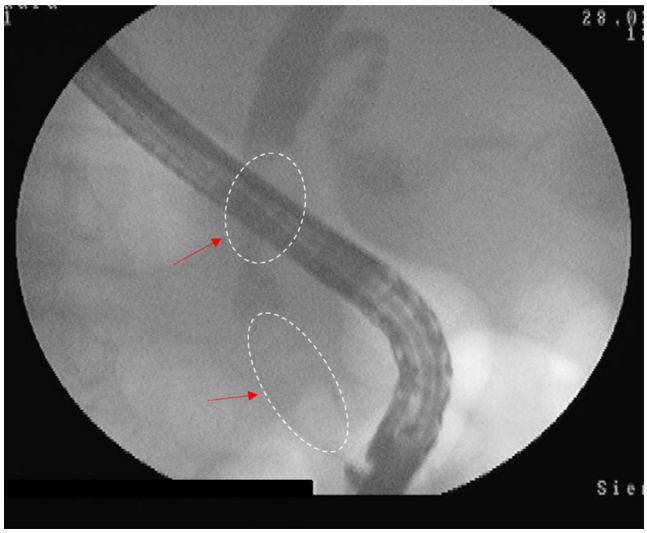

Fig. 2 – An irregular filling defect in the middle and distal portion of the CBD can be appreciated in this side view of ERCP (shown by red arrows and dotted circles).

the gallbladder wall were considered as differential diagnoses (Fig. 4, Video 1 and 2).

MRCP and magnetic resonance imaging (MRI) with contrast were performed for further evaluation, which indicated increased gallbladder wall thickness, containing multiple T2 hyper-signal nodules while the mucosal layer was intact. These findings were consistent with a diagnosis of xanthogranulomatous cholecystitis. Polypoid lesion of the distal portion of the CBD was also persistent in the MRCP (Fig. 5).

Ultimately, the patient underwent cholecystectomy and hepaticojejunostomy afterward. Pathology results from cholecystectomy confirmed the diagnosis of xanthogranulomatous cholecystitis by showing the characteristic foamy histiocytes infiltrates (Fig. 6).

Discussion

XGC is a form of chronic cholecystitis that commonly presents with symptoms of abdominal pain, nausea, vomiting, weight loss, and anorexia [8,9]. It is not possible to clinically distinguish XGC from other forms of chronic cholecystitis; thus in most cases, it is an incidental histopathologic diagnosis that has been reported in roughly 1.3%-1.9% of cholecystectomies in various studies worldwide [9,10]. Theoretically, it is suggested that secondary to the presence of gallstones or other inflammatory triggers, Rokitansky-Aschoff sinuses are ruptured, and bile is extravasated into the gallbladder wall leading to an intense xanthogranulomatous reaction which is characterized by the accumulation of foamy and xanthoma cells [11,12].

The most common sonographic findings of XGC noted in preoperative studies include circumferential thickening of the gallbladder, the presence of gallstones or sludge, and intramural hypoechoic nodules and bands [13,14].

Features of XGC on CT include diffuse or focal gallbladder wall thickening with intramural hypoattenuating nodules [13].

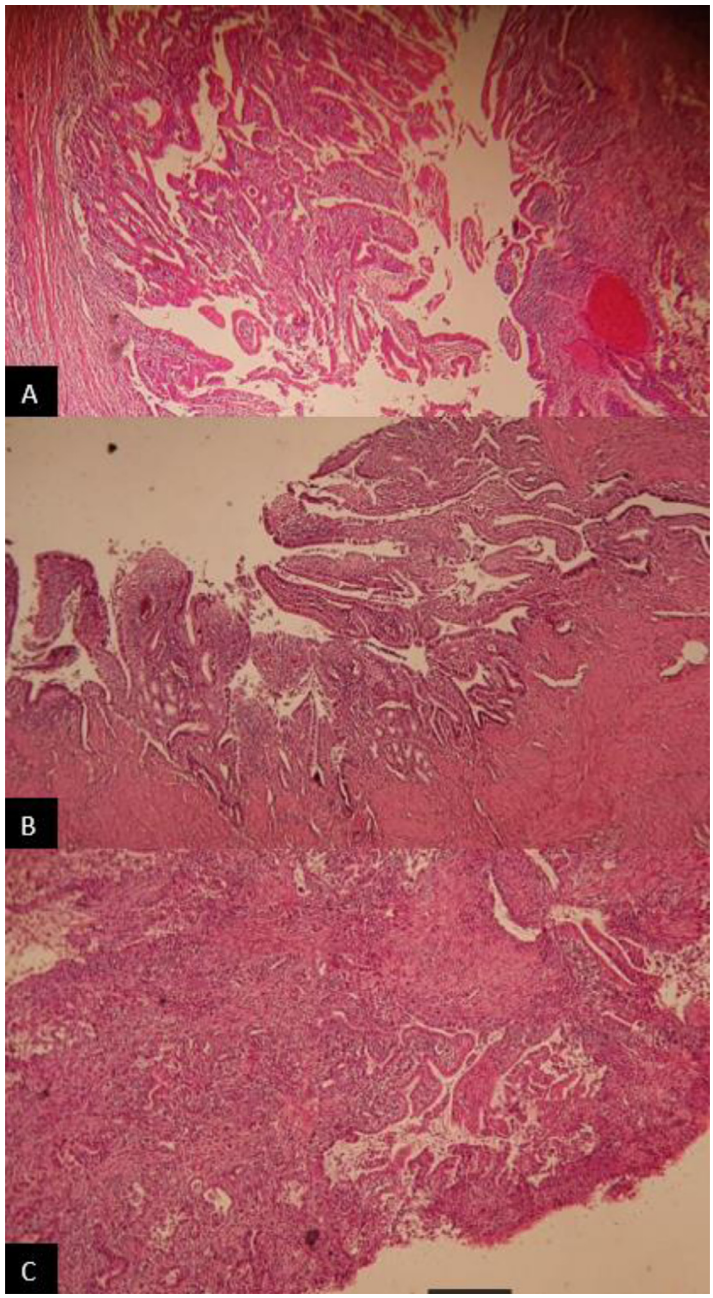

Fig. 3 – Biopsy specimens obtained from the distal CBD lesion, which was diagnosed as intramucosal adenocarcinoma. Villous luminal lesion limited to the mucosal layer can be appreciated, with sparing of the underlying submucosa.

Intramural nodules observed on imaging studies are either xanthogranulomas or abscesses, thus occupation of a large area of the thickened gallbladder wall with nodules highly favors XGC over other diagnoses [15]. Sparing of the continuous mucosal lining in the thickened gallbladder wall with luminal surface enhancement (LSE) is highly suggestive of XGC since it is a pathology of the gallbladder wall and not of mucosal surfaces [16]. Pericholecystic fat stranding and blurring of interface between gallbladder and liver are common findings in all patients, while early liver enhancement, bowel infiltration, stomach infiltration, and invasion of the abdominal wall are mostly observed in rare complicated patients [17].

Intramural nodules in XGC can show signal drops on out-of-phase MRI images because of abundant typical foamy histiocytes in the thickened gallbladder wall containing lipid and bile pigments [18]. Shuto et al. discovered that MRI images and pathologic parameters of XGC may be linked together, thereby iso- to slightly high signal intensity areas on T2-weighted images demonstrating slight and strong enhancement at early and late phases respectively, corresponded with areas of abundant xanthogranulomas [19]. Although sur-

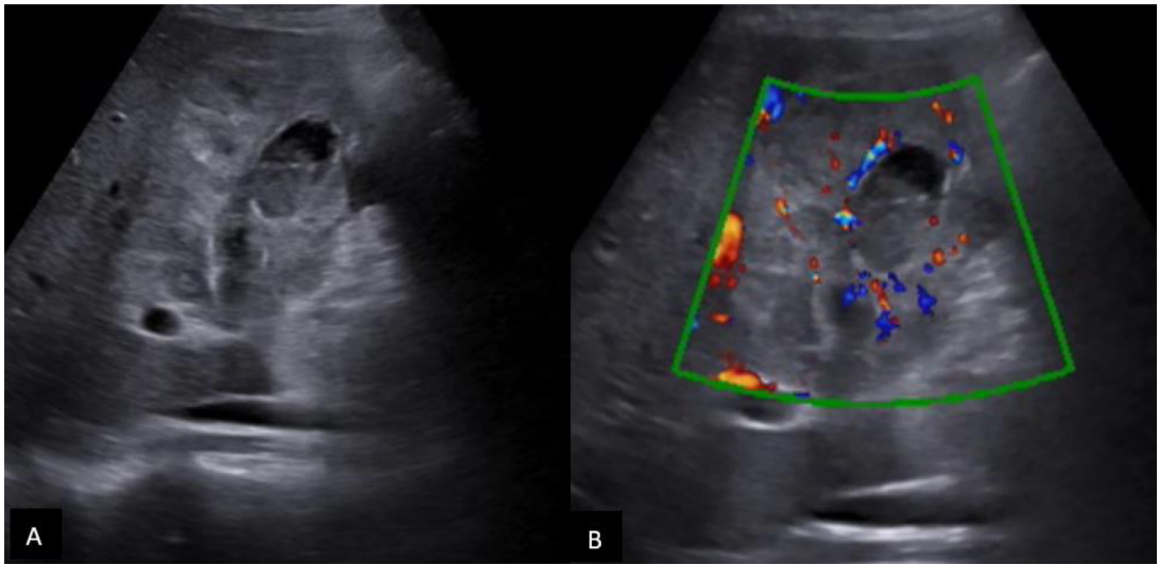

Fig. 4 – Grayscale (A) and Doppler (B) ultrasound images of the gallbladder show a mass-like asymmetrical circumferential gallbladder wall thickening with sparing the mucosal lining. The thickened gallbladder wall contains multiple avascular hypoechoic intramural nodules separated with echogenic vascular bands (Video 1 & 2).

rounding organs, such as the liver, can be infiltrated in XGC, macroscopic hepatic invasion is uncommon [13].

Radiologically, XGC can mimic gallbladder cancers [20–23]. Focal or diffuse asymmetric gallbladder wall thickening with a disrupted mucosal layer, intraluminal polypoid soft tissue mass, hepatic invasion, intrahepatic bile duct dilation, and regional lymphadenopathy are radiologic findings in favor of gallbladder cancer [13,24].

Gallbladder wall enhancement pattern on CT has been classified into 5 types, with type 1 indicating a heterogeneously enhancing 1-layer gallbladder wall or indistinguishable layering of the gallbladder wall [25]. In a study that emphasized the importance of differentiating XGC from gallbladder wall adenocarcinoma, Lee et al. determined that nonfocal GB wall thickening, type I enhancement of the GB wall, transient hepatic attenuation difference in the adjacent liver, mucosal continuity, and the presence of intramural nodules were statistically significant findings supporting XGC [26].

Diffusion Weighted Images (DWI) may have an added benefit to distinguishing XGC from GB cancer, with the apparent diffusion coefficient (ADC) of XGC being significantly higher than the wall-thickening type of GB cancer [27]. There have been reports of positron emission tomography (PET) with fluorine-18-labeled fluoro-deoxyglucose (FDG) scan being a promising tool to differentiate between benign and malignant lesions of the gallbladder wall, with focal uptake being considered as evidence of malignancy [28–30]. However, there have been reports of XGC patients who were tested positive on PET-FDG scan preoperatively [31,32]. The false positivity observed in these cases has been linked to the expression of glucose transporters (GLUT-1 and GLUT3) on inflammatory cells at the gallbladder wall of XGC [32].

Gallbladder actinomycosis, which is a rare chronic suppurative infection of the gallbladder, very closely resembles both gallbladder adenocarcinoma and XGC [33,34]. So much so that it is difficult to differentiate the disease without microscopic evaluation, during which observation of sulfur granules helps diagnose the infection [34].

Gallbladder adenomyomatosis may resemble XGC on imaging. However, ultrasonography often identifies “comet tail” artifacts, while MRCP show characteristic “pearl necklace” sign [35].

There has been a case report of XGC in a patient with PSC by Mori et al. [36] in 2010 and reports of xanthogranulomatous cholangiopathy in patients who underwent transplantation for PSC [37]. However, to the best of our knowledge, our patient is the first case of concomitant UC, PSC, and XGC, along with the presence of intramucosal adenocarcinoma in the distal CBD. XGC in our patient may have resulted from a chronic cholangiopathy in the setting of PSC, as well as the potential microscopic bile duct and cystic duct injuries due to frequent stenting, leading to chronic bile extravasation into the gallbladder wall and a xanthogranulomatous reaction.

Xanthogranulomatous cholangiopathy can occur as an isolated condition or in the setting of XGC or PSC [38,39]. Recently, Zhang et al.’s [39] case report described a patient with a history of recurrent cholangitis and presumed diagnosis of cholangiocarcinoma who was later found to have xanthogranulomatous cholangiopathy without evidence of XGC. The authors performed a PubMed literature search and were able to find only 14 cases of xanthogranulomatous cholangiopathy suspected of malignancy reported thus far [39].

According to the laboratory data described above, the occurrence of XGC and a history of PSC in our patient, the differential diagnosis of the distal CBD lesion found in MRCP/ERCP included an adenocarcinoma of CBD in the setting of PSC, xanthogranulomatous choledochitis in the setting of XGC, or IgG4-related cholangitis due to elevated IgG4 [40,41]. However, a be-

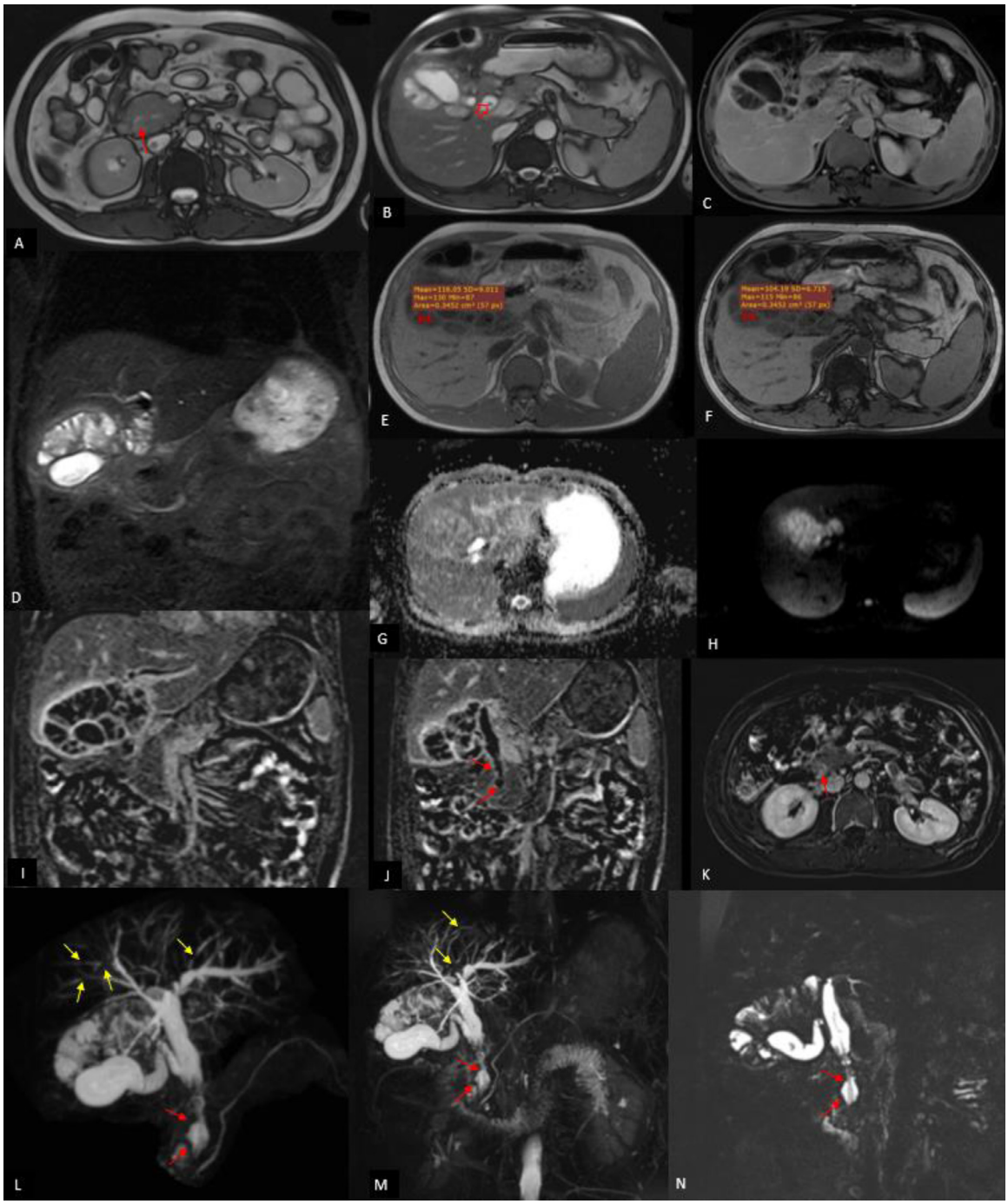

Fig. 5 – Axial T2 weighted MRI (A) demonstrates the persistence and mild enlargement of the distal CBD lesion(shown by red arrowhead). Note the small central low signal filling defect (shown by red hollow arrow in "B") in the proximal portion of CBD indicative of stent. An asymmetrical gallbladder wall thickening containing intramural nodules can be appreciated in MRI images. The nodules are hypersignal on T2 weighted axial (B) and coronal (D) images and hyposignal on T1 weighted in-phase and out-of-phase images (E and F respectively). A mild signal drop in out-of-phase images in an intramural nodule is depicted (E and F) in favor of presence of lipid-containing histiocytes. On DWI imaging (G and H), mild diffusion restriction is highlighted in the gallbladder wall. In postcontrast MRI images (C, I, and J), the surrounding borders of intramural nodules in the gallbladder wall are enhanced. The images show sparing of the mucosal lining in the thickened gallbladder wall (B and D) as well as a continuous luminal surface enhancement (C and I). Abnormal enhancement in distal CBD lesions can be appreciated (J and K). MRCP images (L, M, and N) show gallbladder wall thickening containing hypersignal intramural spaces with sparing of the luminal surface, along with asymmetrical irregular filling defects in the middle and distal portions of the CBD's wall. CBD lesion (shown by red arrows) has enlarged compared with the previous MRCP study shown in Fig. 1 (C). Beaded appearance of intrahepatic bile ducts (shown by yellow arrows) can be appreciated in (L and M).

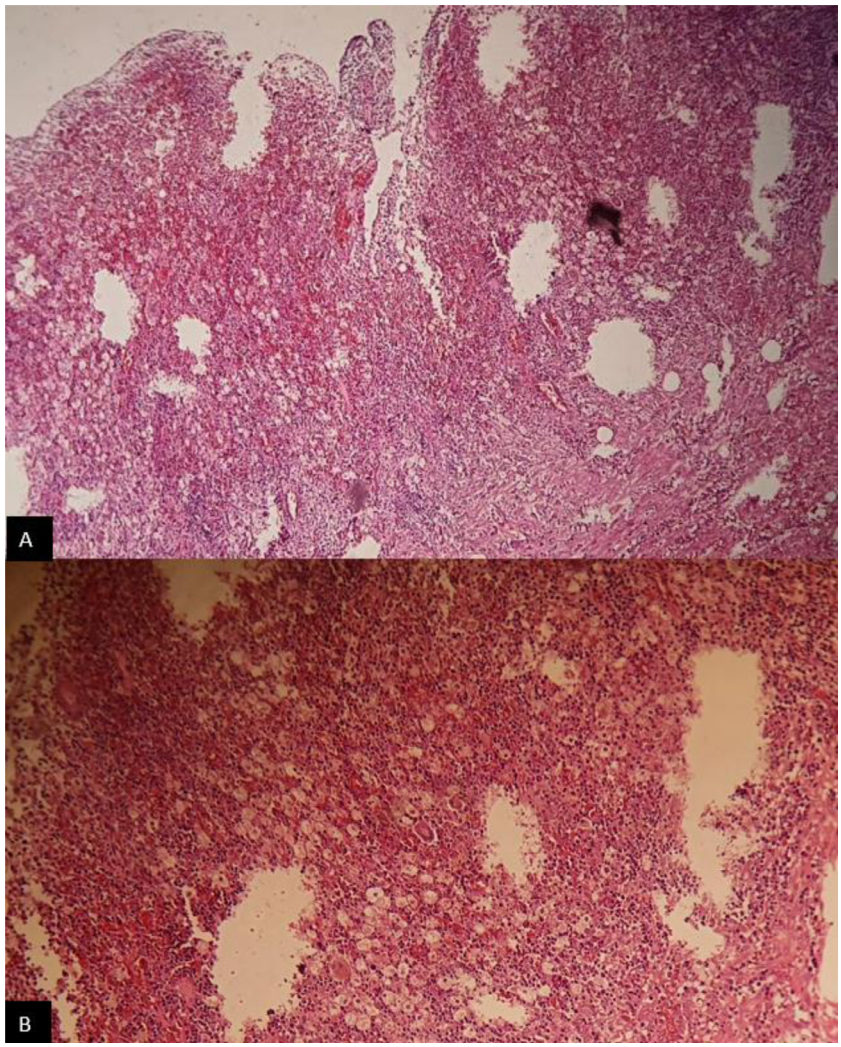

Fig. 6 – Microscopic image of xanthogranulomatous cholecystitis with numerous foamy histiocytes in the gallbladder wall.

nign lesion was not likely since the filling defect of the CBD was irregular and mass-like and was associated with abnormal asymmetrical thickening of CBD and enhancement after contrast injection [42]. The diagnosis was later confirmed to be intramucosal adenocarcinoma via microscopic evaluation.

Conclusion

In this publication, we presented the first documented case of XGC with concomitant distal CBD adenocarcinoma in a patient with a previous diagnosis of PSC and UC. XGC should be included in the differential diagnosis of patients with an established PSC who have evidence of circumferential gallbladder wall thickening on imaging studies, even in the absence of gallstones. It is difficult to diagnose XGC by imaging studies alone. However, the presence of an intact mucosal layer, along with luminal surface enhancement and intramural nodules, are the most frequent radiologic findings associated with XGC.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2023.07.024.

CRediT authorship contribution statement

Mohammad Kazem Tarzamni: Investigation. **Homa Aminzadeh Ghavifekr:** Writing – original draft, Writing – review & editing. **Hadise Zeynalkhani:** Investigation, Writing – orig-

inal draft, Writing – review & editing. **Masoud Shirmohamadi:** Investigation. **Elham Eghbali:** Investigation. **Ali Jafarizadeh:** Writing – original draft, Writing – review & editing, Visualization. **Seyed Siavash Ghareghoran:** Investigation, Writing – original draft, Writing – review & editing. **Seyedeh Elnaz Hashemizadeh:** Investigation. **Masih Falahatian:** Conceptualization, Project administration, Investigation, Writing – original draft, Writing – review & editing, Visualization.

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